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Atropisomerism in a Molecular Gear, 8-Bromo-1,4-dimethyl-9-(2-methylbenzyl)triptycene

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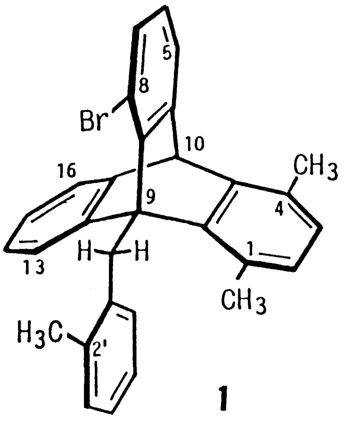
Two rotamers, ap and sc1, of the title compound were separately isolated as stable entities at room temperature. The rotamers gave an equilibrium mixture of the two at elevated temperatures, K([ap]/[sc1]) being 2.26 at 60 °C in toluene-d_8. The kinetic parameters for the sc1 -> ap conversion are as follows: $\Delta H^\ddagger$ = 26.3 ± 0.6 kcal mol^{-1} (1 cal = 4.184 J), $\Delta S^\ddagger$ = -2.7 ± 1.8 cal mol^{-1} K^{-1}, $\Delta G^\ddagger_{350K}$ = 27.2 kcal mol^{-1}.

High rotational barriers about the C_9-C_α bond in a variety of 9-alkyl-substituted triptycene derivatives have well been documented.$^{1)}$ However, isolation of stable rotational isomers, i.e., realization of atropisomerism,$^{2)}$ has so far been attained only in 9-t-alkyltriptycene derivatives$^{3,4)}$ and a triply peri-substituted 9-benzyltriptycene derivative.$^{5a,b)}$ 9-Benzyltriptycenes have a unique feature that the molecules behave as molecular gears composed of a two-toothed wheel and a three-toothed one.$^{5,6)}$ If suitably designed taking advantage of this feature, 9-benzyltriptycene derivatives with only two peri-substituents are expected to give rise to atropisomers. The first example of such cases, atropisomerism in 8-bromo-1,4-dimethyl-9-(2-methylbenzyl)triptycene (**1**), is reported here.

Molecules of 1 are assumed to adopt a conformation in which the 2-methylphenyl group (shown hereafter as Ar) is nearly coplanar with the C_9-CH_2 bond and bisects the notch made



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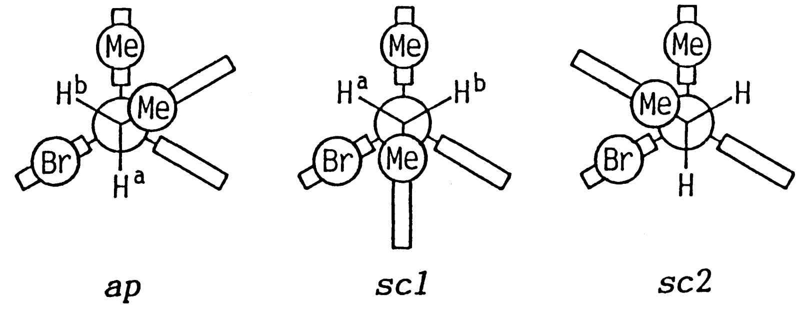

Scheme 1.

by the two benzene rings of the triptycene skeleton, as has been shown in a variety of 9-benzyltriptycene derivatives studied so far.[5-7] Three rotamers, ap, sc1, and sc2, are possible as for the C_9-CH_2 bond as shown by the Newman projections in Scheme 1,[8] where the o-methyl group is reasonably assumed to point outward by the steric reason.[9] The sc2 isomer is expected to be less stable than the other two isomers on steric grounds.[9]

Reaction of 2-methylbenzylmagnesium chloride with 1-bromoanthrone followed by dehydration with thionyl chloride and pyridine afforded 1-bromo-9-(2-methylbenzyl)-anthracene (**2**), mp 135-137 °C.[11] Reaction of **2** in boiling acetone with 3,6-dimethylbenzyne generated in situ by diazotization of 3,6-dimethylanthranilic acid with isopentyl nitrite gave **1** in 90% yield. ^1H NMR spectrum of the product revealed that it consists of two rotational isomers which differ in the conformation about the C_9-CH_2 bond in a ratio of >95:<5. The predominant isomer **1A** was purely isolated by recrystallization of the mixture from dichloromethane-hexane, mp 259-260 °C.[11] **1A** was thermally stable at room temperature not only in the crystalline state but also in solution. At higher temperatures **1A** in solution gradually isomerized to another isomer **1B** to give an equilibrium mixture of the two, the equilibrium constant K=[**1B**]/[**1A**] at 60 °C being 2.26 in toluene-d_8. **1B** was purely separated from the equilibrium mixture by gel permeation chromatography, mp 260-261 °C.

The ^1H NMR spectral data of these isomers are shown in Table 1. With the aid of the decoupling and nuclear Overhauser effect (NOE) experiments, all the signals including the aromatic ones could be unambiguously assigned as given in the Table. The 1-methyl protons of **1A** resonate at a considerably low field of δ 2.85, and upon irradiation of this signal both of the diastereotopic methylene proton signals show NOE enhancements. These features agree only with the sc1 isomer; the 1-methyl group is located in the plane of the 2-methylbenzyl group and thus suffers the deshielding ring-current effect of the aryl group and both of the methylene protons are proximate to the 1-methyl group. The 1-methyl protons of **1B** give the signal at a very high field of δ 2.06 and irradiation of this signal enhances only the lower-field one at δ 5.33 of the methylene proton signals. These facts are compatible with the ap isomer; the 1-methyl group is located above the plane of the 2-methylbenzyl group and thus is shielded by the ring-current effect and only one of the methylene protons is proximate to the 1-methyl group.

Table 1. ^1H chemical shift data (δ) for the two isomers of **1** (500 MHz, $CDCl_3$, 25 °C)

Isomer	$1-CH_3$	$4-CH_3$	$2'-CH_3$	CH_2 a	CH_2 b	10-H	Aromatic[a]	Assign.
1A	2.851 s	2.438 s	2.585 s	5.456 d,	4.198 d	5.639 s	6.42-7.45 m	sc1
				(J=17.6 Hz)				
1B	2.060 s	2.552 s	2.643 s	4.481 d,	5.329 d	5.614 s	6.40-7.46 m	ap
				(J=18.3 Hz)				

a) Details of the aromatic signals are not shown.

Table 2. Kinetic data for the *sc1*-**1** -> *ap*-**1** process

Temp °C	K [*ap*]/[*sc1*]	k 10^{-5} s^{-1}	ΔG‡ kcal mol^{-1}
54.0	2.27	0.501	27.15
66.0	2.26	2.16	27.18
78.0	2.25	8.68	27.20
90.0	2.24	30.2	27.25

$\Delta H^{\ddagger} = 26.3 \pm 0.6$ kcal mol^{-1}

$\Delta S^{\ddagger} = -2.7 \pm 1.8$ cal mol^{-1} K^{-1}

The assignment of *sc1* to **1A** is consistent with the hitherto known stereoselectivity in the formation of triptycene atropisomers by anthracene-benzyne reactions: an atropisomer in which the bulkiest part of the 9-substituent occupies the farthest position from the benzene ring of the triptycene derived from the benzyne is selectively formed.[3,5a,5b]

Kinetics of the isomerization of *sc1*-**1** to *ap*-**1** was studied in toluene-d_8 at four temperatures between 54 and 90 °C by monitoring the change in the intensities of the methyl proton signals and analyzing the data as a reversible first-order rate process. The results are shown in Table 2.

As for the internal motions taking place in **1**, two fundamental processes are to be considered; gear rotation (GR) and isolated rotation of the Ar group (IR).[5b,5c,6] We therefore assume that the rotation about C_9-CH_2 bond by 120° is always accompanied by the rotation about the Ar-CH_2 bond by 180° (GR), while the latter can take place either concomitantly with (GR) or independently of the former (IR). Furthermore, the presence of the *o*-methyl group in the aryl moiety complicates the situation. A single GR or IR step changes a conformer with the *o*-methyl group pointing outward to an unstable conformer with the *o*-methyl group points inward, and another GR or IR step is necessary to form a stable conformer with the *o*-methyl group pointing outward.

Several pathways are possible for the *sc1* -> *ap* conversion in **1**. They are classified into two groups: one contains pathways consisting solely of gear rotational steps, (a) *sc1* -> *sc2*' -> *ap* and (b) *sc1* -> *ap*' -> *sc2* -> *sc1*' -> *ap*, and the other group contains pathways involving an IR step, (c) *sc1* -> *ap*' -> *ap*, (d) *sc1* -> *sc1*' -> *ap*, (e) *sc1* -> *sc2*' -> *sc2* -> *sc1*' -> *ap*, and (f) *sc1* -> *ap*' -> *sc2* -> *sc2*' -> *ap*. As it is impossible to experimentally conclude which among these pathways is the lowest-energy process, computational considerations should be resorted to. A preliminary result of molecular mechanics calculations using the BIGSTRN-3 program suggests that the two-step gear rotational pathway, *sc1* -> *sc2*' -> *ap*, may be the lowest-energy process.[12)]

The origin of the atropisomerism in **1** resides in the fact that the interconversion between the isomers requires a multi-step process which involves a step with a high energy barrier such as passage of the aryl group over a *peri*-substituent and/or isolated rotation of the aryl group. Further study is in progress to explore the possibility of atropisomerism in singly *peri*-substituted 9-benzyltriptycene and related derivatives.

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8) Scheme I shows only one of the enantiomeric sets, in which the configuration of the asymmetric center at C_9 is S. According to the IUPAC nomenclature of stereoisomers, sc1 should be $sc^*(9S^*)$, a racemic mixture of +sc(9S) and −sc(9R), and sc2 should be $sc^*(9R^*)$: L. C. Closs and W. Klyne, Pure Appl. Chem., **45**, 11 (1976).

9) These features are reproduced by molecular mechanics calculations using the MM2 program.10) The relative steric energies for ap, sc1, and sc2 are 0.00, 0.61, and 4.54 kcal mol^{-1}, respectively. The conformers with the o-methyl group pointing inward, designated as ap', sc1', and sc2', are shown to be far less stable, the relative steric energies being 6.98, 7.82, and 11.40 kcal mol^{-1}, respectively.

10) N. L. Allinger and Y. H. Yuh, QCPE Program No. 395. Several parameters in the original force field were modified and some were added.6c)

11) All the new compounds gave satisfactory elemental analyses.

12) In order to adequately reproduce transition states of the internal motions, we chose the BIGSTRN-3 program13) instead of MM2. However, as BIGSTRN-3 does not accept a bromine-containing molecule, calculations have been performed on 8-chloro-1,4-dimethyl-9-(2-methylbenzyl)triptycene. Details of the results will be presented in a full paper.

13) R. B. Nachbar, Jr. and K. Mislow, QCPE Program No. 559.

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