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The synthesis and conformationl studies of 9-monosubstituted-10-Chloro-9H-cyclohepta[def]phenanthrene

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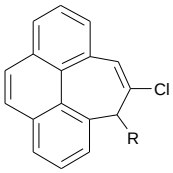
Abstract: Some derivatives of 9-monosubstituted-10-Chloro-9H-cyclohepta[def]phenanthrene have been synthesized in a nucleophlic addition to cyclopropyl ring in 9, 9-dichloro-9H-cyclopropa[e]pyrene. Quantum mechanic calculations indicate that conformation of cycloheptatriene ring in these derivatives has a nearly flatted boat conformation. In this form the C-9 constituent can be oriented in pseudo equatorial (e´) and pseudo axial (a´) directions. The fast interchange process of a´- e´ involves ring inversion of the cycloheptatriene moiety in low level of energy, so in room temperature the conformational diastereomers can not determined by ^{1}H-NMR.

Keywords: Conformational diastereomers**,** Cycloheptatriene**,** Phenanthrene

Introduction

Addition to alkenes represents one of the most common and most commonly investigated reactions of the singlet carbenes and has been widely used for the synthesis of cyclopropanes [1]. On the other hand addition of carbene to polyaromatic compounds is a wellknown reaction [2]. The cyclopropane ring could be opened due a nucleophilic reaction to prepare some derivaties of biphenyl with a chiral center. The diastereomers is due to a combination of the difference in configuration as well as the conformation. In Trephenyls, only the conformational difference is responsible for diastereomerism. Trephenyls with a chiral center, two stereogenic units are responsible for diastereomerism i.e. a chiral axis and a chiral center. It has already reported on the conformational diastereomers of 5-substituted-*5H*-6-chloro-dibenzo-[a,c]-cycloheptene [3]. In the present work we will discuss the conformation of some 9-monosubstituted-10-chloro derivatives of cyclohepta[def]phenanthrene **1**. (Scheme 1)



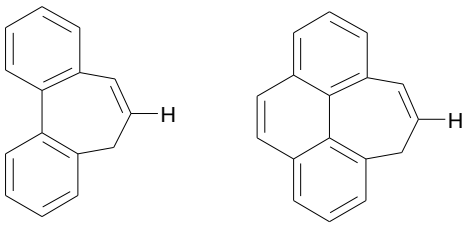
1a OMe
1b OEt
1c O-*i*-Pr
1d O-Bu
1e $O(CH_2)_2OH$
1f NEt_2
1g NHPh
1h $NHCH_2COOH$
1i $NHCH_2CH_2COOH$
1j Cl
1k 

Scheme 1

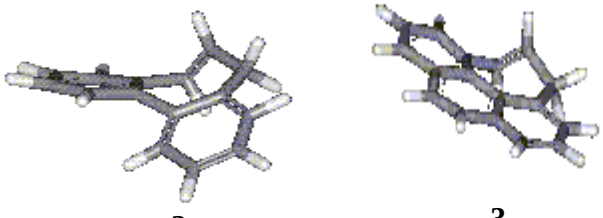
Results and discussion

Empirical force-field calculations on *5H*-dibenzo-[a,c]-cycloheptene **2** and *9H*-cyclohepta[def]phenantherene **3** by the semi-empirical AM1 method [4] predict a boat conformation with ca. 43º dihedral angel for **2** and ca. 17º for **3**.
Enantiomerization of **2** and **3** antipodes happen by ring inversion in cyclohetatriene moiety which accompanied by rotation around the pivot bound of the biphenyl unit from dihedral angel of 43º to -43º and the terphenyl unit from 17º to- -17º in **3** [5].

Fig 1 The structure of **2** and **3** as calculated by MMP2-87 method.



2 **3**



2 **3**

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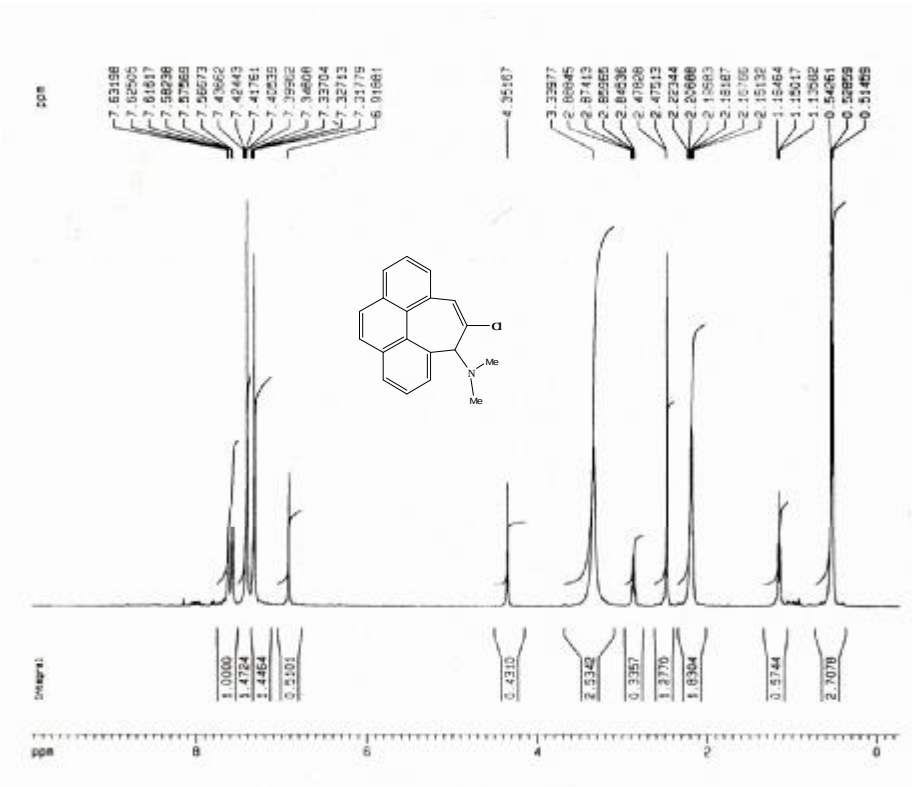
The barrier to these processes in **2** and **3** are determined by dynamic NMR measurement to be 13.3 Kcal/mole and 7.1 Kcal/mole respectively [5]. Cycloheptatriene ring **3** in comparsion with **2** has a flatted boat conformation [6] and positios can be oriented in pseudo equatorial (e'), pseudo axial (a') and constituent at the saturated carbon. Positions give the possibility of two diasteromeric pairs of enantiomers. Diastereomers could rapidly interconvert through the rotation about the chiral axis in the terphenyl unit [7]. ^{1}HNMR spectrum of **1a** - **1i** show just one set of resonance according to fast interconversion of e'and a' conformers. But in previous reports about dibenzocycloheptene derivatives we observed two sets of resonances with different intensity corressponding to the two e'and a' conformers [3]. Table 1 shows the chemical shifts of allylic and vinylic protons in constituents **1** and fig. 2 shows ^{1}H-NMR spectrum of **1a** in C_6D_6 at room temperature.

Table 1. The Chemical shifts of allylic and vinylic protons in subsistent **1**

Compound	Substitute at C_9	δ H_9(PPm) allylic	δ H_{11}(ppm) vinylic
1a	OMe	4.95	7.04
1b	OEt	4.96	7.01
1c	O^{i}Pr	5.09	7.16
1d	OBu	4.93	6.99
1e	$O(CH_2)_2OH$	4.74	6.80
1f	NEt_2	4.53	6.92
1g	NHPh	5.54	6.67
1h	$NHCH_2COOH$	4.06	7.02
1i	$NH(CH_2)_2COOH$	4.49	6.78
1j	Cl	5.02	6.91
1k	Morpholine	4.17	7.02

Fig. 2 The 500MHz ^{1}H-NMR spectrum of **1f** in C_6D_6 at room temperature.



The conformational space of the side chains was systematically searched by dihedral driving in AM1 calculates. The number of independent rotamers thus fund is given in table 2.

Table 2 The number of independet rotamers of **1a-1h** calculated by AM_1 method

Compound	Substitute at C_9	No. of rotamers
1a	OMe	2
1b	OEt	5
1c	O^{i}Pr	5
1d	OBu	40
1e	$O(CH_2)_2OH$	32
1f	NEt_2	1
1g	NHPh	2
1h	$NHCH_2COOH$	10
1i	$NH(CH_2)_2COOH$	31
1j	Cl	1
1k		4

The side chains in **1g**, **1h** and **1i** could each form an internal hydrogen bond. Fig. 3 showes the internal hydrogen bonding in **1h**.

Fig. 3 internal hydrogen bonding in **1h**

Experimental

All of the materials were received from Merk and used without further purification. NMR spectra were recorded on a Bruker 400 MHz spectrometer. Melting points are taken on a Buechi smp 20 apparatus and are uncorrected.

Computation

Initial estimates of the geometry of structures for semi-empirical calculations were obtained by the MMX molecular mechanics method. The semi-empirical AM1 Hamiltonian implemented in the MOPAC 6.0 program was used for full minimization. Conformational space of the side chains in substituted **1** was systematically searched by step size of 15 degrees.

General procedure for preparation of 1a–1l

9, 9-dichloro-9H-cyclopropa[e]pyrene was synthesized according to the published procedure[5] and purified by column chromatography over silica gel using hexane as eluent. The adduct was dissolved in suitable alcohols or amines and the solution was heated at 130º C in a sealed tube for at least two hours. The reaction mixture was poured in water and extracted with CH_2Cl_2 and then was purified by column chromatography over silica gel, using hexane as solvent.

10-chloro-9-methoxy-9H-cyclohepta[def]phenanthrene 1a. Oily viscous. ^{1}H-NMR (C_6D_6, 400 MHz): δ 3.90 (s, 3H), 4.90 (s, 1H), 7.10 (s, 1H), 7.30–7.70 (m, 8H); ^{13}C-NMR (C_6D_6, 100 MHz): δ 56.32, 89.21, 125.90, 127.28, 127.49, 127.93, 128.03, 128.06, 128.13, 128.54, 112.93, 129.37, 131.22, 133.60, 133.80. 133.84, 135.56.

10-chloro-9-ethoxy-9H-cyclohepta[def]phenanthrene 1b. Oily viscous. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.90 (t, *J*=8Hz, 3H), 3.30 (m, 2H), 5.10 (d, *J*=1Hz 1H), 7.20–8.00 (m, 8H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 30.47, 57.08, 87.73, 126.53, 127.49, 127.87, 127.98, 128.66, 128.90, 129.11, 129.96, 130.34, 134.26, and 135.55.

10-chloro-9-isopropoxy-9H-cyclohepta[def]phenanthrene 1c. Oily viscous. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.70 (t, *J*=6.1 Hz, 6H), 3.40

(m, 1H), 5.10 (d, *J*=1Hz 1H), 7.00 (s, 1H), 7.40–8.00 (m, 8H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 21.85, 22.62, 69.37, 126.12, 127.49, 127.75, 128.14, 128.50, 1, 134.33, and 143.00.

10-chloro-9-butoxy-9H-cyclohepta[def]phenanthrene 1d. Oily viscous. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.40 (t, *J*=2.4 Hz, 3H), 0.70 (m, 2H), 1.10 (m, 2H), 5.10 (d, *J*=1,2 Hz 1H), 7.00 (d, *J*=1,2 Hz 1H), 7.10–7.90 (m, 8H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 14.16, 19.49, 32.01, 68.71, 85.19, 126.22, 126.75, 127.72, 128.23, 128.63, 129.54, 132.00, 133.90, 134.02, 134.12,136.20.

2-(10-chloro-9H-cyclohepta[def]phenanthren-9-yloxy)ethanol 1e. Oily viscous. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.30 (br, 1H), 3.46 (m, 4H), 4.74 (br, 1H), 6.80 (s, 1H), 7.19-7.75 (m, 8H).

10-chloro-N,N-diethyl-9H-cyclohepta[def]phenanthren-9-amine 1f. Oily viscous ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.40 (t, *J*=7 Hz, 6H), 2.00 (q, *J*=7 Hz, 4H), 4.50 (d, *J*=2 Hz 1H), 7.00 (d, *J*=1,9 Hz 1H), 7.30–7.90 (m, 8H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 9.20, 41.14, 73.94, 124.32, 125.46, 125.84, 126.89, 127.80, 131.65, 132.56, 133.90, 133.12.

10-chloro-N-phenyl-9H-cyclohepta[def]phenanthren-9-amine 1g Oily viscous ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.54 (s, 1H), 6.67 (s, 1H), 7.16–7.76 (m, 13H).

2-(10-chloro-9H-cyclohepta[def]phenanthren-9-ylamino)acetic acid 1h Oily viscous. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.96 (br, 2H), 3.43 (br, 1H), 4.25 (s, 1H), 7.76 (s, 1H), 7.28–7.90 (m, 8H).

3-(10-chloro-9H-cyclohepta[def]phenanthren-9-ylamino)propanoic acid 1i Oily viscous. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.50 (m, 2H), 3.49 (m, 2H), 3.90 (br, 1H), 4.49 (s, 1H), 6.78(s, 1H), 7.21-7.73 (m, 8H).

9, 10-dichloro-9H-cyclohepta [def]phenanthrene 1j Oily viscous. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.02 (s, 1H), 6.91(s, 1H), 7.20-8.01 (m, 8H).

9-(10-chloro-9H-cyclohepta[def]phenanthren-9-yl)morpholine 1k Oily viscous ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.40 (m, 2H), 3.43 (m, 2H), 4.59 (s, 1H), 6.49 (s, 1H), 7.30–7.90 (m, 8H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 51.52, 67.08, 79.72, 126.09, 127.53, 127.84, 128.56, 129.07, 199.99, 131.57, 133.43, 134.24, 134.39, 135.62.

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