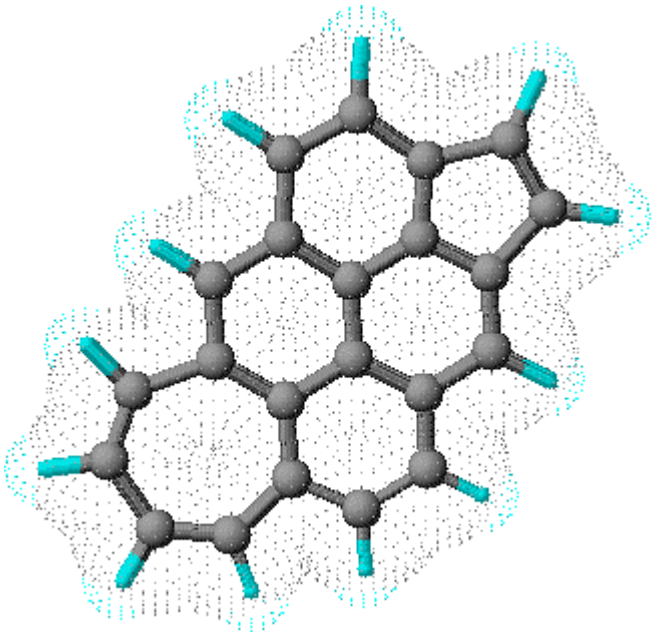
Towards the annealation of a five and seven-membered ring to an alternant polycyclic aromatic hydrocarbon



Report Master's thesis
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Abstract

The anti-symmetric behaviour of cyclohepta-fused and cyclopenta-fused PAHs make these two annealed odd-membered rings interesting moieties to combine and fuse on the same aromatic perimeter, e.g. pyrene. The synthesis of cyclopenta-cycloheptapyrene **11** is attempted with different synthetic strategies, making use of pyrene **(1)** and 1,2,3,6,7,8-hexahydropyrene **(2)** as precursors. However, the use of **2** as starting material turned out to require tedious synthetic procedures and laborious purification steps. A promising effort in the synthesis of **11** is made by acylation of 3,4-dihydrocyclopenta[*cd*]pyrene **(7)**, after which ringclosure of the acylated compound **23** afforded the bis-keto cyclohepta-derivative **24**. Subsequently, **24** is transformed into the suitable FVT precursor **26**, which is obtained properly, though impure containing a lot of salts. Although GC-MS analysis substantiated the obtention of **24**, subjecting it to FVT afforded polymeric material and no desired product.

Contents

1. Introduction

As a compound class, polycyclic aromatic hydrocarbons (PAHs) comprise an innumerable amount of class members and even more isomers. All of them possess different chemical properties, chemical reactivity and biological significances. PAHs are formed during incomplete combustion or pyrolysis of organic material and are also formed to a small extent by microbes and plants.[1] They are ubiquitous environmental contaminants and have been detected in water, plants and earth's atmosphere.[2]

Much attention has been devoted to PAHs due to their impact on health and environment. They are generally persistent in the environment and resistant to enzymatic degradation, while some of them are mutagens and key intermediates in carcinogenic processes. PAHs ranging in molecular weight from 128 (e.g. naphthalene) up to 300 (e.g. coronene) are of particular environmental concern as PAHs within this group have a significant water solubility.[3] This ability increases their bioavailability and mobility within the environment. Besides the fact that some PAHs degrade rapidly under aerobic conditions, the major degradation process is achieved by photolysis. PAHs readily absorb electromagnetic radiation in the visible and in the ultraviolet (UV) region, but are also sensitive to the photochemical effects of UV radiation. Toxicology studies in the discipline of aquatic toxicology presented evidence for the increased toxicity of PAHs upon exposure to UV radiation.[4]

In addition, PAHs have created interest because of their presence in interstellar space.[5] They seem to be responsible for a family of infrared fluorescence bands of the interstellar spectrum.[6] Besides the neutral and cationic species that have been observed also anionic PAHs have been found in the interstellar medium with tremendously large electron affinities.[7] The electron affinities were found to be an important unit for describing the gas-phase oxidation rates of PAHs in combustion gases, hereby using the willingness of a PAH to take up an electron as the initial step for the decomposition.[7]

The classification of PAHs occurs into two distinct classes of alternant and non-alternant PAHs. In contrast to alternant PAHs, which are planar conjugated molecules and consist of even-membered π-conjugated rings, non-alternant PAHs are π-conjugated compounds and contain at least one odd-membered ring, e.g. a five-membered or seven-membered ring. To clarify this criterion, the carbon atoms in a PAH can be divided into two sets, starred and un-starred, with each starred or un-starred carbon having only un-starred or starred neighbours respectively (figure 1). Non-alternant PAHs which contain odd-membered rings therefore contain always either two adjacent starred or un-starred carbon atoms.

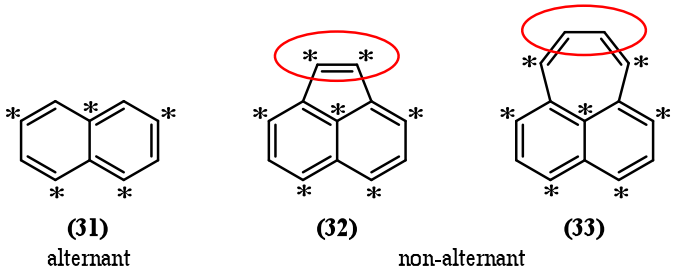


Figure 1. Schematic drawing of naphthalene **(31)**, acenaphthylene **(32)** and pleiadiene **(33)**.

The presence of the odd-membered rings in non-alternant PAHs has a significant effect on the redox properties when compared to their alternant congeners. For example, it is shown that annelation of a peripheral pentagon to an alternant PAH perimeter lowers the reduction potential and notably enhances the electron affinity, which suggest a large localization of the added electron (table 1).[8] In fact, reduction of a cyclopenta-fused PAH is believed to result a 6π-electron containing cyclopentadienide sub-structure (figure 2). On the other hand, PAHs containing cyclohepta-moieties are oxidized more easily than their corresponding PAH and cyclopenta-PAH. The formed positive charge is believed to reside in the cyclohepta-moiety to afford a 6π-electron containing tropylium cation (figure 2).[9]

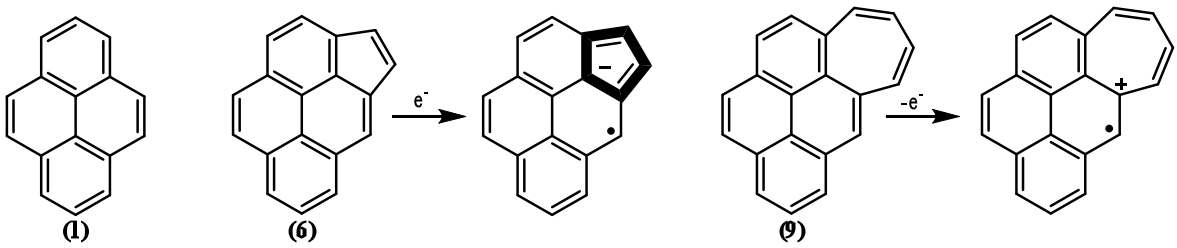


Figure 2. Proposed structures yielded after reduction **(6)** and oxidation of **(9)**.

Table 1. Reduction and oxidation potentials of **(1)**, **(6)** and **(9)**.

	(1)	**(6)**	**(9)**
$\mathbf{E_{ox}(0/+1)}$ (*vs.* SCE)	1.06 V	1.26 V	0.62 V
$\mathbf{E_{red}(0/-1)}$ (*vs.* SCE)	-2.22 V	-1.56 V	-1.81 V

Besides the interesting change in redox properties, annelation of a five or seven-membered ring to an alternant PAH core also has enormous consequences for the electronic charge distribution.[10] As depicted in figure 3, molecular orbital energy levels of alternant PAHs are always symmetrically positioned about the zero energy level, whereas non-alternant PAHs posses an asymmetric charge distribution along their molecules. Another unique result of the charge distribution along non-alternant PAHs is the anti-symmetric electronic relationship between cyclopenta-fused and cycloheptra-fused PAHs (figure 3). By forming a 6π cyclopentadienide sub-structure, cyclopenta-fused PAHs can stabilize negative charges, which account for the high electron affinities, whereas the readily oxidized

cyclohepta-fused PAHs stabilize positive charge by forming 6π-electron containing tropylium sub-structures.[9]

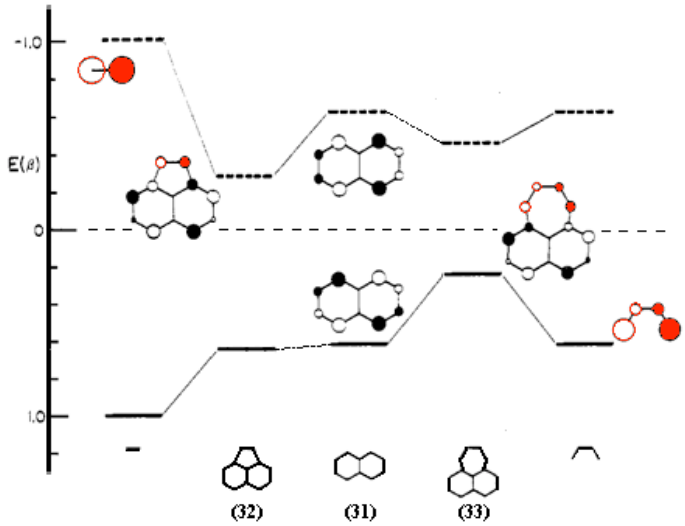


Figure 3. Molecular orbital energy level diagram of **(31)**, **(32)** and **(33)**.

These observed anti-symmetric relationship of cyclopenta and cyclohepta-fused PAHs make cyclopenta-cyclohepta-fused PAHs (CP-CH-PAHs) interesting candidates for investigating their use as electron donor-acceptor compounds. Although many properties of such molecules have been predicted theoretically, the synthesis of CP-CH-PAHs has never been reported in literature. The target of this report is therefore the synthesis of cyclopenta-cycloheptapyrene **(11)**. This molecule exists in three constitutional isomers (figure 4).

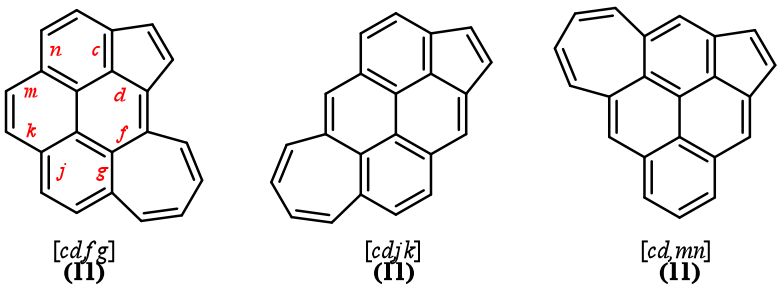


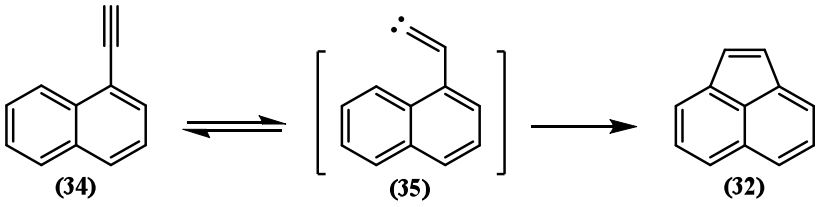
Figure 4. The three constitutional isomers of cylcopenta-cyclohepa-pyrene **(11)**.

2. Background

2.1 Cyclopenta-fused PAHs

A special sub-class of non-alternant PAHs are the cyclopenta-fused PAHs (CP-PAHs). They contain at least one fully unsaturated five-membered ring as integral component on their PAH perimeter. Over the past years they have attracted considerable attention in different research areas. Toxicology studies reported strong evidence that CP-PAHs are responsible for the genotoxicity of combustion mixtures.[11] Besides, CP-PAHs are indentified as precursors for fullerene. Corannulene for example, a bowl shaped CP-PAH, is proposed to constitute building blocks for fullerenes.[12] The presence of both five- and six-membered rings in CP-PAHs gives rise to unique electronic properties. Some of them exhibit extraordinary photophysical behaviour.[13] In line with their non-alternant character, CP-PAHs posses an enhanced electron affinity, which is also a property of fullerenes.[8]

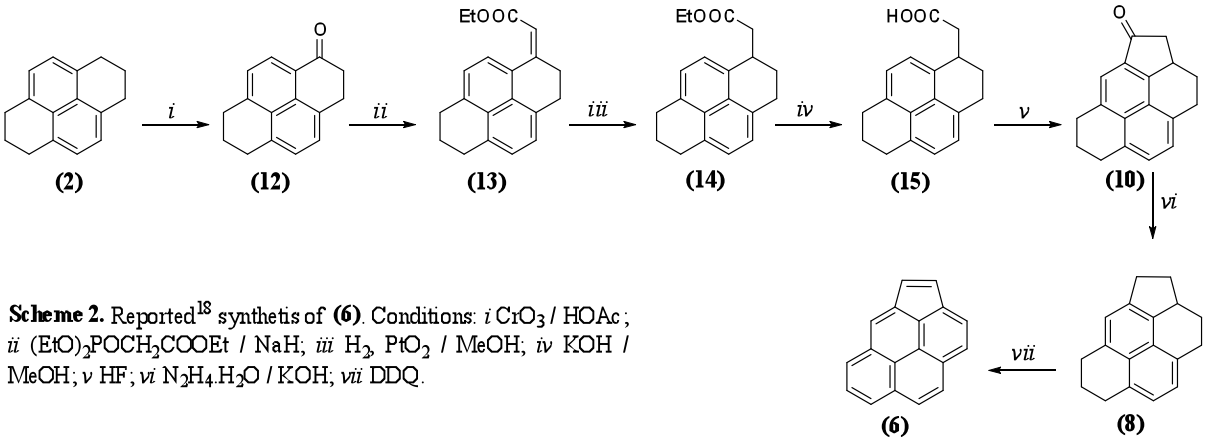
CP-PAHs are of great particular interest due to their abundance in industrial environment. They have been widely found in combustion effluents and soots.[14] An example of one of the most abundant CP-PAH in combustion systems is cyclopenta[*cd*]pyrene **(6)**, which is the most straightforwardly cyclopenta-fused variant of pyrene. It is believed that the cyclopenta-moieties of CP-PAHs are mainly formed by thermal closure of five-membered rings from ethynylarenes during combustion of fossil fuels. These ethynylarenes are expected to arise form PAHs through the addition of acetylenic fragments such as •C=C• or HC=C•.[15] Indeed, many CP-PAHs can be obtained in high yields by flash vacuum thermolysis (FVT) of ethynylarenes. The occurrence of this ethynylarene – CP-PAH rearrangement was observed by Brown and co-workers.[16] They discovered the existence of an ethynyl - ethylidene carbene rearrangement during the efficient conversion of (1-naphthyl)-ethyne **(34)** into acenaphthylene **(32)** under the high temperature conditions of FVT (Scheme 1). Many electronic structure calculations have been employed to elucidate the exact reaction mechanism of the thermal closure of cyclopenta-rings from ethynylarenes.[15] The commonly assumed reaction mechanism involves the generation of (1-naphthyl)-ethylidene carbene **(35)** from (1-naphthyl)-ethyne **(34)** by a 1,2-hydrogen shift, which rearranges to form acenaphthylene **(32)** by an intramolecular C-H insertion of the carbene into a *peri*-carbon-hydrogen bond.[15,16]



Scheme 1. Ethynyl - ethylidene carbene rearrangement after which the carbene C-H insertion yields acenaphthylene **(32)**.

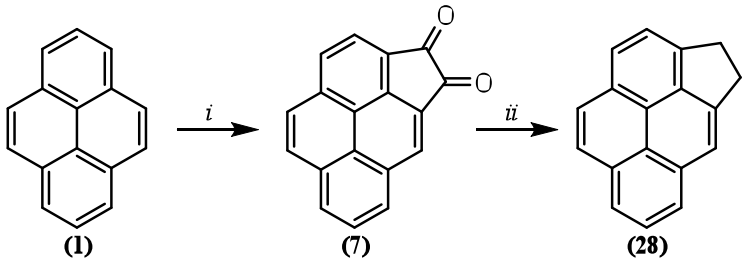
2.1.1. Synthetic pathways for the preparation of CP-PAHs

In the last years lots of research has been devoted to pathways towards the synthesis of CP-PAHs. Of major importance for their identification in combustion systems and their structural assignment, is the availability of reference compounds. For example, because of the abundant presence of cyclopenta[*cd*]pyrene **(6)** in combustion mixtures, lots of synthetic approaches has been developed towards **6** to gain more insight in its physical and biological properties. So far, there are a few reported synthetic routes for cyclopenta[*cd*]pyrene **(6)**. The commonly used precursor before the development of the gas phase approach (i.e. FVT) were 4-pyrenylacetic acid[17] and 1,2,3,6,7,8-hexahydropyrene **(2)** (Scheme 2).[18] Another synthetic route involved the pyrolysis of 2-(pyren-1-yl)ethanol at 850 ^{o}C, which yielded besides cyclopenta[*cd*]pyrene **(6)** (22%) also 3,4-dihydrocyclopenta[*cd*]pyrene **(7)** (7%).[19] However, these classical synthetic routes require lengthy procedures and time-consuming purification steps.



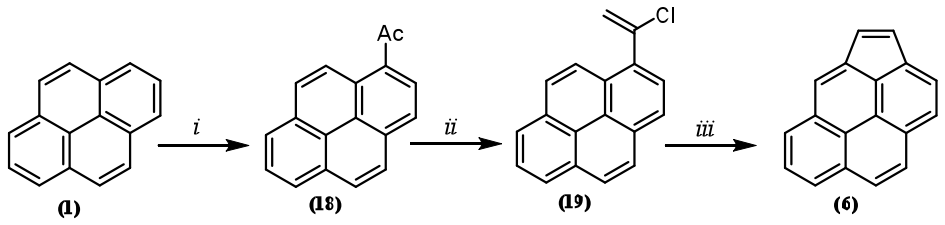
Scheme 2. Reported[18] synthetis of **(6)**. Conditions: *i* CrO_3 / HOAc; *ii* $(EtO)_2POCH_2COOEt$ / NaH; *iii* H_2, PtO_2 / MeOH; *iv* KOH / MeOH; *v* HF; *vi* $N_2H_4.H_2O$ / KOH; *vii* DDQ.

A feasible synthetic route to cyclopenta[*cd*]pyrene **(6)** that requires a minimum amount of steps involves a Friedel-Crafts acylation on pyrene **(1)** using oxalylchloride as reagent. This reaction is expected to generate bis-ketone **28,** which can be reduced to give hydrogenated derivative **7** (Scheme 3). Dehydrogenation of **7** will afford **6.** However, the overall yield of this synthetic route is likely to be minimal due to the harsh reaction conditions.



Scheme 3. Proposed short synthetic route to **(7).** Conditions: *i* $C_2O_2Cl_2$ / $AlCl_3$; *ii* $N_2H_2.H_2O$ / KOH.

After the discovery of the ethynylarene – CP-PAH rearrangements by Brown and co-workers[16], gas phase cyclization reactions became a successful method for the preparation of CP-PAHs. FVT is now commonly used for synthetic purposes. Ethynyl-PAH is a typical FVT precursor for the generation of CP-PAH.[20] However, the reported synthesis by Brown and co-workers of acenaphthylene **(32)** using FVT is only achieved in low yields (18%).[20] This is caused by the fact that (1-naphthyl)-ethyne **(34)** or ethynylarenes in general are susceptible to polymerize at high temperatures rather than to sublime upon heating. To prevent this undesired occurrence, Sarobe and co-workers[16] observed that treatment of l-acetylnaphthalene with phosphorus pentachloride generates l-(naphthy1)-1,1-dichloroethane and l-chloro-(l-naphthy1)-ethene, which appears to be a suitable FVT precursors for acenaphthylene **(32)**. (1-naphthyl)-ethyne **(34)** is generated *in situ* under FVT conditions at relatively low temperatures from l-chloro-(l-naphthy1)-ethene by one fold hydrogen chloride elimination and from l-(naphthy1)-1,1-dichloroethane by two fold hydrogen chloride elimination. The synthesis of **6** using FVT is known and reported in literature.[16] After the synthesis of 1-chloro-1-(pyren-1-yl)ethene **(19)**, it can be subjected to FVT to yield **(6)** (scheme 4).



Scheme 4. Reported[16] synthesis of **(6)**. Conditions: *i* CH_3COCl / $AlCl_3$; *ii* PCl_5; *iii* FVT (1000°C).

2.1.2. Rearrangements of CP-PAHs under high temperature conditions.

Besides the ethynyl-ethylidene carbene rearrangement which is believed to be the major forming pathway of CP-PAHs during incomplete combustion processes, there is another characteristic rearrangement CP-PAHs can undergo. Under high temperature conditions CP-PAHs are able to experience skeletal rearrangement or conversions via ring-contraction or ring-expansion processes including 1,2-H and 1,2-C shifts (figure 5). A clear example of this property of CP-PAHs is the rearrangement of aceanthrylene **(36)** into acephenanthrylene **(37)** into fluoranthene **(38)** with increasing temperatures (>1000^{O}C).[21]

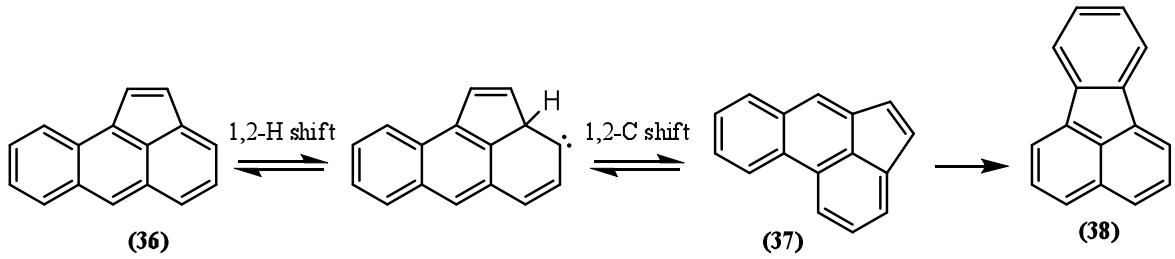


Figure 5. Rearrangement of aceanthrylene **(36)** into acephenanthrylene **(37)** and finally into fluoranthene **(38)** under high temperature conditions.

2.1.3. Biological activity of PAHs.

Cylcopenta[*cd*]pyrene **(6)** is a widespread environmental contaminant and is found in carbon black, cigarette smoke, automobile exhaust and in urban and rural air.[22] It is reported to be a potent mutagen upon metabolic activation by the cytochrome P-450 monooxygenase system, and is known to cause cancer (adenocarcinoma and skin papilomas) in mice.[22] In the past years studies demonstrated the importance of the metabolic route of PAHs and their bio-activation into ultimate mutagenic forms, which starts with the enzymatic oxidation after which the areneoxides are transformed into diol-epoxides.[23] PAHs consisting of a double bond that forms part of a "bay-region", i.e. an indentation between three fused benzene rings, are metabolically activated to a greater extent than PAHs that lack this structural property (figure 6). However, in case of cyclopenta[*cd*]pyrene, a bay-region such as that found in the highly carcinogenic diol-epoxide **39** is absent. Despite the lack of the bay-region, it can form a benzylic carbocation at the C-3 position of the ethylene bridge, which is electronically equivalent to the bay-region C-10 carbocation of **39** (figure 6). These generated carbocations are released from the mitochondria into the living cell as highly reactive electrophiles, becoming ultimate carcinogens as it reacts with negative charges in DNA to from DNA adducts.[22]

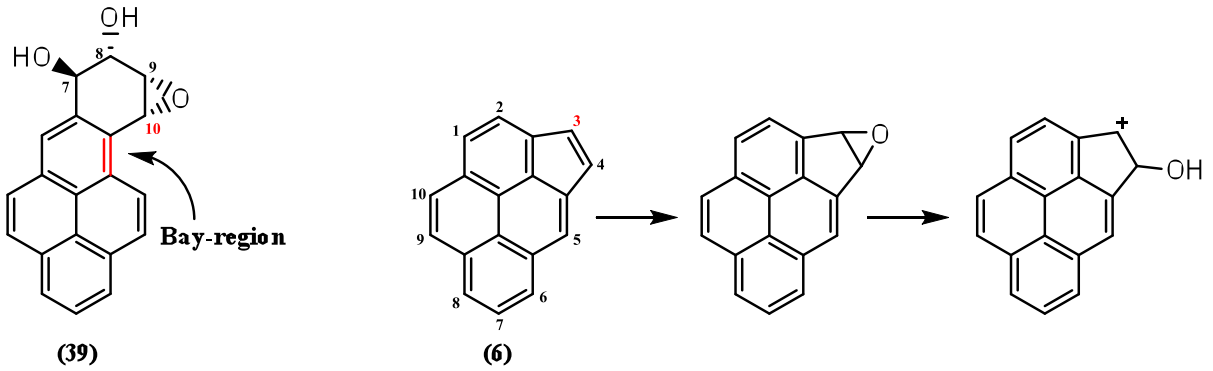


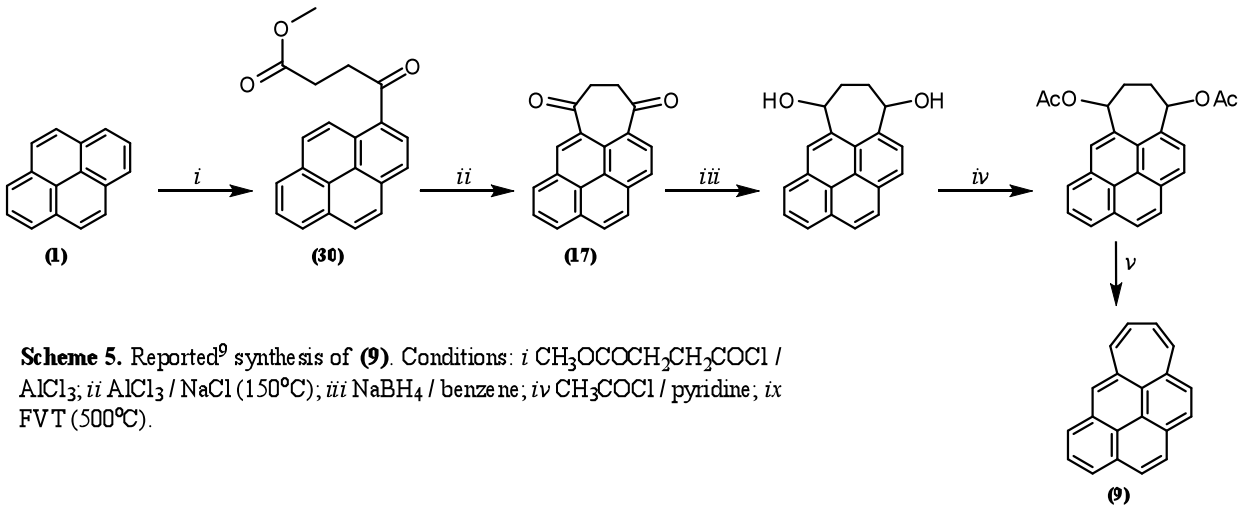
Figure 6. Highly carcinogenic benzo[*a*]pyrene derivative **(39)** and the generation steps of the bioactive carbocation from **(6)**.

2.2 Cyclohepta-fused PAHs.

As described previously, cyclohepta-fused PAHs (CH-PAHs) exhibit some special electronic properties, for example low oxidation potentials.[9] The expected low ionisation potentials render these compounds promising p-type materials. However, in contrast to CP-PAHs, CH-PAHs have not received much attention and not many PAHs containing annealed cyclohepta-moieties are known. An explanation for the lack of synthetic research in this class of non-alternant PAHs is their absence in the environment.

2.2.1 Synthesis of CH-PAHs

A few years ago a synthetic strategy is developed by Koper and coworkers[9] for obtaining cyclohepta-fused PAHs. This strategy is reported to be successful for obtaining cyclohepta[*cd*]pyrene **(9)** and cyclohepta[*cd*]fluoranthene and is drawn out for **9** in scheme 5.



Scheme 5. Reported[9] synthesis of **(9)**. Conditions: *i* $CH_3OCOCH_2CH_2COCl$ / $AlCl_3$; *ii* $AlCl_3$ / NaCl (150°C); *iii* $NaBH_4$ / benzene; *iv* CH_3COCl / pyridine; *ix* FVT (500°C).

2.2.2 High temperature behaviour of CH-PAHs.

Comparable to CP-PAHs, CH-PAHs exhibit also characteristic behaviour at elevated temperatures. During the FVT of pleiadiene **(33)** at 900^{O}C the formation of acenaphthylene **(32)** is observed.[24] This observation suggests that under these conditions CH-PAHs behave like transitory intermediates that readily undergo interconversions to give the more stable cyclopenta-derivatives. The proposed mechanism for this behaviour is reported to generate intermediate **(40)**, after which extrusion of a C_2H_2-fragment is believed to occur (figure 7). This proposed mechanism is corroborated by FVT of **40** and yielded as expected **32** at 900^{O}C.

This observed behaviour of CH-PAHs provides a rational explanation for the fact that CH-PAHs up to date have not been identified as environmental contaminants. CH-PAHs are unstable at high temperatures and interconvert readily to yield the thermodynamically more stable CP-PAHs.

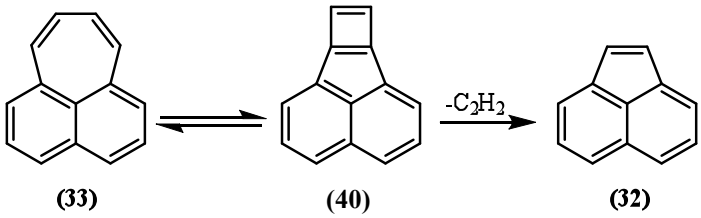


Figure 7. Interconversion of pleiadiene **(33)** into acenaphthene **(32)**.

3. Approach

3.1 Suitable precursors.

The synthesis of target molecule cyclohepta-cyclopentapyrene **(11)** can theoretically be performed in many different synthetic pathways. Unfortunately, a successful synthetic strategy for obtaining CH-CP-PAHs is not reported. Retrosynthetic analysis for the development of a promising synthetic approach to obtain the desired target molecule is essential and required. Choosing a suitable key synthon is of major importance and will fix the continuation of the synthetic progress. For the synthesis of **11** a few compounds are qualified as possible starting materials. Each precursor depicted in figure 8 has its advantages but also its unfavourable conditions that reduces the chances of effectiveness.

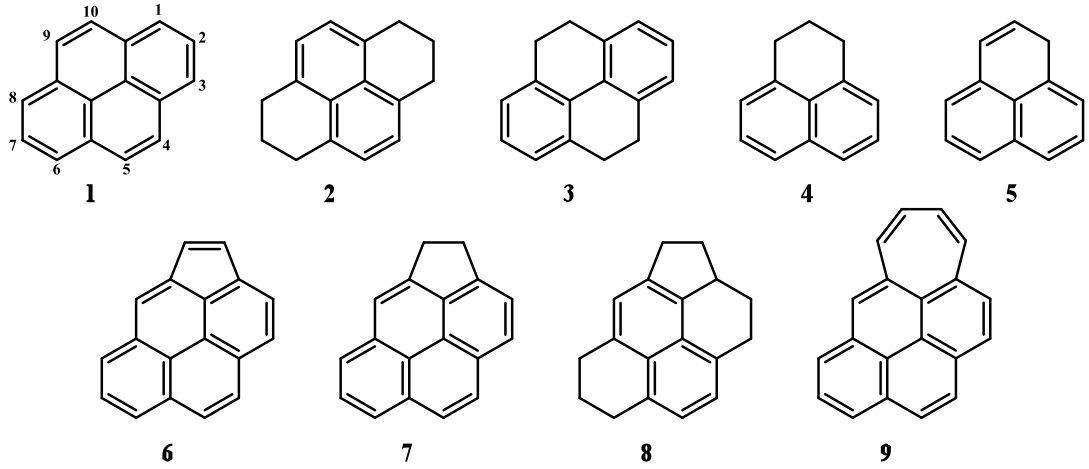


Figure 8. Possible synthons, namely pyrene **(1)**, 1,2,3,6,7,8-hexahydropyrene **(2)**, 4,5,9,10-tetrahydropyrene **(3)**, perinaphthane **(4)**, perinaphthene **(5)**, cyclopenta[*cd*]pyrene **(6)**, 3,4-dihydrocyclopenta[*cd*]pyrene **(7)**, 1,2,2a,3,4,6,7,8-octahydrocyclopenta[*cd*]pyrene **(8)**, cyclohepta[*cd*]pyrene **(9)**.

With the exception of pyrene **(1)** and 1,2,3,6,7,8-hexahydropyrene **(2)**, none of the other compounds in figure 8 are commercially available. For the use of pyrene as starting material many investigations and publications are dedicated to its behaviour in various reactions. An electrophilic attack on pyrene is reported to usually occur at site 1.[25] This reveals the position at which electrophilic aromatic substitution like Friedel-Crafts acylations take place. One of the consequences of the selective reactivity of pyrene is that formation of a *cd*-fused ring by intramolecular Friedel-Crafts acylation of 1-pyrenylacetic acid cannot be achieved, due to the lack of reactivity towards electrophilic substitution at position 4.[26] Besides the use of Friedel-Crafts acylations as cyclization strategy, there are other reported synthetic routes for the introduction of a cyclopenta or cyclohepta-moiety on pyrene. Flash vacuum thermolysis (FVT), as described previously, is now commonly used as method of choice for the preparation of CP-PAHs.[16] It is also reported that acylation of 1-substituted pyrene occurs at the 3-, 6-, and 8-position.[25] After introducing the first ring moiety onto pyrene, the formation of three different isomers in the next acylation step can be expected.

Also the use of 1,2,3,6,7,8-hexahydropyrene **(2)** as starting compound is well documented.[18,26] It can be used as a pyrene derivative for specific acylation on the 4-position, which is impossible to achieve on pyrene. By dehydrogenation of the two hydrogenated six-rings, the 1,2,3,6,7,8-hexahydropyrene **(2)** framework can be converted into pyrene. This is a cunning method for obtaining 4-pyrenylacetid acid that can be easily cyclised onto the 1 position. In addition, it is also possible to reach the same molecule, i.e. cyclopenta[*cd*]pyrene, in the opposite pathway. Oxidation of 1,2,3,6,7,8-hexahydropyrene **(2)** by CrO_3 is a suitable reaction for yielding a carbonyl-moiety at the 1-position.[18] After obtaining a carboxylic acid at position 1, cyclization by intramolecular Fried-Crafts acylation is possible. An additional advantage of 1,2,3,6,7,8-hexahydropyrene as starting material is the lack of available substitution positions. After the introduction of the first ring-moiety there are less positions available for substitution, which results in less possible isomers.

4,5,9,10-Tetrahydropyrene **(3)** is in contrast to **1** and **2** commercially not available. It can be obtained as a 85/15 mixture of respectively **(3)** and **(2)** by dehydrogenation of desulfurized pyrene (10% Pd/C, wet EtOAc, 40 psi for 64-72 h).[27] Besides, the usage of **(3)** as precursor is unfavourable and will require more reaction steps due to its uncomfortably hydrogenated rings in comparison with pyrene **(1)**. The induced selectivity of **3** is undesirable for the synthesis of the target compound since direct electrophilic aromatic substitution (Friedel-Craft acylation) of **3** is known to occur selectively at the 2- and 7-position.[27]

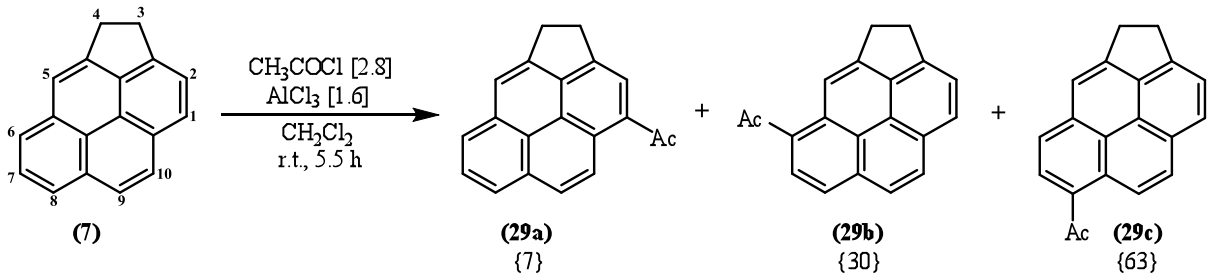
Syntheses involving the functionalization of perinaphthene **(5)** received considerable attention in the past years due to the observed unusual properties of perinaphthene derivatives.[28] Because of the symmetry of perinaphthene **(5)**, the corresponding ions and radicals have a relatively high degree of stabilization due to resonance. Using **5** as precursor for target compound **11** seems at first sight also an inventive strategy to decrease the possible substitution positions. However, perinaphthene **(5)** is highly unstable in air, discolouring in a matter of hours and finely becomes black in a couple days. It is also commercially unavailable and can be prepared by the dehydration of perinaphthanol-7 using alcoholic hydrogen chloride as catalyst (yield 65-85%).[29] Lock and co-workers[30] observed the catalytic reduction of **5** to **4** and the oxidation of **4** to perinaphthenone in air. Although the preparation of monosubstituted perinaphthene has been described previously (e.g. 1-methylperinaphthene[28]), it was found to isomerise readily to give all the possible isomers. Perinaphthane **(4)** seems to be more accessible and selective towards acyl substitution, however its use as precursor is not an option since it decomposes readily in solution and air.[31]

In doing the retrosynthetic analysis to obtain **11** a decision must be made whether the 5-membered or 7-membered ring will be chosen to start synthesising first. Another important decision in the analysis is choosing in which stage of the synthetic route the 2nd Friedel-Crafts acylation will have to take place.

The reactions of a few compounds with electrophiles have been studied in order to obtain further insight in their reactivities. Substitution reactions on cyclopenta[*cd*]pyrene **(6)** for instance, are known to occur exclusively on the etheno-bridge. Nitration of **6** in the presence of silver nitrate, sodium nitrite and iodine in acetonitrile is reported to yield 4-nitrocyclopenta[*cd*]pyrene (43%).[32] Also methyl substitution on **6** is observed to take place on the etheno-brigde.[18]

On the other hand, the butadiene-moiety of **9** is sensitive towards substitution reactions. In contrast to the ethene-moiety of **6**, cylcohepta[*cd*]pyrene **(9)** is expected to be selective towards nucleophilic substitution. Although substitution onto **9** is never reported, nucleophilic replacement of substituents in the seven-membered ring of azulene is known to proceed under mild conditions.[33] As described previously, CH-PAHs rearrange under enhanced FVT conditions to give the thermodynamically more stable CP-PAHs. As a consequence, it is not possible to proceed with the synthesis of the cyclopenta-ring after obtaining compound **9**. In addition, CH-PAHs are also known to decompose under oxidative reaction conditions. Attempts to introduce full pi-conjugation in the cyclohepta-moieties of both cyclohepta[*fg*]aceanthrylene and cyclohepta[*kl*]anthracene with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) are reported to yield unidentified and decomposed products.[34]

However, electrophilic substitution of **7** is well documented and the isomeric distributions of the obtained products are known (scheme 6).[25] The Friedel-Crafts acetylation of **7** with acetyl chloride in the presence of aluminium chloride is reported to yield three isomers, i.e. 1-acetyl-, 6-acetyl-, and 8-acetyl-3,4-dihydrocyclopenta[*cd*]pyrene. The isomeric distribution of the obtained isomers was 1-acetyl **29a** : 6-acetyl **29b** : 8-acetyl **29c** = 7 : 30 : 63. Although the electrophilic substitution reaction is carried out with acetyl chloride, it is expected to obtain the same isomers for the acylation of **(7)** when methyl succinyl chloride is used as reagent.



Scheme 6. Reported[25] products afforded by the Friedel-Crafts acetylation of **(7)**. []: Molar ratio of reagent. {}: Isomeric distribution.

Although compound **2** has been used in literature as starting material for obtaining 1,2,2a,3,4,6,7,8-octahydrocyclopenta[*cd*]pyrene **(8)**, no further substitution reactions have been performed on **8**.[18] It is used as a convenient method to obtaine cyclopenta[*cd*]pyrene **(6)** by means of the liquid phase approach. It is expected that acylation of **8** will afford also three isomers due to the strongly activating and ortho/para-directing property of alkyl- substituents. For this reason, acylation of **(8)** is expected to yield 5-substituted, 9-substituted and 10-substituted 1,2,2a,3,4,6,7,8-octahydrocyclopenta[*cd*]pyrene **(8)** (figure 9). However, if the choice is made to perform a Friedel-Crafts acylation on compound **10**, substitution is supposed to take place on the 9 and 10 position. Due to the presence of a deactivating and meta-directing keto-functionality on the 4 position, substitution on the 5 position is not likely to occur. As a result of this regioselectivity, compound **10** is expected to be the most promising precursor to perform the acylation on.

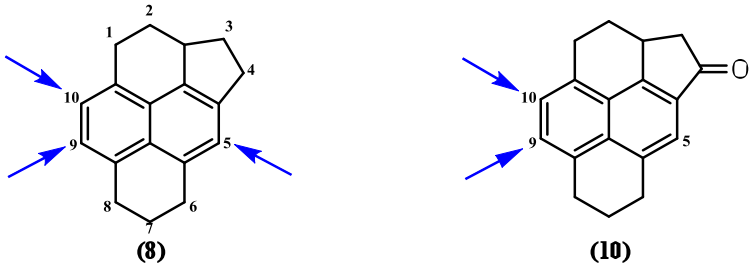


Figure 9. Expected possible electrophilic aromatic substitution positions of **(8)** and **(10)**.

On the other hand, substitution can also be performed onto **17** and is likely to pose a regioselectivity similar to that of **10**. Although nothing is known about compound **10** in literature, it can be suggested that acylation will take place on the 6 and 8 position (figure 10). However, there is a lack of certainty about position 1. In spite of the meta-directing property of the neighbouring keto-functionalities, there will also be a certain deactivation and a disadvantageous steric influence for the acylation to occur on the 1 position.

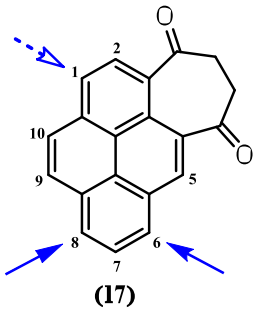
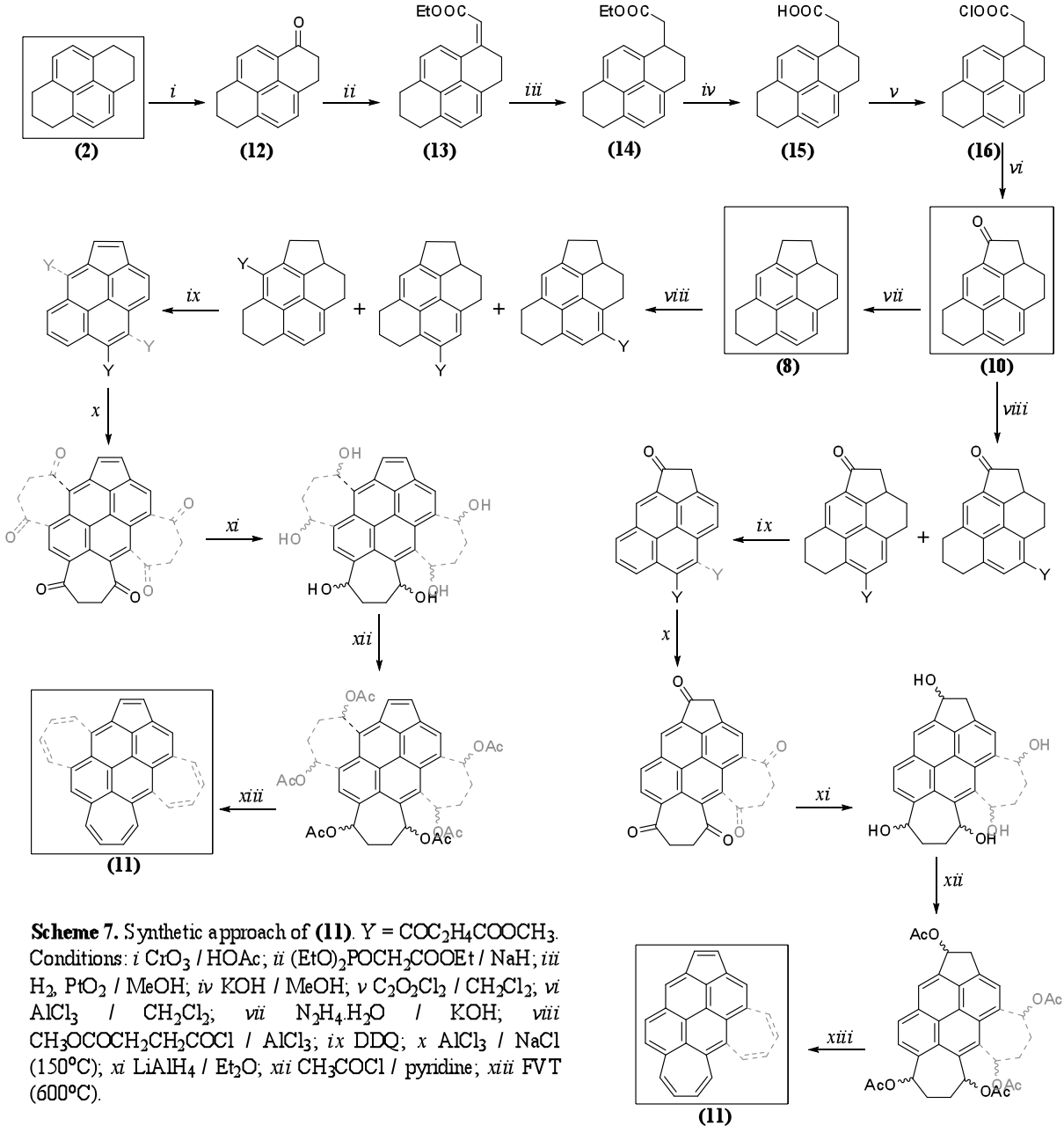


Figure 10. Possible electrophilic substitution positions of **(17)**.

3.2 Approach towards the synthesis of cyclohepta-cyclopentapyrene (11).

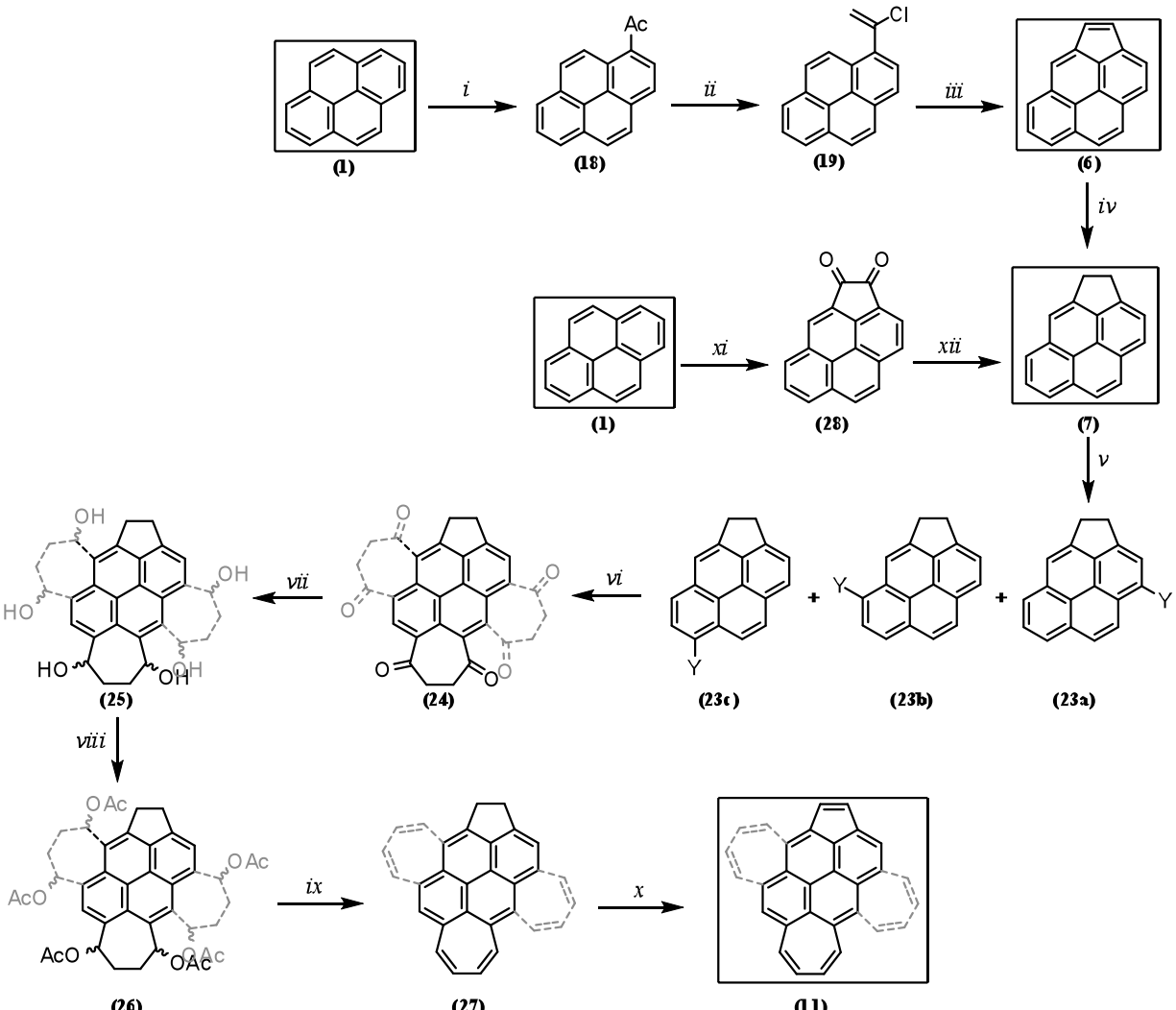
The synthesis of **11** can be achieved by various synthetic routes. As described previously, it is inevitable to synthesize the cyclopenta-moiety onto the pyrene framework before the annulation of the seven-membered ring. This can also be achieved in different ways. In Scheme 7 the synthetic approach for obtaining **11** is outlined, making use of compound **2** as starting material. A small deviation is made in the cyclization step for obtaining **10**. Instead of performing the cyclization step using the hazardous hydrogen fluoride as reported[18], cyclization of acid **15** is thought to be achieved by an internal Friedel-Crafts acylation after carboxylic acid **15** is turned into acid chloride **(16)**.



Scheme 7. Synthetic approach of **(11)**. Y = $COC_2H_4COOCH_3$. Conditions: *i* CrO_3 / HOAc; *ii* $(EtO)_2POCH_2COOEt$ / NaH; *iii* H_2, PtO_2 / MeOH; *iv* KOH / MeOH; *v* $C_2O_2Cl_2$ / CH_2Cl_2; *vi* $AlCl_3$ / CH_2Cl_2; *vii* $N_2H_4.H_2O$ / KOH; *viii* $CH_3OCOCH_2CH_2COCl$ / $AlCl_3$; *ix* DDQ; *x* $AlCl_3$ / NaCl (150°C); *xi* $LiAlH_4$ / Et_2O; *xii* CH_3COCl / pyridine; *xiii* FVT (600°C).

Directly after the acyl substitution of **8** and **10**, the pyrene-framework needs to be aromatized to enable the second ring closure of the methyl succinyl-moiety. From this point the cyclization and the aromatization of the seven-membered ring can be accomplished according to published procedures.[9] However, the 4-keto-moiety remaining on the acylated **10** compound brings in a few uncertainties about the following reactions. The removal of the carbonyl on the 4-position is supposed to be achieved by the same procedure as the other carbonyl-moieties, i.e. elimination of acetic acid under FVT conditions.

Another synthetic route can be drawn up for the synthesis of **11** starting with compound **1** (scheme 8). As mentioned earlier, 3,4-dihydrocyclopenta[*cd*]pyrene **(7)** can be rapidly obtained in more than one way. A drawback in this synthetic approach is that it is not possible to avoid hydrogenating the five-membered ring. Dehydrogenation of the cyclopenta-ring has to be carried out as last step with palladium on carbon in mesitylene.



Scheme 8. Synthetic approach of **(11)**. Y = $COC_2H_4COOCH_3$. Conditions: *i* CH_3COCl / $AlCl_3$; *ii* PCl_5; *iii* FVT (1000°C); *iv* H_2 / Pd/C; *v* $CH_3OCOCH_2CH_2COCl$ / $AlCl_3$; *vi* $AlCl_3$ / NaCl (150°C); *vii* $LiAlH_4$ / Et_2O; *viii* CH_3COCl / pyridine; *ix* FVT (600°C); *x* Pd/C / mesitylene; *xi* $C_2O_2Cl_2$ / $AlCl_3$; *xii* $N_2H_4.H_2O$ / KOH.

4. Results

4.1 Synthesis of 1,2,2a,3,4,6,7,8-Octahydrocyclopenta[*cd*]pyrene (8).

Similar to the reported data[18], oxidation of the commercially available 1,2,3,6,7,8-hexahydropyrene **(2)** with CrO_3 in acetic acid afforded the 1-oxo derivative **12** in a yield of 43%. Subsequently, ketone **12** was subjected to a Wittig reaction. The reaction of **12** with triethyl phosphonoacetate in benzene gave olefinic ester **13** in 73% yield. However, in contrast to the reported data[18], a mixture of two products were obtained in a ratio of 1:1. Further ^{1}H NMR analysis and proton decoupling experiments indicated the presence of a pair of stereoisomers, namely an E and a Z isomer as a consequence of the exocyclic double bond (figure 11). GC-MS analysis confirmed this result by showing two products in the GC chromatogram having a small difference in their retention times and their associated mass spectra showing the same molecular ion mass and fragmentation patterns (figure 12).

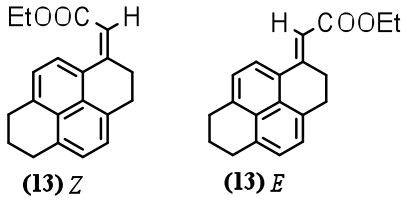
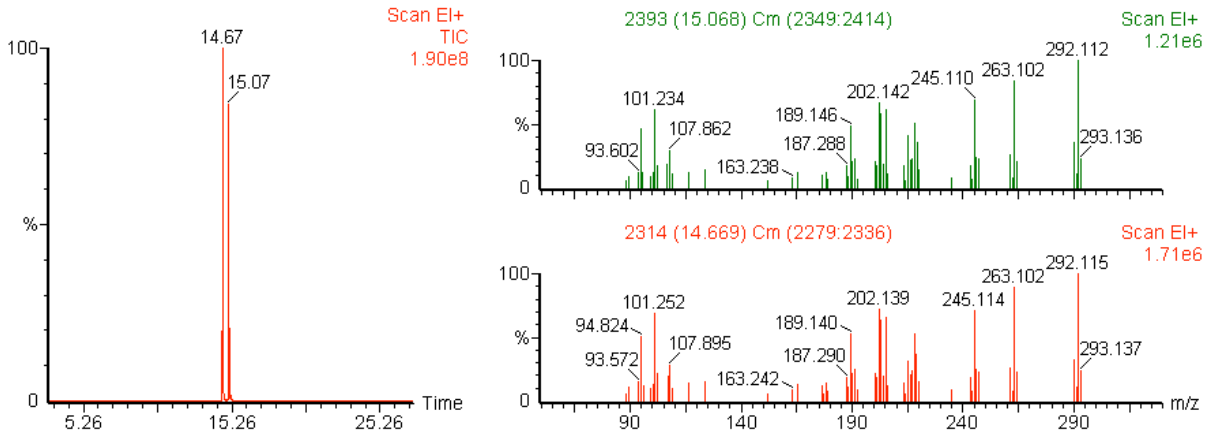


Figure 11. Cis-trans (*Z/E*) isomerism of **(13)**.

Figure 12. GC chromatogram and mass spectra of **(13)**.



The olefinic bond of ester **13** was reduced by hydrogenation using PtO_2 as catalyst and yielded the corresponding aliphatic ester **14** (83%). Subsequently, the ester underwent a saponification step to give carboxylic acid **15** as a potassium salt in a 90% yield. The carboxylic acid functionality of **15** was turned quantitatively into an acid chloride **16** by stirring with oxalylchloride at room temperature. Ring closure of **16** was achieved successfully by an internal Friedel-Crafts acylation and afforded **10** in 45% yield. Wolff-Kishner reduction of the carbonyl-moiety of **10** gave the cyclopenta-fused octahydropyrene **8** (75% yield).

4.2 Friedel-Crafts acylation of 4-oxo-1,2,2a,3,4,6,7,8-Octahydrocyclopenta[*cd*]pyrene (10) and 1,2,3,4-tetrahydro-dioxo-cyclohepta[*cd*]pyrene (17).

Although acylation onto **10** was expected to be the most promising strategy for obtaining the lowest amount of isomers, Friedel-Crafts acylation of **10** resulted in the obtention of only starting material. Increasing the amount of acid chloride had no effect on the reaction and still only starting material was obtained. The characteristic three aromatic resonances in the ^{1}H NMR spectrum of compound **10)**remain unaffected after the reactions. GC-MS also confirms this result by showing only one signal in the GC chromatogram with the characteristic retention time as well as the parent ion mass of **10**. The deactivation by the meta-directing carbonyl-moiety which was expected to occur only on the 5 position appears to be responsible for the deactivation of the whole aromatic framework of **10**. This is in line with the observed unsuccessful acylation of **17.** After the synthesis of **30,** ringclosure of **30** afforded **17**. Friedel-Crafts acylation of **17** resulted in obtaining unreacted starting material.

4.3 Friedel-Crafts acylation of 1,2,2a,3,4,6,7,8-Octahydrocyclopenta[*cd*]pyrene (8).

Wolff-Kishner reduction of ketone **10** afforded compound **8** in 75% yield. However, it is noteworthy to mention that the obtained product contained some impurities which showed a large quantity of aromatic signals in the ^{1}H NMR spectrum. Despite the presence of those signals, it could be seen from the other characteristic resonances that the Wolff-Kishner reduction of **10** was successful. Attempts to purify the impure oily **8** by recrystallization as well as column chromatography were unsuccessful. Friedel-Crafts acylation of the impure **8** yielded the acylated product, however the signals of the impurities interfere to a large extent within the aromatic range of the ^{1}H NMR spectrum. Analysis by GC-MS showed various signals of pollution, thought no signals of the desired product were present. Purification attempts by have been made, however, just as in the step before column chromatography was not able to separate the desired compound from the impurities. The presence of the desired product can be based on the aliphatic signals in the ^{1}H NMR spectrum, particularly the singlet at 4.2 ppm belonging to the methyl group of the ester. Unfortunately, not much insight into the isomer distribution of the obtained product could be gained from the analysis results.

4.4 Synthesis of 3,4-dihydrocyclopenta[*cd*]pyrene (7), the FVT route.

In an earlier stage[35] the synthesis of cyclopenta[*cd*]pyrene **(7)** had been accomplished by FVT procedures. At first, acylation of pyrene **(1)** afforded 1-acetylpyrene **(18)** in a 76% yield, which was reacted with PCl_5 to give 1-(1-chloroethenyl)pyrene **(19)** and a small amount of the bis-chlorinated product **20** (83%). The obtained mixture of **19** and **20** was subjected to FVT experiments in portions of 50 milligrams due to the small capacity of the sublimation glassware. After sublimation ($2.8 \cdot 10^{-2}$ Torr, sublimation temperature: 135^{o}C) and exposure to the hot zone (1000^{o}C) of FVT precursors **19** and **20**, cyclopenta[*cd*]pyrene **(6)** deposited in the cold zone as an orange solid. FVT afforded pure **6** in an average yield of 93% and an average mass recovery of 90%. In order to obtain **7**,

cyclopenta[*cd*]pyrene **(6)** had to undergo a hydrogenation step. The hydrogenation was performed, using palladium on carbon as catalyst and under atmospheric hydrogen pressure. The reaction yielded **7** as a white solid (72%).

4.5 Synthesis of 3,4-dihydrocyclopenta[*cd*]pyrene (7) by diacylation of pyrene.

The proposed route for obtaining 3,4-dihydrocyclopenta[cd]pyrene **(7)** by simultaneous diacylation of pyrene **(1)** followed by a Wolff-Kishner reduction turned out to be an excellent timesaving method. Friedel-Crafts acylation of pyrene **(1)** using oxalylchloride as reagent and a triple excess of $AlCl_3$, due to the presence of two carbonyl-moieties, yielded a dark solid mass containing a large amount of aluminium-salts. Extraction of these salts with an organic solvent gave bis-ketone **28** as an orange solid in a 16% yield. Wolff-Kishner reduction of **28** afforded pure **7** as a white solid after purification by flash chromatography using hexane as eluent (yield: 11%). Although it is possible to obtain pure 3,4-dihydrocyclopenta[cd]pyrene **(7)** rapidly in this way, it is noteworthy to mention that these two reactions require a bit more intensive workup procedures, especially when they are carried out with large amounts of starting materials. Performing the Friedel-Crafts acylation of pyrene in gram-scale with oxalylchloride as reagent requires a tremendous amount of $AlCl_3$ and generates a large quantity of gaseous hydrogen chloride during the reaction. After stirring the reaction mixture overnight at room temperature, the reaction mixture turned into a black solid mass containing the desired **28** enclosed in aluminium-salts, after which tedious extraction procedures are necessary to obtain the raw product.

4.6 Friedel-Crafts acylation of 3,4-dihydrocyclopenta[*cd*]pyrene (7).

As reported in an earlier stage of research[35], Friedel-Crafts acylation of **7** using methyl succinyl chloride as reagent (ratio **7** : methyl succinyl chloride : $AlCl_3$ = 1 : 1.05 : 3) afforded three isomers analogous to the reported isomers in literature in which acetyl chloride is used as reagent.[25] The presence of the three isomers in the yielded mixture **23a**, **23b** and **23c** was deduced from comparison of the obtained UV-Vis spectra from HPLC analysis (solvent gradient: 70% Acetonitrile – 30% H_2O to 100% Acn in 15 min.) with the reported data in literature (solvent gradient: 98% Hexane – 2% THF).[25] As clearly depicted in figure 13, the UV-Vis spectra corresponding to peaks *2*, *3* and *4* show similar absorbance curves, which indicate to be originated from the same compound. Peak *1* is thought to be a combination of peak *2* and *3* due to the presence of both absorption maxima between 330 and 440 nanometers. Combining the found absorption maxima with the reported[25] data, as listed in table 2, show great similarity.

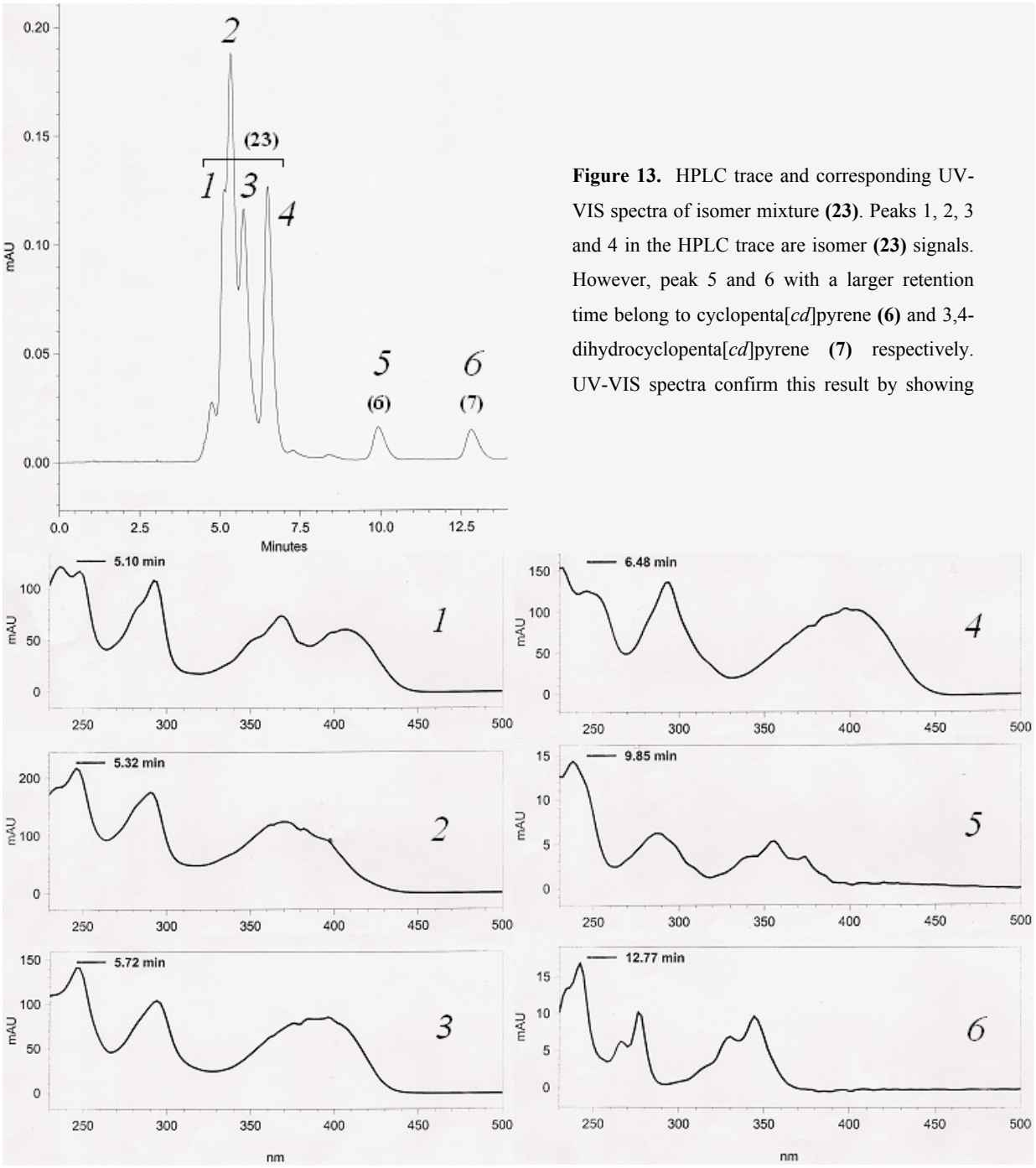


Figure 13. HPLC trace and corresponding UV-VIS spectra of isomer mixture **(23)**. Peaks 1, 2, 3 and 4 in the HPLC trace are isomer **(23)** signals. However, peak 5 and 6 with a larger retention time belong to cyclopenta[*cd*]pyrene **(6)** and 3,4-dihydrocyclopenta[*cd*]pyrene **(7)** respectively. UV-VIS spectra confirm this result by showing

Table 2. Listed UV absorption maxima of the reported[25] and obtained products.

Reported[25] UV λ_{max}					
- (29b)	400 nm	364 nm	349 nm	290 nm	**244 nm**
- (29c)	391 nm	377 nm		291 nm	**245 nm**
Measured UV λ_{max}					
- peak 1	408 nm	368 nm	351 nm	290 nm	**249 nm**
- peak 2	398 nm	370 nm		290 nm	**246 nm**
- peak 3	400 nm	371 nm		294 nm	**246 nm**
- peak 4	**402 nm**	**373 nm**		**294 nm**	**246 nm**

The mixture of the three constitutional isomers **23a**, **23b** and **23c** is also analyzed later on by GC-MS (figure 14). As expected from earlier measurements, the GC chromatogram showed the presence of three compounds with different peak intensities (retention time: 24.58, 27.91 and 29.20 min.). The first peak (24.58 min.) of the chromatogram differs slightly from the other two peaks by having a lower intensity and a larger difference in retention time. This peak is thought to be resulted from the 1-isomer **23a**. However, the other two signals could not specifically be assigned to isomers **23b** and **23c**. The corresponding mass spectra are in agreement with these results and show equal fragmentation patterns and the same molecular ion mass of 342, i.e. the molecular mass of **23**.

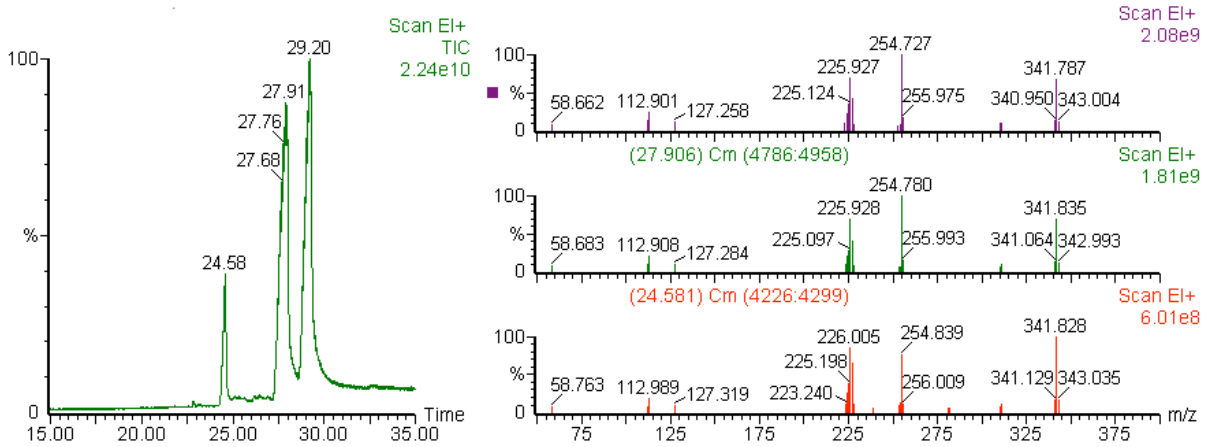


Figure 14. GC-MS data of isomeric mixture **23**.

^{1}H NMR measurements of mixture **23** showed the presence of three products as expected from earlier analysis. The interpretation of the ^{1}H NMR spectrum of **23** was facilitated by comparing the data with those of the parent compound **7**. By comparing the ^{1}H NMR signals with the reported[25] data of compound **29,** it was possible to assign the signals with more certainty. It was expected to observe a lower field shift of the protons peri and ortho to the methyl succinyl substituent than the corresponding protons of the parent compound **7**. The same observed low field shifts on the protons peri and ortho to acetyl group of **29** are reported in literature[25] to be $\Delta\delta_{peri}$= +0.97 to +1.16 ppm and $\Delta\delta_{ortho}$= + 0.39 to 0.50 ppm. Also the $^{3}J_{H\text{-}H}$ coupling constants peri and ortho to the acetyl group are observed and reported to be ΔJ= 0.4-0.5 Hz larger than that of **7**. These reported[25] values are consistent with the obtained data from ^{1}H NMR measurements (figure 15).

Table 3. Reported[25] ^{1}H NMR

(29a)	7.90 (H_5, bs), 8.00 (H_7, t, *J*=7.9), 8.32 (H_2, s), 9.10 (H_{10}, d, *J*=9.6).
(29b)	7.94 (H_2, d, *J*=7.7), 8.02 (H_9, d, *J*=9.1), 8.05 (H_8, d, *J*=8.1), 8.15 (H_{10}, d, *J*=9.1), 8.20 (H_1, d, *J*=7.7), 8.38 (H_7, d, *J*=8.1),
(29c)	7.81 (H_5, t, *J*=1.6), 7.95 (H_2, d, *J*=7.8), 8.07 (H_6, d, *J*=8.1), 8.21 (H_1, d, *J*=7.8), 8.22 (H_{10}, d, *J*=9.6), 8.40 (H_7, d, *J*=8.1),

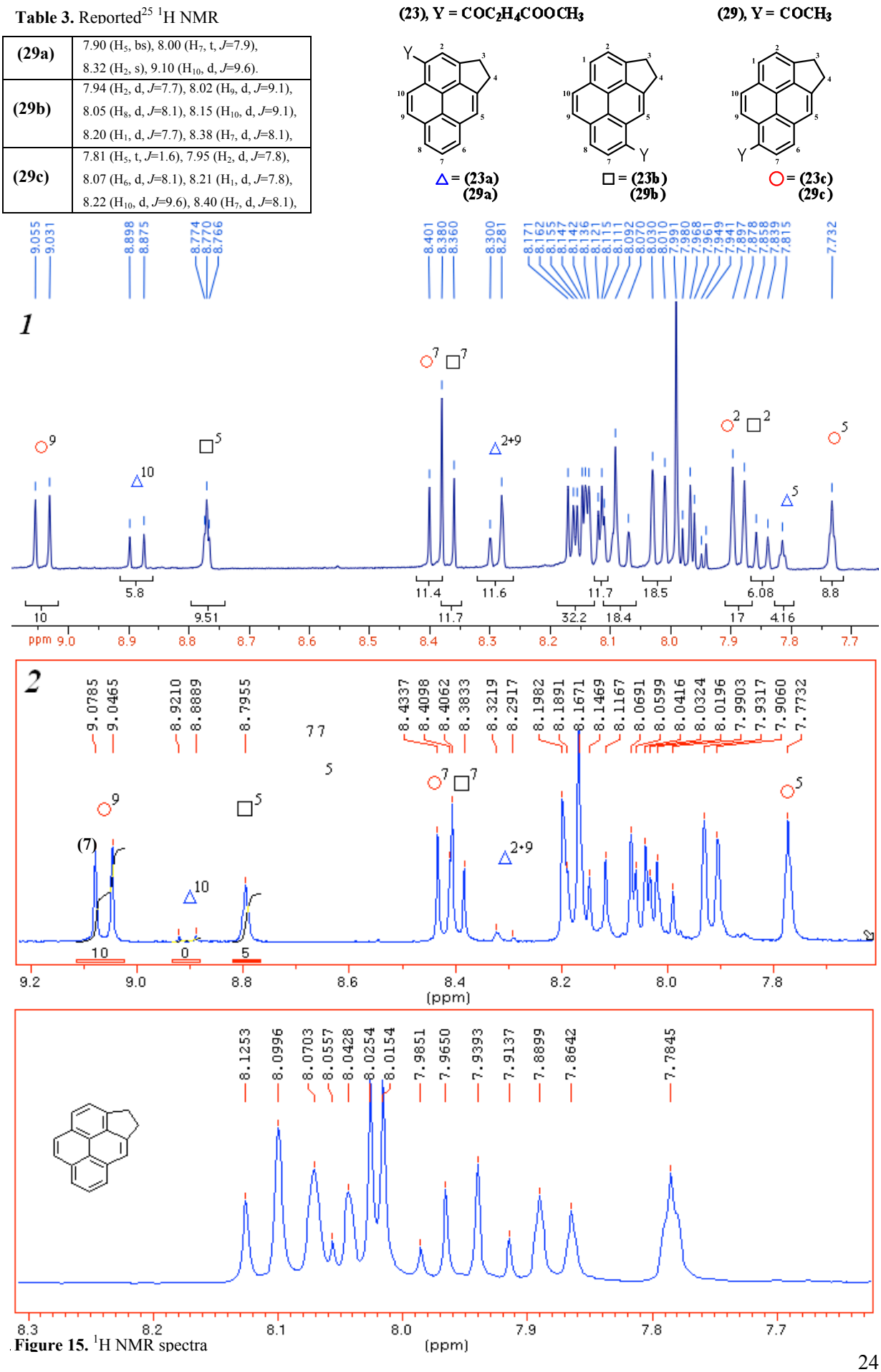


Figure 15. ^{1}H NMR spectra

The ^{1}H NMR spectra shown in figure 15 are from different reaction mixtures. Spectrum 1 is obtained for a reaction mixture of which starting material **7** is added to the generated acylium ion at room temperature. However, spectrum 2 is obtained from a reaction mixture of which starting compound **7** is added to the reaction mixture at 0^{O}C, after which the reaction mixture is stirred overnight at room temperature. Although both spectra show similar signals, spectrum 2 seems to contain a smaller amount of one isomer. From the available data can be deduced that these missing signals in spectrum 2 are originating from the 1-isomer **23a**. In addition, spectrum 1 contains a small amount of pyrene **1** with characteristic signals (8.16, 8.01 and 7.99 ppm), and is responsible for the singlet at 8.01 ppm with high intensity.

A characteristic signal for all the three constitutional isomers **23** is originating for proton 5. This signal is observed as a broad singlet due to the meta-coupling resulting from its structure. The largest low field shifted singlet can be assigned to H_5 of **23b** owing the lower field shift to the methyl succinyl substituent on the 6 position. The methyl succinyl group causes also the resonances of peri protons H_9 of **23c** and H_{10} of **23a** to shift down field to 9.05 ppm and 8.90 ppm respectively.

As can be calculated from the ^{1}H NMR spectra in figure 15, the protons peri as well as the protons ortho to the methyl succinyl groups resonate at lower fields as expected. For the ortho protons, the low field shifts are $\Delta\delta_{ortho}$= + 0.4430 ppm for the 1-isomer **23a,** $\Delta\delta_{ortho}$= + 0.4502 ppm for the 6-isomer **23b** and $\Delta\delta_{ortho}$= + 0.4732 ppm for the 8-isomer **23c.** The peri protons shift are found to be $\Delta\delta_{peri}$= + 0.8760-1.0190 ppm for the 1-isomer **23a,** $\Delta\delta_{peri}$= + 1.0035 ppm for the 6-isomer **23b** and $\Delta\delta_{peri}$= + 1.0034 ppm for the 8-isomer **23c.** The isomeric distributions of the obtained mixtures **23** are calculated from proton integrals and are listed below.

	1-isomer 23a : 6-isomer 23b : 8-isomer 23c
[addition of **(7)** at room temperature]	5.8 : 9.5 : 10.0
[addition of **(7)** at 0^{O}C]	0.9 : 5.2 : 10.0

Attempts to separate the obtained isomers **23** by recrystallization, column chromatography and HPLC were unsuccessful and mixture **23** was used for further synthesis.

4.7 Internal Friedel-Crafts acylation of ester 23.

Ringclosure of ester **23** by an internal Friedel-Crafts acylation in a melt (150^{O}C) of $AlCl_3$/NaCl afforded bis-ketone **24** as a mixture of isomers in a yield of 75%. Analysis of the obtained mixture by GC-MS showed two large signals in the GC chromatogram (retention time: 28.7 and 32.6 min.) corresponding to mass spectra with a molecular ion peak of 310, which is in agreement with the molecular mass of **24** (figure 17). Analysis by ^{1}H NMR showed also the presence of mainly two isomers. From comparison of the obtained spectra with the spectrum of **17** and **23** can be deduced that these isomers must be the ringclosed [*cd*,*fg*] **24b** and [*cd*,*jk*] bis-ketones **24c** resulting from esters **23b** and **23c**. Again there is a small difference in isomer distribution of **24** between spectrum 1 and 2 (figure 16).

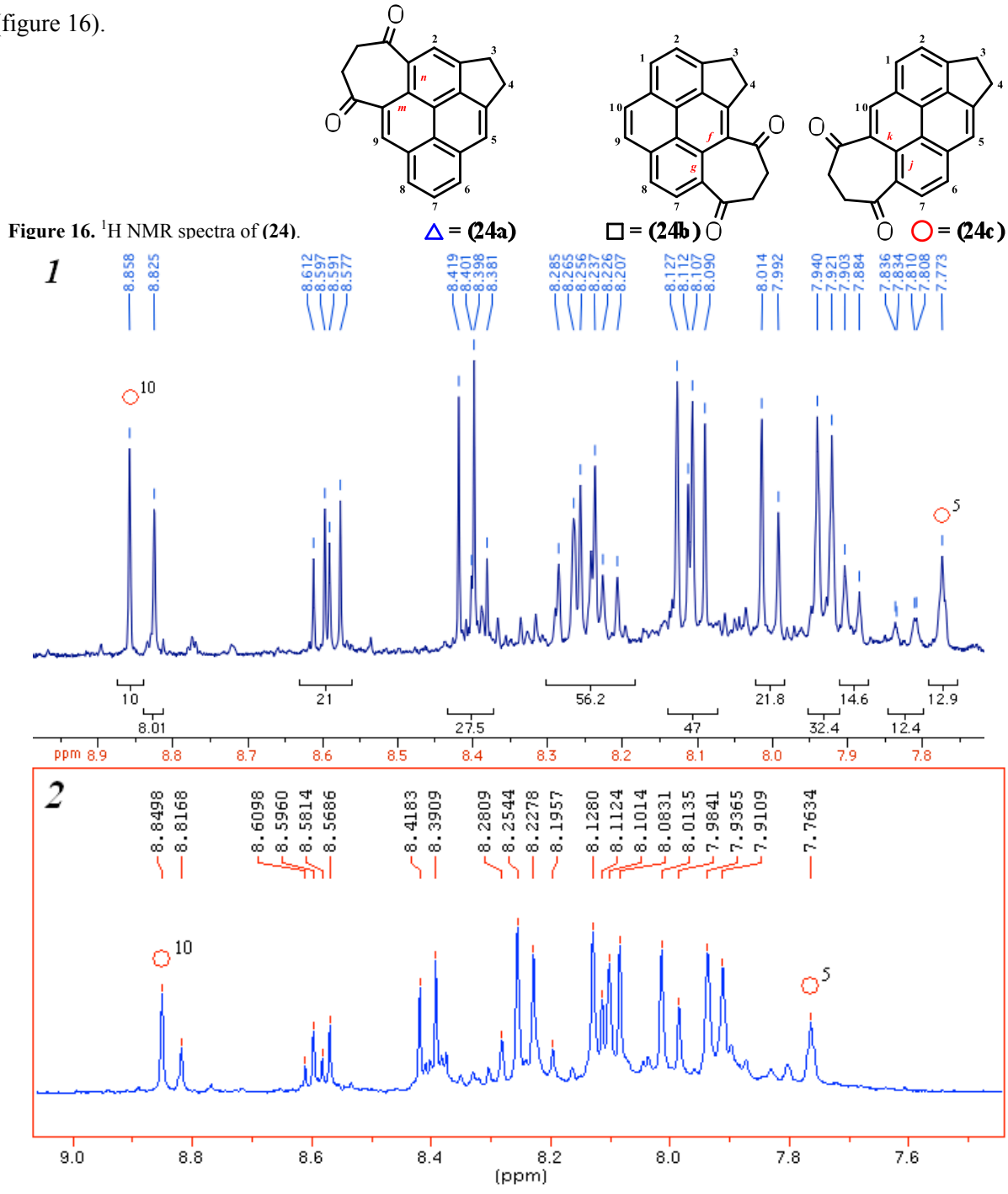


Figure 16. ^{1}H NMR spectra of **(24)**.

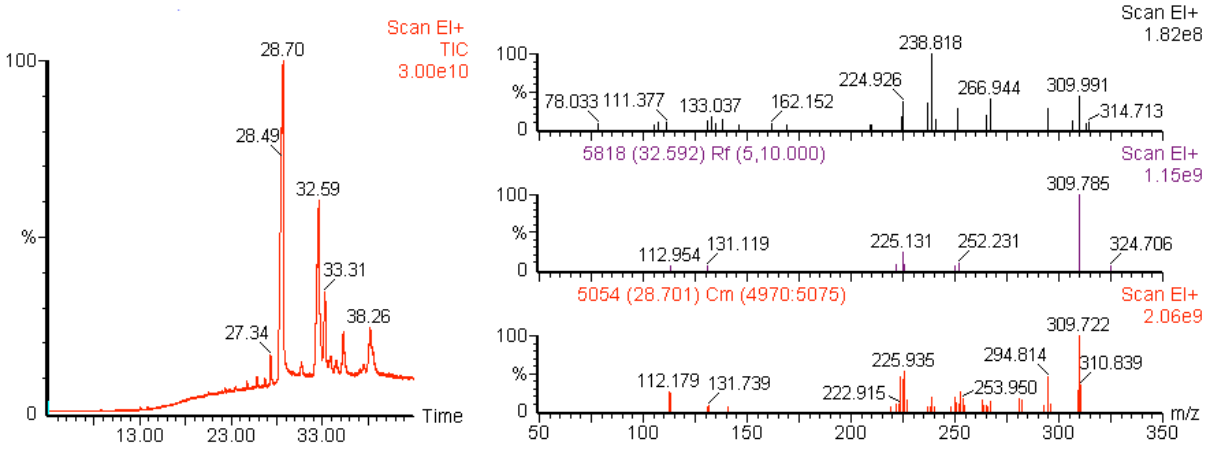


Figure 17. GC-MS results of **(24)**.

Attempts for purifying the isomeric mixture **24** by column chromatography were unsuccessful, and mixture **24** was used for further synthesis.

4.8 Synthesis of cyclohepta-cyclopenta[*cd*]pyrene (11).

Reduction of bis-ketone **24** was achieved by $LiAlH_4$ in dry diethylether in a yield of 80%. Expected was to obtain for each isomer of bis-ketone **24** a mixture of four stereoisomers; two diastereomeric pairs of enantiomers (figure 18).

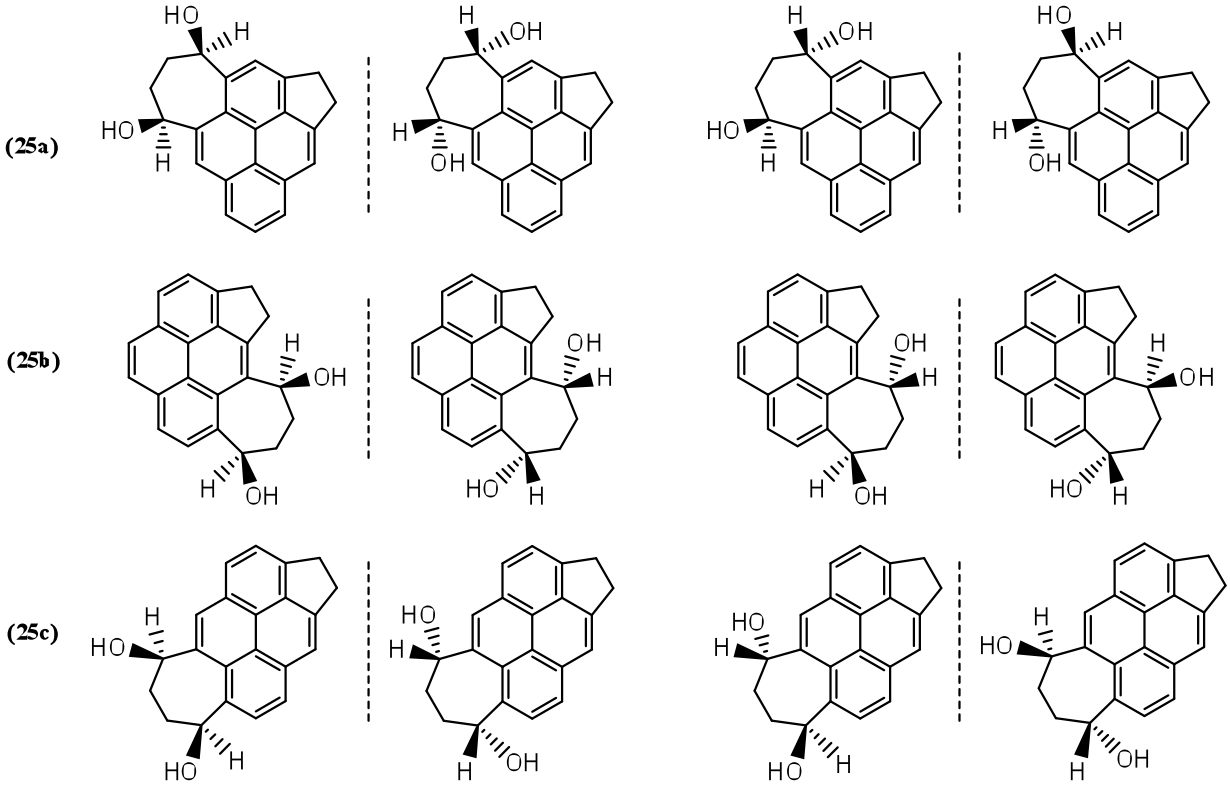


Figure 18. Expected stereoisomers resulting from the reduction of **(23)**.

The presence of bis-hydroxyl **25** was shown by ^{1}H NMR analysis. However, the obtained spectrum could not be interpreted correctly. The characteristic resonances at 5.60-5.63 ppm and 5.71-5.72 ppm originating from the methylene protons next to the hydroxyl groups were observed (figure 19). From these broad resonances can be concluded that they result from more than one **25** isomer.

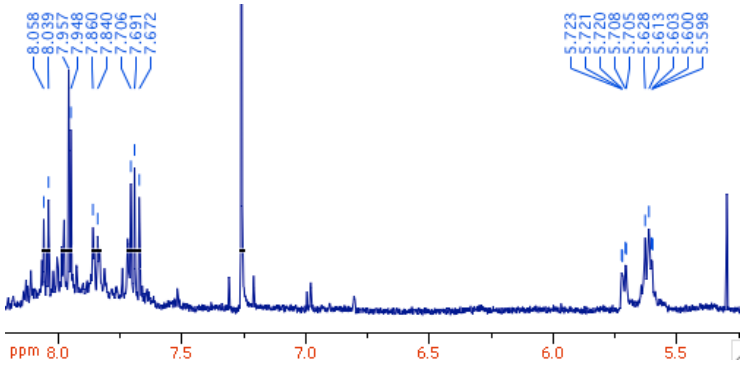


Figure 19. ^{1}H NMR spectrum of **(25)**.

GC-MS analysis of **25** showed besides the various signals in the GC chromatogram, no molecular ion peak in the mass spectra (m/z 314). However, peaks were observed at m/z 296. These are in correspondence with **25** since elimination of one water molecule (m/z 314-18) is possible to occur in the injector of the GC-MS. Two fold elimination of water is not observed in the mass spectra. The bis-hydroxyl **25** was acylated without further purifications.

Acetylation of **25** was performed with acetyl chloride and pyridine in dichloromethane. The reaction yielded an orange solid, containing a large amount of pyridinyl salts. However, it was still possible to detect the ^{1}H NMR resonances of the two acetyl groups at 2.1-2.2 ppm. Analysis of the obtained product by GC-MS showed the desired characteristic behaviour of bis-acetyl **26**. The mass spectrum originating from a signal (retention time: 11.63 min) in the GC chromatogram showed a m/z value of 278, which corresponds to the mass of the conjugated cyclohepta-ring.

Subjecting the obtained impure bis-acetyl **26** to FVT, yielded a small amount of yellow solid. The recorded ^{1}H NMR spectrum showed besides the large water peak an intense signal at 1.28 ppm and another broad signal at 0.8-1.0 ppm. This is thought to result from polymer material and **26** is believed to tend to polymerize under FVT conditions. Analysis of the obtained product by GC-MS showed besides the earlier observed GC-peak (retention time: 11.63 min) with a corresponding m/z value of 278, also an intense peak in the GC chromatogram at 14.26 min. The m/z value belonging to this peak is found to be 276, which is corresponding to the molecular mass of cyclohepta-cyclopentapyrene **(11)** (figure 20).

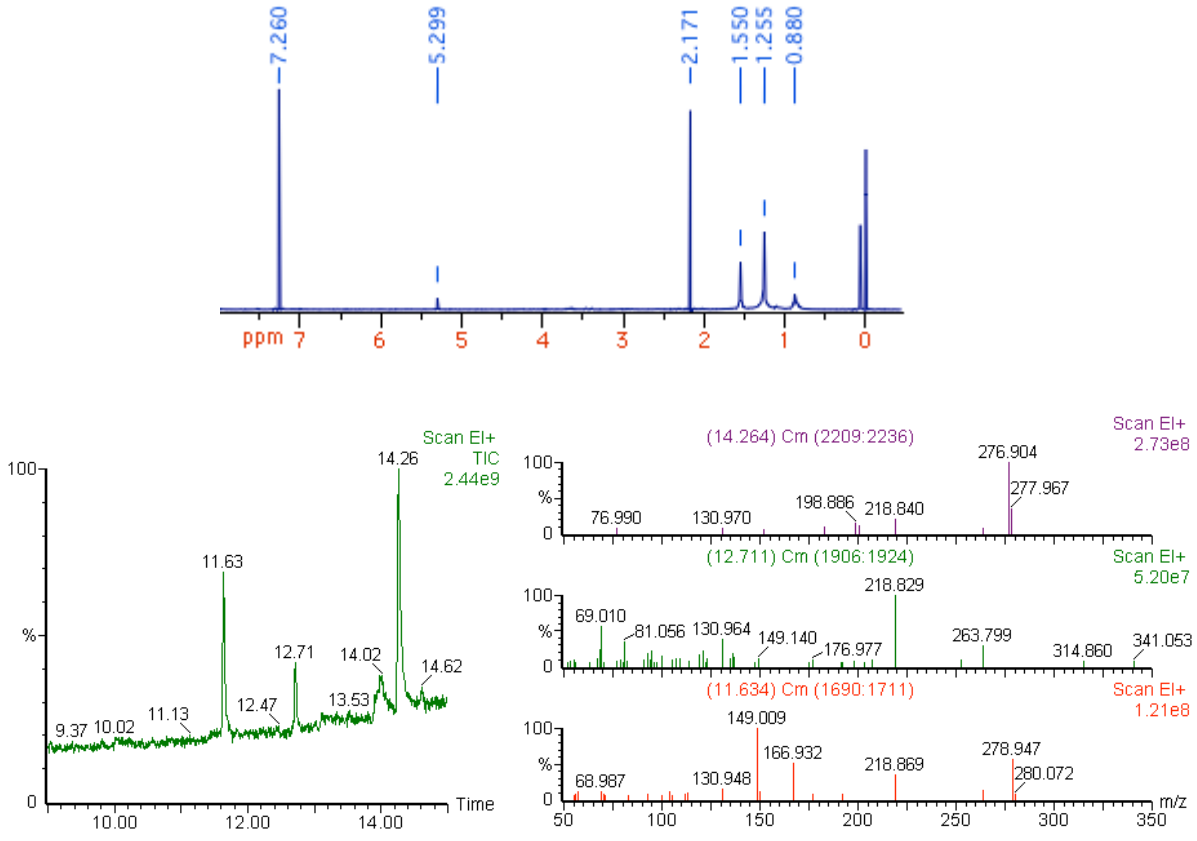


Figure 20. Corresponding ^{1}H NMR spectrum and GC-MS spectrum of the FVT products.

5. Conclusion and discussion

The goal of this report, i.e. the synthesis of cyclopenta-cycloheptapyrene **(11)**, has unfortunately not been achieved. Although the cyclohepta-derivatives were obtained and characterized properly, the last step of the proposed synthetic strategy, that is FVT of the bis-acetyl **26,** afforded an undesired product. FVT of **26** at 600^{O}C (sublimation temperature 170-190^{O}C) yielded polymeric material. Bis-acetyl **26** is thought to polymerize under the used FVT conditions, but can also be a consequence of the impurities of the used FVT precursor **26**. However, GC-MS analysis of bis-acetyl **26** substantiates the ability of **26** to eliminate two molecules of acetic acid to give the conjugated seven-membered ring derivative **27** with the corresponding m/z value of 278 (retention time: 11.63 min), which is generated in the GC-injector. GC-MS analysis of the product obtained from FVT experiments showed also the formation of the desired **27**. Moreover, also another peak appeared in the GC chromatogram with a corresponding m/z value of 276 and is supposed to originate from the fully conjugated **11**.

In addition, the most promising strategy proposed for obtaining **11** turned out to be not feasible. At first, Friedel-Crafts acylation of ketone **10** failed to fulfill the expectation of affording only two constitutional isomers. The carbonyl-moiety on the 4-position was expected to deactivate the 5-position of **10**, but appears to be responsible for the deactivation of the whole aromatic core. This observed effect of the carbonyl-substituents on the aromatic core was corroborated from the obtention of starting materials after the attempted acylation of bis-ketone **17**.

Friedel-Crafts acylation of **8** yielded unidentified products, and is observed to be not a convenient method for obtaining the desired compound **11**. The synthetic strategy has shown to involve many steps and the use of HF for achieving the ringclosure of carboxylic acid **15** was avoided for security reasons. To carry on with this strategy it is of crucial importance to obtain pure products, which is impossible due to the lots of steps involving harsh reaction conditions, accompanied by low yields.

6. Outlook

The most promising results are obtained making use of the synthetic strategy depicted in scheme 3. This route is still believed to be the most feasible one for obtaining cyclopenta-cycloheptapyrene **(11)**. However, more time has to be devoted to the purification of the starting materials before carrying on with the next synthetic steps. Future work that would facilitate the characterization of the obtained products is the separation of the obtained isomers in the acylation step of 3,4-dihydrocyclopenta[*cd*]pyrene **(7)**. Obtaining a considerable amount of the pure FVT precursor **26** will make it possible to investigate the behaviour of **26** under FVT conditions. This is the only way that will provide the opportunity to exclude the unknown effects of the pyridinyl salts that caused the reported FVT results to be unreliable.

7. Experimental

7.1 General

Following syntheses were all carried out under a nitrogen atmosphere. All the solvents were distilled before usage. Column chromatography: Merck kieselgel 60 silica (230 – 400 ASTM). ^{1}H-NMR (300.13 and 399.94 MHz) NMR spectra were recorded in $CHCl_3$, unless stated otherwise. All chemical shifts reported are in ppm and referenced to TMS (δ = 0.00 ppm) and $CDCl_3$ (δ = 7.26 ppm). For the ^{1}H-NMR multiplicity is denoted as following: s = singlet, d = doublet, t = triplet, m = multiplet. GC-MS spectra were measured on a Perkin Elmer Turbomass upgrade (Mass spectrometer) Autosystem XL (gas chromatograph) (column J&W Scientific DB-5, length 30 m, ID 0.32 mm and film thickness 0.25 μm; injector temperature 150ºC, temperature program 10ºC min^{-1}, final temperature 280ºC, carrier gas He; mass spectrometer 70 eV). GC were recorded with a Varian 3400 (column: IB17, length 30, ID 0.25 mm and film thickness 0.25 μm; injector temperature 150 ºC, temperature program 2 min 150 ºC - 10 ºCmin^{-1}, final temperature 280 ºC, detector temperature 300 ºC). IR spectra were measured on a Perkin Elmer with ATR unit.

Caution: (Non-)alternant (CP)-PAHs are potential genotoxic compounds.

7.2 Synthesis

1-Acetylpyrene (18)

Anhydrous $AlCl_3$ (1.6 g, 12.0 mmol) was added to 30 ml of dry CH_2Cl_2 under stirring, after which (0.824 g, 10 mmol) acetyl chloride was added to this cooled (0^{o}C, ice bath) suspension. After stirring for 1 hour 2.0 g (9.90 mmol) of pyrene was added at room temperature in small portions. During the addition of pyrene a color change was observed from yellow into deep red. The reaction mixture was stirred at room temperature overnight. Workup of the reaction mixture was achieved by addition of water (50 ml) and 30% HCl (5 ml). The water layer was extracted two times with 25 ml of CH_2Cl_2, after which the organic layers were combined, washed with a saturated sodium bicarbonate solution (30 ml) and water (30 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude acetylpyrene was purified by recrystallization from methanol and yielded pure 1-acetylpyrene **(18)** (yield 1.9 g, 7.79 mmol, 79%)

^{1}H NMR ($CDCl_3$); δ 9.06 (1H, d, *J*=9.3 Hz), 8.38 (1H, d, *J*=8.0 Hz), 8.22 (3H, m), 8.16 (2H, d, *J*=8.8 Hz), 8.04 (2H, m), 2.90 (3H, s) ppm.

1-(1-chloroethenyl)pyrene (19)

1-Acetylpyrene (1.5 g, 6.16 mmol) **(18)** was added under stirring to PCl_5 (1.35 g, 6.45 mmol) in 50 ml CH_2Cl_2. The suspension was stirred and heated at reflux temperature for 18 hours. After cooling the reaction mixture to room temperature water (50 ml) was added. The organic layer was washed with a saturated sodium bicarbonate solution an twice with 50 ml of water. The remaining yellowish organic layer is dried over $CaCl_2$, concentrated under reduced pressure, and purified by flash chromatography (silica, eluent: hexane:CH_2Cl_2 9:1), yielding 1-(1-chloroethenyl)pyrene **(19)** as yellow solid (yield 1.34 g, 5.12 mmol, 83%).

^{1}H NMR ($CDCl_3$); δ 8.45 (1H, d, *J*=9.3 Hz), 8.10 (8H, m), 6.00 (1H, d, *J*=1.1 Hz) and 5.68 (1H, d, *J*=1.1 Hz) ppm.

GC-MS; t_r=15.04 min; *m/z* 262 (M^+), 226 (M – 2HCl).

Cyclopenta[cd]pyrene (6)

1-(1-chloroethenyl)pyrene **(19)** was inserted in portions of approximately 0.050 grams into the FVT tube. An orange solid deposits during FVT (970-1000 ^oC, sublimation temperature 120-150 ^oC, $2{,}8 \cdot 10^{-2}$ mbar) in the cold zone of the FVT tube. Pure cyclopenta[cd]pyrene **(6)** (0.7922 g, 3.50 mmol) was obtained after FVT as an orange solid, with an average yield of 93% and an average mass recovery of 90%.

^{1}H NMR ($CDCl_3$); δ 8.41 (1H, d, *J*=7.7 Hz), 8.37 (1H, s), 8.28 (1H, d, *J*=7.7), 8.11 (3H, m), 8.03 (2H, m), 7.42 (1H, d, *J*=5.2 Hz) and δ 7.24 (1H, d, *J*=5.2) ppm.

3,4-Dihydrocyclopenta[cd]pyrene (7)

Cyclopenta[cd]pyrene (0.6433 g, 2.83 mmol) **(6)** was hydrogenated at room temperature in three portions in 40 ml of ethanol and under one atmosphere of H_2-pressure. A catalytic amount of palladium on activated carbon (10%) is used as catalyst. After the color of the solution changed from yellow/orange into colorless (1.5 hours), the solution is filtered and concentrated under reduced pressure, yielding pure 3,4-dihydrocyclopenta[cd]pyrene **(7)** as a white solid (yield 0.4752 g, 0.210 mmol, 72%).

^{1}H NMR (300.13 MHz, $CDCl_3$); δ 8.02 (6H, m), 7.88 (1H, d, *J*=7.7 Hz), 7.78 (1H, s), 3.67 (2H, m), 3.63 (2H, m) ppm.

^{13}C NMR (75.46 MHz, $CDCl_3$); δ 145.10, 142.25, 136.81, 133.81, 131.42, 128.41, 127.09, 126.35, 126.26, 125.10, 124.13, 123.91, 122.99, 122.54, 121.73, 118.74, 31.95, 30.68 ppm.

GC-MS; t_r=13.16 min; *m/z* 228 (M^+), 226 (M – 2H), 200 (M – C_2H_4).

Cyclopenta[cd]pyrene-3,4-dione (28)

To a cooled suspension (0°C, ice bath) of anhydrous $AlCl_3$ (15.0 g, 0.11 mol) in dry CH_2Cl_2 (250 ml), 6.35 g (0.050 mol) oxalylchloride was added under stirring. After the yellow suspension was stirred for 1 hour, 10.0 g (0.050 mol) pyrene **(1)** was added in small portions at room temperature. A color change was observed from yellow into dark red/black accompanied. The reaction mixture was stirred overnight at room temperature, after which water (250 ml) and 30% HCl (25 ml) was added. The quenched mixture was left overnight to dissolve the formed aluminum salts. Subsequently, the water layer was extracted 5 times with CH_2Cl_2 (25 ml) and the organic layers were combined, washed with water (50 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. Crude cyclopenta[cd]pyrene-3,4-dione **(28)** was obtained as an orange solid (yield 2.7 g, 0.011 mol, 22%). Cyclopenta[cd]pyrene-3,4-dione was used for further synthesis without any further purification.

^{1}H NMR (300.13 MHz, $CDCl_3$); δ 8.43 (1H, d, *J*=7.6 Hz), 8.42 (1H, d, *J*=7.4 Hz), 8.38 (1H, s), 8.32 (1H, d, *J*=4.38 Hz), 8.30 (1H, d, *J*=5.52 Hz), 8.2 (3H, m) ppm.

3,4-Dihydrocyclopenta[*cd*]pyrene (7) (Wolff-Kishner)

After 2.7 g (0.011 mol) unpure cyclopenta[*cd*]pyrene-3,4-dione **(28)** was dissolved in diethylene glycol (150 ml), 10.5 ml (0.22 mol) of hydrazine monohydrate was added at room temperature. Subsequently, the reaction mixture was refluxed for 1 hours. The excess of hydrazine was then removed from the reaction mixture by distillation (120°C), after which 11.0 g (0.20 mol) of KOH was added to the reaction mixture and refluxed for 1 hour. After the reaction mixture was cooled to room temperature, it was poured into water (250 ml) and 30% HCl (25 ml). The water was extracted with CH_2Cl_2 (8 x 25 ml), and the organic layers were combined, washed with water (30 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was obtained as a red solid and purified by flash chromatography over silica with hexane as eluent. Pure 3,4-dihydrocyclopenta[*cd*]pyrene **(7)** was collected as a white solid (0.200 g, 0.87 mmol, 8%)

^{1}H NMR (300.13 MHz, $CDCl_3$); δ 8.02 (6H, m), 7.88 (1H, d, *J*=7.7 Hz), 7.78 (1H, s), 3.67 (2H, m), 3.63 (2H, m) ppm.

^{13}C NMR (75.46 MHz, $CDCl_3$); δ 145.10, 142.25, 136.81, 133.81, 131.42, 128.41, 127.09, 126.35, 126.26, 125.10, 124.13, 123.91, 122.99, 122.54, 121.73, 118.74, 31.95, 30.68 ppm.

GC-MS; t_r=13.16 min; *m/z* 228 (M^+), 226 (M – 2H), 200 (M – C_2H_4).

Friedel-Crafts acylation of 3,4-dihydrocyclopenta[*cd*]pyrene (23)

Methyl succinyl chloride (58 µl, 0.50 mmol) was added to a cooled (0°C, ice bath) suspension of $AlCl_3$ (0.2014 g, 1.51 mmol) in 10 ml dry CH_2Cl_2. After the $AlCl_3$ is dissolved, the ice bath is removed. 3,4-Dihydrocyclopenta[cd]pyrene **(7)** (0.0929 g, 0.438 mmol) was added in small portions at room temperature to the yellow suspension. During addition the color of the suspension turned immediately deep red. The suspension was stirred overnight at room temperature. The reaction was worked up by

adding 30% HCl (10 ml) and water (50 ml) to hydrolyzing the reaction mixture. Subsequently, the organic layer was separated and washed with sodium bicarbonate (50 ml) and twice with water (50 ml). The remaining red solution was dried over magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by recrystallization from toluene, hexane and methanol was attempted but unsuccessfully. Purification of the compound by column chromatography (silica; eluent dichloromethane) afforded three isomers **(23)** as a red oil (yield 0.1234 g, 0.36 mmol, 88%), namely methyl-4-(3,4-dihydrocyclopenta[*cd*]pyren-1-yl)-4-oxobutanoate, methyl-4-(3,4-dihydrocyclopenta[*cd*]pyren-6-yl)-4-oxobutanoate and methyl-4-(3,4-dihydrocyclopenta[*cd*]-pyren-8-yl)-4-oxobutanoate.

^{1}H NMR (300.13 and 400 MHz, $CDCl_3$); δ see figure 15.

GC-MS; see figure 14.

HPLC; see figure 13.

Tetrahydro-dioxo-cyclohepta-cyclopenta[cd]pyrene (24)

0.154 g NaCl (2.63 mmol) was added to a solution of 0.0642 g (0.1877 mmol) of **(23)** in CH_2Cl_2 (3 ml). The suspension was concentrated under reduced pressure to distribute the red oil equally in NaCl. Subsequently, 0.750 g (5.63 mmol) of $AlCl_3$ was added to the mixture of **(23)** and NaCl. The reaction flask was poured into a hot oil bath (150^{o}C) for 30 minutes, after which the reaction mixture was hydrolyzed by pouring the reaction flask overnight in water (150 ml) and 30% HCl (25 ml). The water layer was extracted with CH_2Cl_2 (3 x 25 ml). The organic layers were combined, washed with water (30 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (silica, eluent: $CHCl_3$), which gave a mixture of mainly two isomers (0.035 g, 0.1130 mmol, 60%), namely **(24b)** and **(24c)**.

^{1}H NMR (300.13 and 400 MHz, $CDCl_3$); δ see figure 16.

GC-MS; see figure 17.

Tetrahydro-dihydroxy-cyclohepta-cyclopenta[cd]pyrene (25)

To a solution of 0.020 g (0.065 mmol) **(24)** in diethyl ether (2 ml), 0.0074 g (0.1935 mmol) $LiAlH_4$ was added at room temperature. The reaction mixture was stirred at room temperature for 3 days, after which water (2 ml) was added to quench the excess $LiAlH_4$. The organic layer was separated and dried over magnesium sulfate, filtered and concentrated under reduced pressure. The resulting yellow oil **(25)** (yield 0.017 g, 0.054 mmol, 83%) was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$); δ see figure 19.

GC-MS; *m/z* 296 (M - H_2O)

Tetrahydro-diacetyl-cyclohepta-cyclopenta[cd]pyrene (26)

To an cooled (0°C, ice bath) solution of 0.017 g (0.054 mmol) **(25)** in CH_2Cl_2 (2 ml) and pyridine (21 µl , 0.2592 mmol), acetylchloride (19 µl, 0.27 mmol) was slowly added. The reaction mixture was stirred for 4 days at room temperature, after which the water (20 ml) was added. The organic layer was washed with water (3 x 5 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product **(26)** was obtained as a red oil (yield 0.020 g), and used without further purification. The crude product contained a significant amount of pyridinyl salts.

^{1}H NMR (400 MHz, $CDCl_3$); δ 2.1 – 2.2 ppm

GC-MS; t_r=11.63 min; *m/z* 278 (M – 2 x AcOH)

FVT of tetrahydro-diacetyl-cyclohepta-cyclopenta[cd]pyrene (26)

FVT of 0.020 g (0.050 mmol) tetrahydro-diacetyl-cyclohepta-cyclopenta[cd]pyrene **(26)** at an oven temperature of 600°C and a sublimation temperature 170-190°C, yielded a yellow product. The product was dissolved in CH_2Cl_2 and removed from the tube. The product was concentrated enough for GCMS analysis, but too diluted to perform good ^{1}H NMR measurement. However, ^{1}H NMR analysis showed the presence of polymer material in the FVT product and residue.

GC-MS; t_r=11.63 min; *m/z* 278 (M – 2 x AcOH); t_r=14.26 min; *m/z* 276 (M – 2 x AcOH – 2H)

l-Oxo-1,2,3,6,7,8-hexahydropyrene (12)

1,2,3,6,7,8-Hexahydropyrene (2.12 g, 10.17 mmol) **(2)** was added to acetic acid (25 ml) and benzene (5 ml) to dissolve the pyrene derivative. The solution was heated to 80°C and stirred, after which a solution of CrO_3 (1.33 g, 13.5 mmol) in water (5 ml) and acetic acid (10 ml) was added drop wise at 80°C. The reaction mixture was stirred for 45 min at 80°C and for 4 hours at room temperature. Work up was achieved by pouring the reaction mixture into water (200 ml), and extraction of the water layer with ether (3 x 25 ml). The organic layers were combined, washed with water (50 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure, yielding a brown solid. The crude product was purified by column chromatography (silica, eluent: dichloromethane:hexane 9:1). A blue fluorescence band afforded pure ketone **(12)** as a yellow solid (yield 0.8456 g, 3.80 mmol, 37%).

^{1}H NMR (300.13 MHz, $CDCl_3$); δ 8.10 (1H, d, *J*=7.4 Hz), 7.34 (2H, d, *J*=7.4 Hz), 7.22 (1H, d, *J*=7.40 Hz), 3.36 (2H, t, *J*=7.0 Hz), 3.14 (2H, t, *J*=7.0 Hz), 3.12 (2H, t, *J*=6.2 Hz), 2.91 (2H, t, *J*=7.1 Hz), 2.08 (2H, quintet, *J*=6.2 Hz) ppm.

1-(Carbethoxymethylene)-1,2,3,6,7,8-hexahydropyrene (13)

First the sodium hydride (0.180 g, 4.5 mmol) was washed with dry pentane (2 x 10 ml), after which dry benzene (15 ml) was added. The suspension was cooled (0°C, ice bath) and triethyl phosphonoacetate (0.620 ml, 3.06 mmol) in dry benzene (10 ml) was added drop wise. The reaction mixture was stirred at room temperature for 1 hour. Subsequently, ketone **(12)** (0.6731 g, 3.03 mmol)

was added drop wise at 0°C in dry benzene (10 ml) to the reaction mixture. During the addition of the ketone a color change is observed from colorless into dark yellow. The reaction mixture was heated to reflux temperature and stirred for 72 hours. The dark green reaction mixture was cooled to room temperature and treated with water (100 ml) and the benzene layer was separated. The water layer was washed with ether (3 x 20 ml), and the organic layers were combined, washed with water (25 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified twice by column chromatography (silica, eluent: dichloromethane:hexane 9:1) and yielded 0.2727 g of pure **(13)** as a red oil (0.934 mmol, 31%).
^{1}H NMR (300.13 MHz, $CDCl_3$); δ 7.64 (1H, d, *J*=7.44 Hz), 7.20 (3H, m), 6.43 (1H, s), 4.25 (2H, quartet, *J*=7.15 Hz), 3.47 (2H, t, *J*=6.14 Hz), 3.18 (2H, t, *J*=6.14 Hz), 3.10 (4H, m), 2.08 (2H, quintet), 1.36 (3H, t, *J*=7.15 Hz) ppm.

Ethyl-(1,2,3,6,7,8-hexahydropyrenyl)-acetate (14)
To a solution of 0.1567 g (0.536 mmol) of **(13)** in methanol (20 ml) a catalytic amount of platinum(IV)oxide was added. The reaction mixture was stirred under H_2 (1 atm.) overnight. Subsequently, the reaction mixture was filtered and the solvent was evaporated. Analysis of the crude product showed the presence of a reasonable amount of pollution, after which the product was purified by column chromatography (silica, eluent: CH_2Cl_2). 0.1231 g of pure **(14)** was obtained as yellow oil (0.418 mmol, 78%).
^{1}H NMR (300.13 MHz, $CDCl_3$); δ 7.22 (1H, d, *J*=7.33 Hz), 7.21 (2H, s), 7.16 (1H, d, *J*=7.33 Hz), 4.20 (2H, quartet, *J*=7.15 Hz), 3.65 (1H, m), 3.09 (6H, m), 2.69 (1H, dd, *J*=1406, 6.19 Hz), 2.62 (1H, dd, *J*=14.6, 8.9 Hz), 2.06 (4H, m), 1.28 (3H, m, *J*=7.15 Hz) ppm.

(1,2,3,6,7,8-Hexahydropyrenyl)-acetic acid (15)
0.3039 g (1.034 mmol) of **(14)** was dissolved in methanol (25 ml) and aqueous potassium hydroxide (20%, 10 ml). The reaction mixture was refluxed for 1 hour, after which the methanol was evaporated. The aqueous solution was diluted with water (25 ml) and acidified with 30% HCl (10 ml) to precipitate acid **(15)** as a brown solid (yield 0.275 g, 1.03 mmol, 100%). The crude product was used without further purification.
IR; C=O 1683, C-O 1278, C-H 2929, 2864, 2829

(1,2,3,6,7,8-Hexahydropyrenyl)-acetic chloride (16)
0.100 g (0.376 mmol) of acid **(15)** was dissolved in dry CH_2Cl_2 (20 ml). The solution was cooled (0°C, ice bath) and 0.0440 ml (0.50 mmol) oxalyl chloride was added. The reaction mixture was stirred during the weekend at room temperature. Subsequently, the CH_2Cl_2 was evaporated under reduced pressure and yielded acetic chloride **(16)** as a red oil (yield 0.1037 g, 0.365 mmol, 97%)
GC-MS; t_r=14.47 min; *m/z* 248 (M - HCl).

4-Oxo-1,2,2a,3,4,6,7,8-octahydrocyclopenta[*cd*]pyrene (10)

Acid **(16)** (0.3214 g, 1.130 mmol) was dissolved in dry CH_2Cl_2 (15 ml) and cooled (0°C, ice bath). To the cooled solution $AlCl_3$ (0.2934 g, 2.20 mmol) was added in portions, and the reaction mixture was stirred overnight at room temperature. The next day the reaction mixture was poured into water (50 ml) and 30% HCl (10 ml). The water layer was extracted with CH_2Cl_2 (3 x 25 ml) and the organic layers were combined, washed with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (silica, eluent: CH_2Cl_2). Collection of the methanol fraction afforded **(10)** as a red oil (yield 0.1838 g, 0.74 mmol, 65%)

^{1}H NMR (300.13 MHz, $CDCl_3$); δ 7.38 (1H, s), 7.31 (1H, d, *J*=7.14 Hz), 7.26 (1H, d, *J*=7.44 Hz), 3.38 (1H, m), 3.08 (6H, m), 2.50 (1H, m), 2.14 (1H, dd, *J*=17.6, 5.25 Hz), 2.05 (2H, m), 1.63 (1H, dd AB, *J*= Hz) ppm.

^{13}C NMR (75.46 MHz, $CDCl_3$); δ 205.34 (C=O), 157.95, 136.72, 135.08, 134.69, 132.36, 131.16, 127.39, 127.23, 124.71, 116.20, 45.40, 36.39, 31.35, 30.68, 30.01, 29.33, 23.46 ppm.

GC-MS; t_r=14.56 min; *m/z* 248 (M^+), 220 (M - C=O).

Friedel-Crafts acylation of 4-Oxo-1,2,2a,3,4,6,7,8-octahydrocyclopenta[*cd*]pyrene (10)

To a cooled (0°C, ice bath) suspension of $AlCl_3$ (0.120 g, 0.897 mmol) in dry CH_2Cl_2 (5 ml), 0.0277 ml (0.2250 mmol) methyl succinylchloride was added. After stirring the reaction mixture for 1 hour, a solution of 0.056 (0.224 mmol) **(10)** in dry CH_2Cl_2 (2 ml) was added. The reaction mixture was stirred at room temperature overnight, after which water (25 ml) and 30% HCl (3 ml) was added. The water layer was extracted with CH_2Cl_2 (3x 15 ml), the organic phases were combined, washed with water (20 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. Analysis of the obtained red oil showed the presence of mainly starting material.

1,2,2a,3,4,6,7,8-Octahydrocyclopenta[*cd*]pyrene (8) (Wolff-Kishner)

To a solution of 0.1036 g (0.4177 mmol) of **(10)** in diethylene glycol (100 ml), hydrazine monohydrate (0.42 ml, 8.35 mmol) was added at room temperature. The reaction mixture was refluxed for 1 hour, after which the excess of hydrazine monohydrate was removed by distillation (120°C). Potassium hydroxide (0.50 g, 0.091 mmol) was added to the solution and refluxed for 1 hour. The reaction was worked up by addition of water (100 ml) and 30% HCl (25 ml). The water layer was extracted with CH_2Cl_2 (8 x 25 ml) and the organic extracts were combined, washed with water (50 ml), dried over magnesium sulfate, filtered and concentrated under reduced pressure. Crude **(8)** was obtained as red oil (yield 0.0582 g, 0.249 mmol, 60%) and was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$); δ 7.13 (1H, s), 7.10 (1H, d, *J*=7.2 Hz), 7.04 (1H, d, *J*=6.8 Hz), 3.30 (1H, m), 2.86-3.14 (8H, m), 2.32-2.49 (1H, m), 2.05 (2H, quintet, *J*=6.4 Hz), 1.47-1.58 (2H, m) ppm.

GC-MS; t_r=10.82 min; *m/z* 234 (M^+), 206 (M – C_2H_4).

Friedel-Crafts acylation of 1,2,2a,3,4,6,7,8-Octahydrocyclopenta[*cd*]pyrene (8)

0.133 g (1.0 mmol) of $AlCl_3$ was added to dry CH_2Cl_2 (10 ml). To the cooled (0°C, ice bath) suspension 50 µl (0.40 mmol) methylsuccinylchloride was added and stirred for 1 hour. At room temperature a solution of 0.0868 g (0.371 mmol) **(8)** in dry CH_2Cl_2 (3 ml) was added, and the reaction mixture was stirred overnight. Standard workup yielded a mixture of unidentified compounds as red oil (0.085 g).

Methyl-4-(1-pyrenyl)-4-oxo-butanoate (30)

Methyl succinylchloride (3.37 ml, 0.025 mol) was added to a cooled (0°C, ice bath) suspension of $AlCl_3$ (6.50 g, 48.6 mmol) in CH_2Cl_2 (250 ml). The suspension was stirred for 1 hour at room temperature, after which 5.00 g (0.025 mol) pyrene **(1)** was slowly added in portions. The reaction mixture was stirred overnight at room temperature, and hydrolyzed by adding water (225 ml) and 30% HCl (25 ml). The water layer was extracted with CH_2Cl_2 (3 x 50 ml). The organic extracts were combined, washed with water, dried over magnesium sulfate, filtered and concentrated under reduced pressure. 6.50 g (0.0215 mol) of **(30)** was obtained as an orange solid (yield 85%).

^{1}H NMR (300.13 MHz, $CDCl_3$); δ 8.94 (1H, d, *J*=9.42), 8.39 (1H, d, *J*=8.06), 8.23 (2H, m), 8.17 (2H, m), 8.05 (3H, AB), 3.75 (3H, s), 3.56 (2H, t, *J*=6.65), 2.94 (2H, t, *J*=6.55)

1,2,3,4-tetrahydro-dioxo-cyclohepta[*cd*]pyrene (17)

1.00 g (3.16 mmol) of **(30)** was added to a melt (150°C) of $AlCl_3$ (13.0 g, 95 mmol) and NaCl (2.6 g, 44 mmol). During the addition the color of the reaction mixture changed immediately from yellow into dark red. After heating the reaction (150°C) for 30 minutes, the reaction was quenched by pouring the reaction flask in water (250 ml) and 30% HCl (15 ml). The water layer was extracted with CH_2Cl_2 (3 x 50 ml) after which the organic layers were combined and washed with water (50 ml). After drying the organic extract over magnesium sulfate, it was filtered and concentrated under reduced pressure. 0.1860 g (0.624 mmol) of **(17)** was obtained as a red/orange oil (yield 20%).

^{1}H NMR (300.13 MHz, $CDCl_3$); δ 8.81 (1H, s), 8.56 (1H, d, *J*=8.13 Hz), 8.37 (2H, AB, *J*=8.54, 8.27 Hz), 8.25 (1H, d, *J*=8.16), 8.17 (1H, d, *J*=8.68), 8.10 (2H, m), 3.33 (4H, s) ppm.

Friedel-Crafts acetylation of 1,2,3,4-tetrahydro-dioxo-cyclohepta[*cd*]pyrene (17)

To a cooled (0°C, ice bath) suspension of acetyl chloride (14 µl, 0.201 mmol) and $AlCl_3$ (0.090 g, 0.67 mmol) in dry CH_2Cl_2 (10 ml), a solution of 0.050 g **(17)** (0.168 mmol) in dry CH_2Cl_2 (2 ml) was added. The reaction mixture was stirred overnight at room temperature, after which standard workup yielded mainly starting material **(17)** (0.043 g). The synthesis was redone and instead of adding an 1.2 equivalence of acetyl chloride, it was used as solvent (5 ml). Workup and analysis of the reaction mixture showed a product in which the dioxo-cyclohepta ring was destroyed.

Friedel-Crafts acetylation of acenaphtylene (32)

28 µl (0.40 mmol) of acetyl chloride was added to a cooled (0°C, ice bath) suspension of $AlCl_3$ (0.18 g, 0.67 mmol) in dry CH_2Cl_2 (10 ml). This suspension was stirred for 1 hour at room temperature. Subsequently, 0.050 g (0.33 mmol) of acenaphtylene **(32)** was added slowly at room temperature. The reaction mixture was stirred overnight at room temperature, after which standard workup yielded the acylated compound. ^{1}H NMR showed that the acetylation had taken place on the ethenobridge.

Dehydrogenation of 3,4,8,9-tetrahydrocyclohepta[fg]acenaphthylene-7,10-dione (41)

Dehydrogenation of 0.050 mg (0.21 mmol) **(41)** was attempted by dissolving it in mesitylene (10 ml). To this solution a catalytic amount of palladium on carbon is added and the suspension is refluxed for 2 hours. Analysis of the obtained product showed the presence of only starting product, after which the reaction mixture is refluxed overnight. Analysis showed a small amount of the desired product accompanied with mainly starting material.

References

1. J. Borneff, F. Selenka, H. Kunte, A. Maximomos, *Environ.* **1968**, *2*, 22 – 29.
2. D.P. Arfsten, D.J. Schaeffer, D.C. Mulveny, *Ecotoxicology and environmental safety* **1996**, *33*, 1-24.
3. D. Mackay, W.Y. Shiu, *J. Chem. Eng. Data* **1977**, *22*, 399 – 402.
4. O.G. Mekenyan, G.T. Ankley, G.D. Veith, D.J. Call, *Daphnia magna. Chemosphere* **1994**, *28*, 567 – 582.
5. D. J. Cook, S. Schlemmer, N. Balucani, D. R. Wagner, B. Steiner and R.J. Saykally, *Nature* (London) **1996**, *380(6571)*, 227-9.
6. D. M. Hudgins, C.W. Bauschlicher, L.J. Allamandola, J.C. Fetzer, *Journal of Physical Chemistry* **2000**, *104(16)*, 3655-3669.
7. A. Modelli, L. Mussoni, D. Fabbri, *J. Phys. Chem.* **2006**, *110*, 6482-6486
8. C. Koper, M. Sarobe, L.W. Jenneskens, *J. Phys. Chem.* **2004**, *6*, 319-327.
9. Koper C., *Ph.D. Thesis*, Utrecht University, Utrecht, The Netherlands, **2003**
10. J. Michl, *JACS* **1976**, *98:15*, 4546
11. J.B. Howard, J.P. Longwell, J.A. Marr, C.J. Pope, W.F. Busby, A.L. Lafleur, K. Taghizadeh, *Combust. Flame* **1995**, *101 (3)*, 262.
12. G. Mehta, G. Panda, *Tetrahedron Lett.* **1997**, *38*, 2145.
13. B.F. Plummer, Singleton, F. Scott, *Journal of Physical Chemistry* **1990**, *94(19)*, 7363-7366.
14. G. Grimmer, J. Jacob, K.W. Naujack, G. Dettbarn, *Anal. Chem.* **1983**, *55*, 892.
15. J. Cioslowski, M. Schimeczek, P. Piskorz, and D. Moncrieff, *J. Am. Chem. Soc.* **1999**, *121*, 3773-3778.
16. M. Sarobe, J.W. Zwikker, J.D. Snoeijer, U.E. Wiersumb, L.W. Jenneskens, *J. Chem. Soc., Chem. Commun.* **1994**, 89.
17. M. Konienczny and R. G. Harvey, *J. Org. Chem.* **1979**, *44*, 2158.
18. R. Sangaiah, A. Gold, *J. Org. Chem.* **1991**, *56*, 6717-6720.
19. J. Jacob, G. Grimmer, *Zentralbl. Bakteriol., Parasitenkd., Infectionskr. Hyg. Abt. Orig. Reihe B,* **1977**, *165*, 305.
20. L.W. Jenneskens, U.E. Wiersum, *Gas Phase Reactions in Organic Synthesis*, Gordon and Breache science publishers **1997**, 143.
21. M. Sarobe, *Ph.D. Thesis*, Utrecht University, Utrecht, The Netherlands, **1999**
22. H. Yagi, H. Frank, A. Seidel, and D.M. Jerina, *Chem. Res. Toxicol.* **2007**, *20*, 650-661.
23. R.E. Lehr, C.W. Taylor, S. Kumar, *JOC* **1978**, *43*, 3462.

24. J.E. Shields, D. Gavrilovic, J, Kopecky, W. Hartmann, H.G. Heine, *JOC* **1974**, *39*, 515-520.
25. M. Minabe, R. Nishimura, T. Kimura, M. Tsubota, *The Chemical Society of Japan* **1993**, *66*, 1248-1253.
26. A. Gold, J. Schultz, E. Eisenstadt, *Tetrahedron Letters* **1978**, *46*, 4491-4494.
27. D.M. Connor, S.D. Allen, D.M. Collard, C.L. Liotta, D.A. Schiraldi, *J. Org. Chem.* **1999**, *64*, 6888-6890.
28. V. Boekelheide, C.E. Larrabee, *J. Am. Chem. Soc.* **1950**, *37*, 1240-1245
29. V. Boekelheide, C.E. Larrabee, *J. Am. Chem. Soc.* **1950**, *37*, 1245-1249
30. Lock, Gergely, *Ber.* **1944**, *79*, 461.
31. L.F. Fieser, E.B. Hershberg, *J. Am. Chem. Soc.* **1938**, *60*, 1658-1665.
32. A.M. van den Braken-van Leersum, J. Cornelisse, J. Lugtenburg, *Tetrahedron Letters* **1985**, *26*, 4823-4824.
33. D.H. Reid, *Tetrahedron.* **1958**, *3*, 339-352.
34. K. Morita, T. Aida, K. Morinaga and J. Tsunetsugu, *J. Chem. Soc. Perkin Trans* **1994**, *1*, 1215-1220.
35. A.B. Chakiri, *Bachelorthesis*, Utrecht University, **2007**
36. A. Violi, *J. Phys. Chem.* **2005**, *109*, 7781-7787.