

SYNTHESIS AND ATROPISOMERISM OF HINDERED

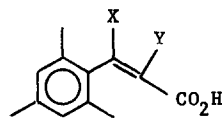
CIS- β -ALKYL STYRENES

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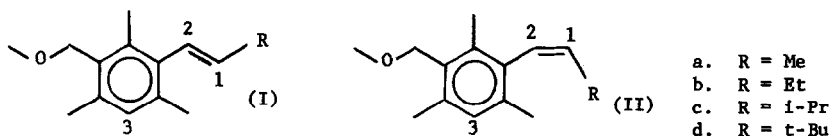
(Received in USA 30 August 1973; received in UK for publication 16 October 1973)

Atropisomerism in hindered aryl olefins was reported in the 1940's by Adams and coworkers in a series of papers.¹ By optical resolution of compounds of the general structure shown it was shown that atropisomerism results in enantiomerism. The similarities between this series of compounds and those of hindered biphenyls are evident. However, unlike the biphenyl series, practically no additional work has been done since Adams'. Therefore only compounds with a limited number of substituents have been studied and even so using the only method available then (optical resolution) for a study of properties associated with restricted rotation of the alkenyl group. More detailed systematic studies appear desirable particularly using modern instrumentation methods which allow direct examination of the hindered rotation process.



Our recent discovery of one way photochemical conversion of the trans alkene to the corresponding more hindered olefins made the preparation of hindered cis- β -alkyl styrenes relatively easy.² We now have prepared a homologous series of such hindered styrenes with appropriate substituents for nmr studies. The results are described below.

Compounds Ia-d were prepared by the identical sequence of reactions involving Friedel-Craft acylation of mesitylene followed by chloromethylation, nucleophilic substitution, sodium borohydride reduction, and acid catalyzed dehydration. All compounds showed expected spectroscopic properties, (selected nmr data shown in Table I). Sensitized irradiation of a benzene solution of the trans isomer under conditions for selective one-way isomerization² resulted in quantitative conversion to the cis isomer (IIa-d). The photo-products again showed expected spectroscopic properties. For example, their nmr spectra (Table I) typically show smaller (\sim 11 Hz)



coupling constants for the *cis* vicinal vinyl hydrogens and the chemical shift of the β -alkyl hydrogens substantially shifted upfield as a result of their being forced into a position above or below the aromatic ring as clearly suggested by space-filling models.

Compounds IIa-d, therefore, should exist as a mixture of the two rotamers which because of the presence of the ether groups are also enantiomers. Interconversion of these enantiomers by rotation of the alkenyl group clearly is an activated process. However, based on known

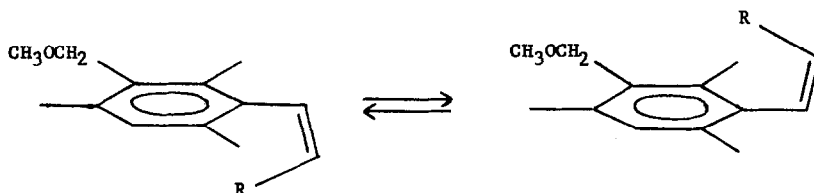


Table I. Selected PMR Data for Compounds I and II^a

Cpd.	R	H ₁	H ₂	H ₃
Ia	1.86(<u>CH</u> ₃ , d x d) J = 6.5 x 1.5	5.44(1H, q x d) J = 16.2, 6.5	6.22(1H, d) J = 16.2	6.69(1H, s)
IIa	1.42(<u>CH</u> ₃ , d x d) J = 6.6 x 1.5	5.78(1H, q x d) J = 11.0, 6.6	6.32(1H, d) J = 11.0	6.83(1H, s)
Ib	1.03(<u>CH</u> ₃ , t) 2.1(<u>CH</u> ₂ , m)	5.45(1H, t x d) J = 16.0 x 6.2	6.20(1H, d) J = 16.0	6.70(1H, s)
IIb	0.90(<u>CH</u> ₃ , t) 1.74(<u>CH</u> ₂ , m)	5.68(1H, t x d) J = 11.2, 6.6	6.24(1H, d) J = 11.2	6.80(1H, s)
Ic	1.10(6H, d) 2.47(<u>CH</u> , m)	5.42(1H, d x d) J = 15.8, 6.8	6.16(1H, d) J = 15.8	6.69(1H, s)
IIc	0.90(6H, d) 2.2(<u>CH</u> , m)	5.47(1H, d x d) J = 11.0, 9.8	6.08(1H, d) J = 11.0	6.74(1H, s)
Id	1.14(9H, s)	5.48(1H, d) J = 16.4	6.13(1H, d) J = 16.4	6.69(1H, s)
IIId	0.86(9H, s)	5.53(1H, d) J = 12.5	6.13(1H, d) J = 12.5	6.76(1H, s)

a. Taken on Varian HA-100 or A-60. Solvent: CCl₄ with TMS as internal standard. Chemical shift in δ ; J in Hz.

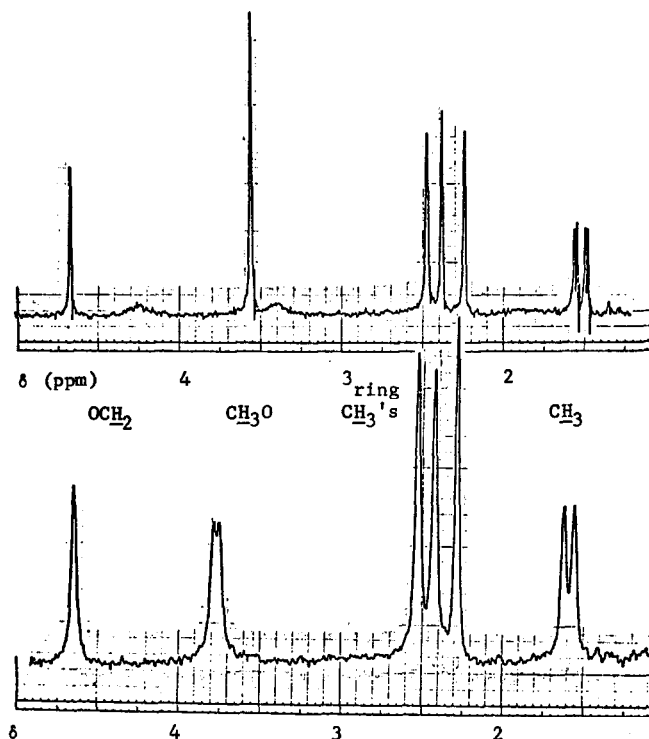


Figure I. Partial (high field) pmr spectrum of compound IIa in the presence of "Optishift" at room temperature (upper) and at -64° (lower)

rotational barriers of related β -ionyl compounds³ we did not expect these compounds, even in the case of IIId, to be resolvable. We, instead, decided to use pmr methods to study the expected restricted rotation, and in order to distinguish the two enantiomers, an optically active shift reagent was used.⁴

The pmr spectra taken at room temperature and at -64° of IIa in CDCl_3 in the presence of Eu-OPTISHIFT I⁵ in a molar ratio of 4:1 are shown in Figure I. The room temperature spectrum only shows the expected downfield shift of signals due to the presence of the paramagnetic shift reagent without showing separation of peaks to suggest the presence of enantiomers. Although most of the peaks remain unchanged at -64° (with some broadening only) the methoxy methyl singlet has clearly separated into two. We believe these two peaks are the methoxy hydrogens of the two enantiomers which inter-convert at a sufficiently slow rate at this temperature for nmr detection. Indeed, chemical shift differences of the two peaks are a function of temperature

and they coalesce at -44° ; the phenomenon is totally reversible. As expected, the coalescence temperature is a function of the size of the β -alkyl group (Table II). For IID the methoxy peak shows considerable

broadening even at the room

temperature. Unfortunately up

to now we have been unable to

use line shape analysis to

obtain accurate rate constants

for calculation of activation

parameters for the hindered

rotation process. The difficulty

stems from the small difference in chemical shift of the methoxy peaks further complicated by the presence of the expected temperature dependence of shift reagent-substrate equilibrium.

However, such problems could be overcome by employing hindered styrenes which are potentially diastereomeric and/or mesomeric. Such compounds are being prepared in this laboratory.⁶

Table II. Coalescence Temperature
of Compounds IIa-d.

Compound	T_c
IIa	-44°
IIb	-33°
IIc	-29°
IID	18°

References

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2. V. Ramamurthy, Y. Butt, C. Yang, P. Yang and R. S. H. Liu, J. Org. Chem., **38**, 1247 (1973).
3. V. Ramamurthy, T. T. Bopp and R. S. H. Liu, Tetrahedron Letters, 3915 (1972).
4. (a) G. M. Whitesides and D. W. Lewis, J. Amer. Chem. Soc., **92**, 6976 (1970); (b) H. L. Goering, J. N. Eikenberry and G. S. Koermer, ibid, **93**, 5913 (1971).
5. Eu-OPTISHIFT I is tris-[3-trifluoromethylhydroxymethylene)-d-camphorato]-europium III (ref. 4b).
6. The work was partially supported by a grant from NIH (ROI EY-AM 00918-01). Helpful discussions with Professors T. T. Bopp and R. E. Cramer are acknowledged.