NOTE

Molecular mechanics calculation of the rotational barriers of 2,2′,6-trialkylbiphenyls to explain their GC-elution behaviour

ADRI C.T. VAN DUIN[1], BART HOLLANDERS[1], RENÉ J.A. SMITS[1],
JAN M.A. BAAS[1], BASTIAAN VAN DE GRAAF[1], MARTIN P. KOOPMANS[2],
JAAP S. SINNINGHE DAMSTÉ[2] and JAN W. DE LEEUW[2]

[1]Laboratory of Organic Chemistry and Catalysis, Delft University of Technology, Julianalaan 136,
2628 BL, Delft, The Netherlands and [2]Netherlands Institute for Sea Research (NIOZ), Department
of Marine Biogeochemistry and Toxicology, P.O. Box 59, 1790 AB Den Burg. Texel,
The Netherlands

Abstract—Application of molecular mechanics enabled calculation of the rotational barrier between the two atropisomers of 2,3,5′,6-tetramethyl-2′-(2-butyl)biphenyl. The calculated energy barrier, 149.4 kJ/mol, is in good agreement with the experimental value of 155 kJ/mol reported by Koopmans *et al.* (1996) for a similar 2,3,5′,6-tetramethyl-2′-(2-alkyl)biphenyl compound, supporting their interpretation of the GC–MS data of these compounds. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Recently, Koopmans *et al.* (1996) reported the abundant presence in sedimentary rocks of a series of *ortho*-alkyl substituted biphenyls diagenetically derived from carotenoids, in particular isorenieratene and β-carotene. GC–MS analysis of these compounds showed several completely or partially separated pairs of isomers with identical mass spectra. These compounds possess only one chiral carbon atom and it was concluded that the separation by GC strongly suggested atropisomerism due to the significant barrier for rotation around the phenyl–phenyl bond. The GC-elution behaviour of these compounds, tentatively identified as the 2,3,5′,6-tetramethyl-2′-alkyl biphenyl compound **I** (Fig. 1) was studied by isothermal gas chromatography at various temperatures (Fig. 2). The decreasing resolution at increasing temperatures supports the presence of atropisomers. Applying the method of König *et al.* (1993), the time/temperature profiles in Fig. 2 were used by Koopmans *et al.* (1996) to estimate the rotational barrier $\Delta H^{\#}$ between the two atropisomers of **I** at 155 kJ/mol.

To further support the identification of this type of atropisomerism, an attempt was made to calculate the energy barrier of 2,3,5′,6-tetramethyl-2′-(2-butyl)biphenyl (**II**, Fig. 1) by molecular mechanics.

METHODS

Calculations were performed on Silicon Graphics Indigo R4400 and DEC 5000/200 computers. A conformational search for the energy minima of compound **II** was performed using the Delphi molecular mechanics program (van de Graaf and Baas, 1984) using the 1989 version of the MM3 force field that includes specific parameters for benzene type carbon atoms (atom type 50; Operating Instructions for MM3 Program, updated as of January 19, 1990, p. 9). To include the influence of the delocalization of the π-electrons in the calculations, the geometries of the energy minima thus obtained were used as input geometries for the MM3(92) molecular mechanics program (Allinger *et al.*, 1990). The resulting geometries from this MM3 calculation were checked for being energy minima by the absence of imaginary vibrations in the calculated vibrational spectra. To locate the transition states the rotation around the C-1–C-1′ bond of compound **II** was investigated by calculations with various stepped and constrained torsion angles.

RESULTS AND DISCUSSION

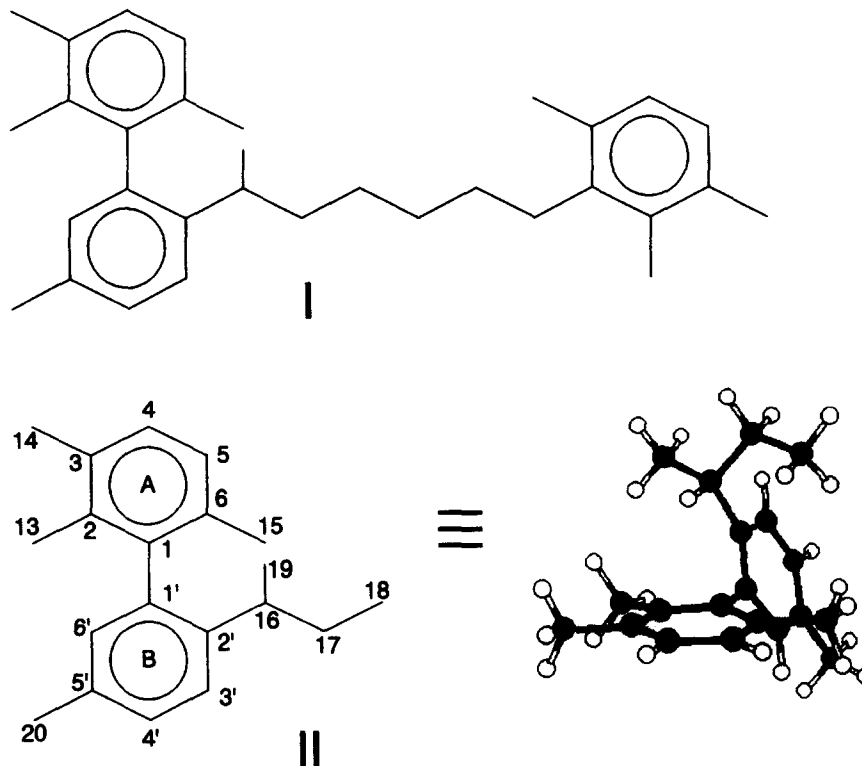To find the energy minima of compound **II** a conformational search was performed to identify the

Fig. 1. Structures of compound I and II, atom numbering and ground state geometry for compound II.
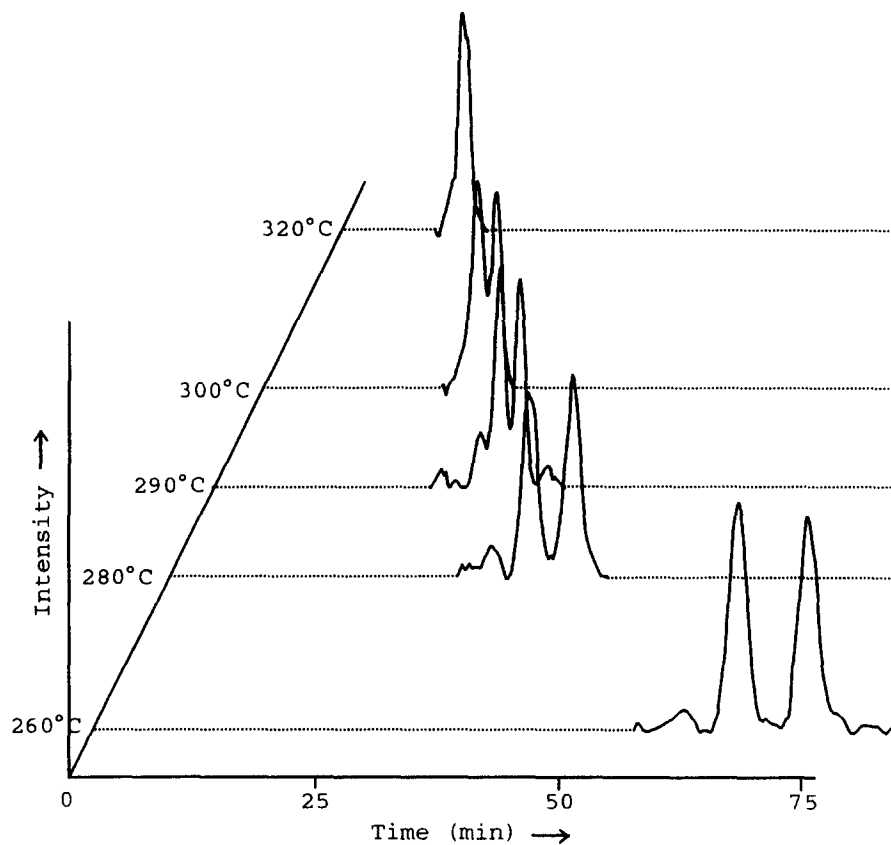

Fig. 2. GC-elution behaviour at different temperatures for the two atropisomers of compound I (after Koopmans *et al.*, 1996).

Table 1. Calculated equilibrium ratio between the two atropisomers at temperatures ranging from 260 to 320°C

Temperature	Equilibrium ratio[a]
260 C	48.8:51.2
280 C	48.6:51.4
300 C	48.7:51.3
320 C	48.7:51.3

[a] Ratio defined as atropisomer $(\omega_{2,1,1',2'} = -85°)$: atropisomer$(\omega_{2,1,1',2'} = 86°)$. Ratio is based on calculated $\Delta\Delta G$ between the atropisomers. Entropy and enthalpy of the atropisomers have both been corrected for temperature.

most favourable forms of the 2-butyl group at C-2' in each atropisomer (see Fig. 1). It was found that the energy minima for the two atropisomers (torsion angle $\omega_{2,1,1',2'} = 86°$ or $-85°$) were almost isoenergetic $(\Delta\Delta G_{25} = 0.04$ kJ/mol). This agrees well with the equal areas of the GC-peaks observed for compound I (Fig. 2). Table 1 shows that the equilibrium ratio between the two atropisomers at temperatures between 260 and 320°C based on the calculated $\Delta\Delta G$ is ca. 50:50.

The presence of the 2-butyl group at C-2' in compound II inhibits a straightforward calculation of the rotational barrier around the C-1–C-1' bond. Figure 3 clarifies the complexity due to this structural feature. The values shown in curve (a) of Fig. 3 are obtained by stepping torsion angle $\omega_{2,1,1',2'}$ upwards from 100° to 240°, whereas those in curve (b) are obtained by starting at $\omega_{2,1,1',2'} = 260°$ and stepping downwards towards $\omega_{2,1,1',2'} = 120°$. Curves (a) and (b) both show a discontinuity at $\omega_{2,1,1',2'} = 210°$ and $\omega_{2,1,1',2'} = 150°$, respectively. Similar discontinuities are observed when torsion angle $\omega_{2,1,1',2'}$ is stepped around 0°.

The points of highest energy in both curves in Fig. 3 show that the 2-butyl group at C-2' hooks behind the methyl group at C-2 (or C-6) during rotation around the central C-1–C-1' bond. This explains the differences in position between the points of highest energy in Fig. 3. As Fig. 4 shows, the discontinuities shown in Fig. 3 are caused by the sudden release of the 2-butyl group at C-2' from its hindrance by the methyl group at C-2 (or C-6) when $\omega_{2,1,1',2'}$ reaches a sufficiently low or high value.

The geometries of the transition states for the rotation around C-1–C-1' were identified by unconstrained geometry optimization using the points of highest energy (Fig. 3) as input. The same procedure was followed in the region between $\omega_{2,1,1',2'} = +60$ to $-60°$. In this way, two of the four transition states were identified, one at $\omega_{2,1,1',2'} \approx 160°$ and one at $\omega_{2,1,1',2'} \approx -30°$. Transition states possibly present at $\omega_{2,1,1',2'} \approx 200°$ and at $\omega_{2,1,1',2'} \approx 30°$ were not found, but no points were found with energies higher than those of the identified transition states. Figure 5 shows the geometries of the two transition states at $\omega_{2,1,1',2'} \approx 160°$ and $\omega_{2,1,1',2'} \approx -30°$. The calculated vibrational spectra of these conformations both show one vibration with an imaginary wavenumber. In Fig. 5 the atomic movements corresponding with these vibrations are indicated. These movements clearly correspond to rotation around the C-1–C-1' bond, which implies that these geometries indeed reflect the transition states searched for. Figure 5 also shows that this rotation is accompanied by large movements of the interacting methyl and 2-butyl groups (see also Fig. 4).
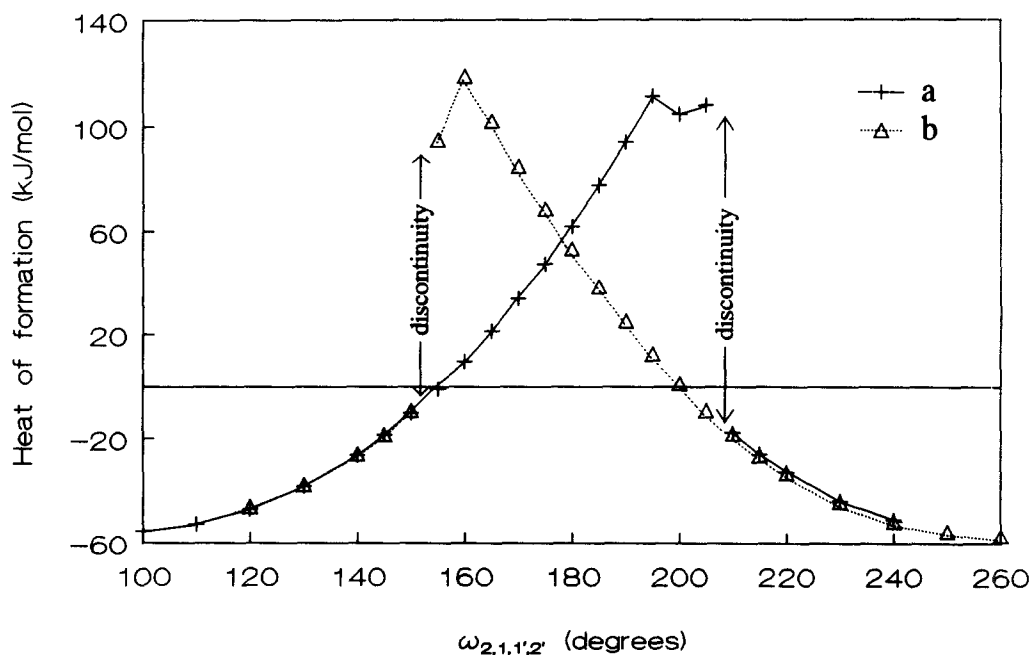

Fig. 3. Results from the calculations with (a) $\omega_{2,1,1',2'}$-constraint varying from 100° to 240° and (b) $\omega_{2,1,1',2'}$-constraint varying from 260° to 120°.
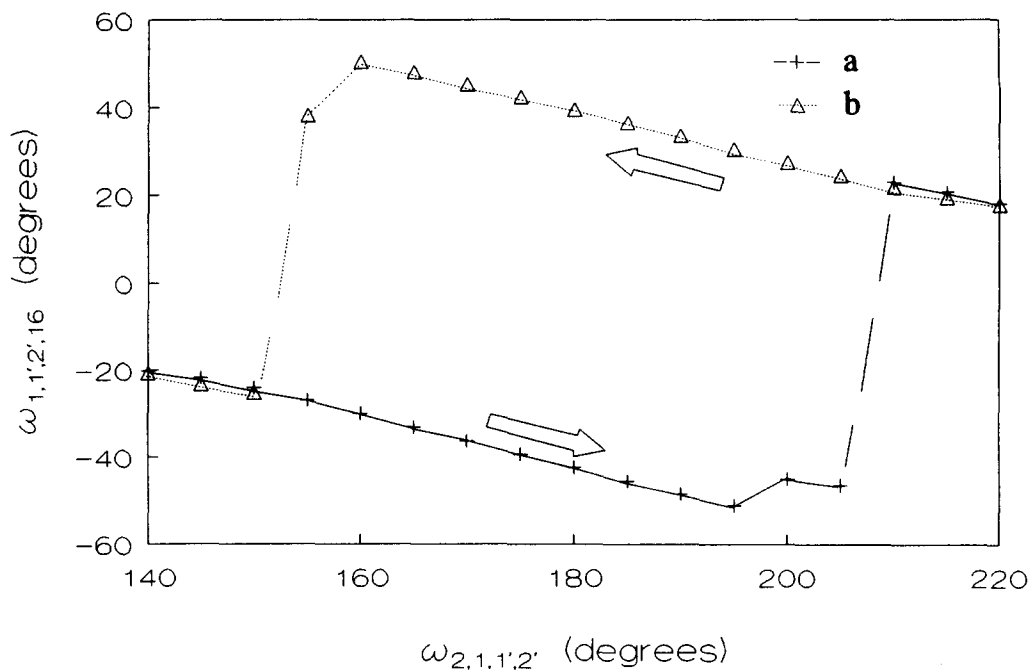
Fig. 4. Values for $\omega_{1,1',2',16}$ during constrained rotation around the C-1–C-1' bond by means of constraining $\omega_{2,1,1',2'}$ from (a) 140° to 220° and from (b) 220° to 140°.

The calculated heat of formation for the transition state depicted in Fig. 5a is + 92 kJ/mol. The geometry shown in Fig. 5b has a calculated heat of formation of + 97.5 kJ/mol. By subtracting the energy of the ground state geometry (− 57.4 kJ/mol) from these calculated heats of formation, rotational barriers around the $\omega_{2,1,1',2'} = 180°$ and $\omega_{2,1,1',2'} = 0°$-sides of respectively 149.4 and 154.9 kJ/mol are obtained. This result corresponds very well with the rotational barrier between the atropisomers of compound I of about 155 kJ/mol, as determined by isothermal gas chromatography at different temperatures (Fig. 2, Koopmans *et al.*, 1996).

CONCLUSIONS

The calculations resulted in the identification of two transition states for rotation around the central C-1–C-1' bond of compound II. Based on the energies of these transition states, rotational barriers of 149.4 ($\omega_{2,1,1',2'} = 180°$-side) and 154.9 kJ/mol ($\omega_{2,1,1',2'} = 0°$-side) have been calculated. The values of these barriers agree very well with that of the rotational barrier of compound I, 155 kJ/mol, as experimentally derived from GC-measurements. Hence, the presence of *o*-alkylsubstituted biphenyl atropisomers is supported fully by these calculations.
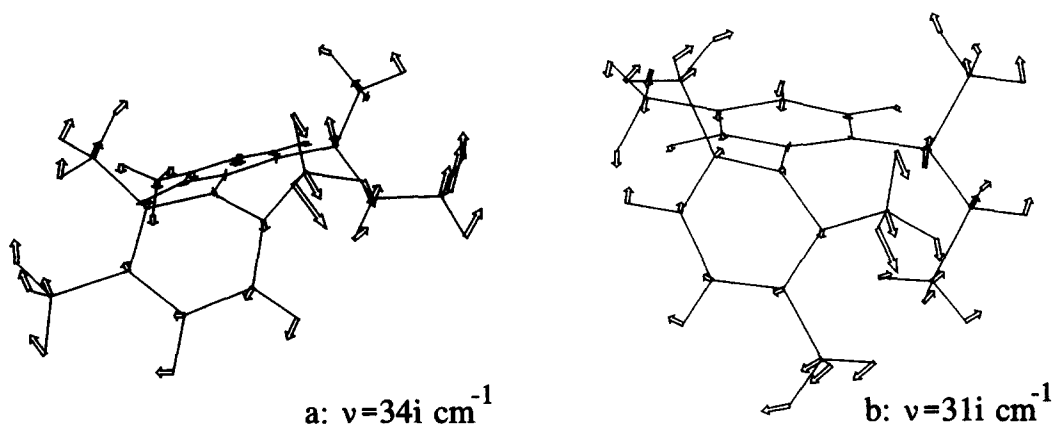
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Fig. 5. Intermediate geometries in the rotation around the C-1–C-1' bond. The atomic movements according to the negative eigenvector are indicated. (a) $\omega_{2,1,1',2'} \approx 160°$; (b) $\omega_{2,1,1',2'} \approx − 30°$. Atomic movements have been calculated using the Delphi molecular mechanics program (van de Graaf and Baas, 1984) and the MM3 1989 force field (Allinger *et al.*, 1990).

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