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# Variable-Temperature NMR Studies of 6-(*o*-Tolyl)-8-methoxy-1,8-dimethylbicyclo[2.2.2]oct-5-en-2-ones

**A. Srikrishna* and S. Danieldoss**
Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

**Variable temperature NMR studies, establishing the presence of atropisomers, of β-(*o*-tolyl)-carvone (2) and the bicyclo[2.2.2]octene derivatives 4 and 5 mentioned in the title are described.** © **1997 John Wiley & Sons, Ltd.**

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*Keywords:* $^{1}$H NMR; $^{13}$C NMR; variable-temperature studies; orthogonal styrenes; atropisomers; 2-arylbicyclo[2.2.2]oct-2-enes

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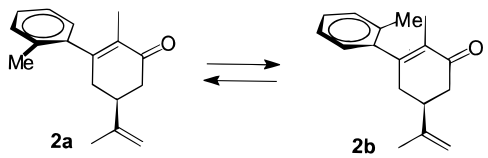
## INTRODUCTION

During our studies directed towards the chiral isotwistanes en route to pupukeanones[1] starting from (*R*)-carvone,[2] we have discovered novel styrenic systems[3] exhibiting atropisomerism which were established employing variable-temperature $^{1}$H and $^{13}$C NMR spectroscopy. It is of interest to note that the title compounds show coalescence behaviour at room temperature. Even though atropisomerism is very common in biphenyl systems, it is relatively less documented in olefinic or styrenic systems.

## RESULTS AND DISCUSSION

(*R*)-Carvone was converted into β-(2-methylphenyl) carvone employing a 1,3-arylative enone transposition[4] protocol (Scheme 1). Thus, reaction of (*R*)-carvone (**1**) with 2-methylphenyllithium, generated from 2-bromotoluene and *n*-butyllithum at −78 °C, and oxidation of the resulting *tert*.-allyl alcohol with pyridinium chlorochromate (PCC)–silica gel[5] gave β-(2-methylphenyl)carvone (**2**), m.p. 104 °C, whose structure was established from its spectral data. The existence of two diastereomers, **2a** and **2b**, due to atropisomerism was inferred from the presence of two sets of signals due to some protons and carbons in the respective NMR spectra. In the $^{1}$H NMR spectrum, resonances appeared at δ 7.3–7.2 due to three of the aromatic protons, but the fourth (H-6′) one appeared at an upfield position at 7.19 and 6.96 ppm, probably due to the shielding effect of the enone. The signal due to aromatic methyl group also shifted upfield and resonated at δ 2.19 and 2.17 ppm. Similarly, the $^{13}$C NMR spectrum exhibited signals at δ 156.4 and 155.9 due to C-3 quaternary olefinic carbon, and at 38.0 and 37.7 ppm due to C-4 methylene carbon. The presence of two sets of peaks for some protons and carbons in the $^{1}$H and $^{13}$C NMR spectra, respectively, can be readily explained by the visualization of the existence of two diastereomers, **2a** and **2b** (atropisomers), due to the restricted rotation of the C—C single bond between the enone and aryl moieties.




**2a** **2b**

To prove the existence of atropisomerism in **2**, high-temperature NMR studies in DMSO-$d_6$ were carried out. In the $^{1}$H NMR spectrum of the enone **2** in DMSO-$d_6$ at room temperature, resonances appeared at δ 7.13 and 7.02 due to the H-6′ aromatic proton and at 2.16 and 2.14 ppm due to the aromatic methyl group. With a gradual temperature increase to 353 K and finally to 373 K, as expected, the two singlets due to the aromatic methyl group first merged into a broad singlet and finally a sharp singlet. Similarly, in the $^{13}$C NMR spectrum of the enone **2** in DMSO-$d_6$ at room temperature, resonances appeared at δ 156.4 and 155.6 due to C-3 and at 37.1 and 37.6 due to C-4 carbons, whereas at 373 K both carbons exhibited single peaks at δ 155.3 and 37.1 ppm, respectively.

As depicted in Scheme 2, regiospecific bromomethoxylation[6] of the electron-rich double bond in the dienone **2** with *N*-bromosuccinimide (NBS) in methylene chloride–methanol medium generated a diastereomeric mixture of bromoenones **3**, which also exhibited atropisomerism, analogous to **2**. The bromoenones **3** were transformed into the bicyclic ketones **4** and **5** employing an intramolecular alkylation reaction via the dienolate.[7] Thus, treatment of a mixture of the

* *Correspondence to*: A. Srikrishna.

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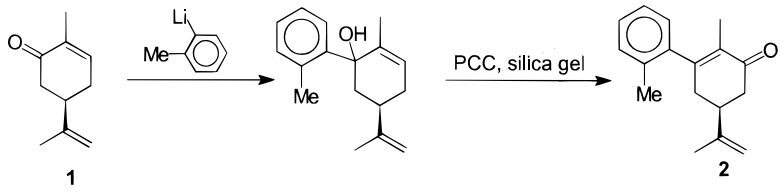


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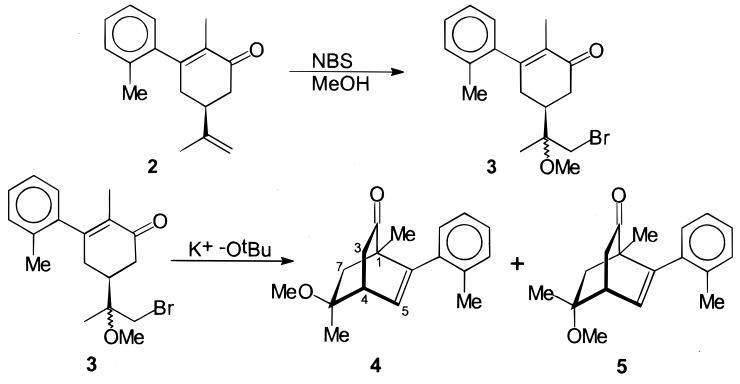
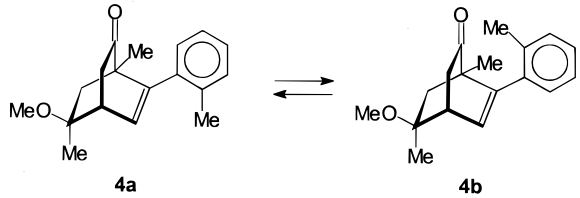
**Scheme 1**




**Scheme 2**

bromoenones **3** with potassium *tert*-butoxide in 1:1 *tert*-butanol and dry THF gave a 1:1 mixture of the epimeric bicyclic ketones **4** and **5** in 76% yield. Careful separation of the mixture using a silica gel column resolved the individual epimers **4** and **5**, whose structures were delineated from their interrelated spectral data. The orthogonal nature of the olefinic and aromatic moieties was supported by the upfield shift of the C-1 methyl group to $\delta$ 0.85 and 0.87 ppm, respectively, in the $^1$H NMR spectrum of **4** and **5** due to their presence in the shielding region of the aromatic ring. The major difference between the two epimers **4** and **5** in their $^1$H NMR spectra was the chemical shift difference between the two methylene protons adjacent to the carbonyl group which was exploited for establishing the relative stereochemistry of the methoxy group. In **4**, in which the methoxy group is *syn* to the $CH_2C{=}O$ bridge, the two protons differ considerably; a downfield shift was observed for the proton *syn* to the methoxy group resonating at $\delta$ 2.69 and the second proton resonated at 2.09 ppm. On the other hand, in the epimer **5**, where the methoxy group is *anti* to methylene, the methylene attached to carbonyl group resonated as a singlet at $\delta$ 2.29 ppm.

The most interesting and intriguing aspect of the $^1$H NMR spectra of the two ketones **4** and **5** was the absence of a sharp singlet due to the aromatic methyl group; instead, a very broad hump appeared for three protons. Furthermore, one doublet of the AB spin system due to C-7 methylene protons was missing. This can be rationalized by visualizing the presence of two atropisomers, e.g. **4a** and **4b**, due to the orthogonal




**4a** **4b**

arrangement of the aryl and olefinic moieties and was established by carrying out variable-temperature $^1$H NMR studies.

The $^1$H NMR spectrum of **4** at 273 K in $CDCl_3$ showed clearly two sets of peaks due to two atropisomers. In contrast to the spectrum recorded at room temperature, the $^1$H NMR spectrum at 273 K exhibited two doublets due to the aromatic C-6′ proton, two broad singlets due to the aromatic methyl group, while the singlets due to C-1 and C-8 methyl groups were broadened. On further lowering the temperature, the $^1$H NMR spectrum at 253 K clearly exhibited the resonances due to a 2:1 mixture of the atropisomers **4a** and **4b**. All the methyl groups exhibited sharp singlets, the aromatic methyl group at $\delta$ 2.0 and 2.24, the C-8 methyl group at 1.41 and 1.45 and the C-1 methyl group at 0.83 and 0.84 ppm for the major and minor rotational isomers, respectively, of **4**. Similarly, the C-7 methylene protons exhibited two sets of AB pattern at 1.88 and 1.68 and at 1.89 and 1.81, and the aromatic C-6′ proton doublets at 6.92 and 6.78 ppm for the major and minor atropisomers, respectively. For the high-temperature NMR studies, the solvent DMSO-$d_6$ was chosen as before. The room temperature $^1$H NMR spectrum of **4** in DMSO-$d_6$ showed a multiplet at $\delta$ 2.2–1.9 ppm for the H-3b and aromatic methyl protons. As expected, the $^1$H NMR spectrum (DMSO-$d_6$) at 393 K exhibited only one set of peaks due to the fast rotation of the aryl moiety. It exhibited a sharp singlet at $\delta$ 2.1 ppm due to the aromatic methyl group.

Similarly, the $^1$H NMR spectrum of the epimer **5** at 253 K exhibited two sets of peaks due to a 1.7:1 mixture of rotational isomers. In contrast to the room temperature spectrum, the $^1$H NMR spectrum at 253 K exhibited two sets of sharp singlets for all the methyl groups including the methoxy group. The resonances due to the methoxy group appeared at $\delta$ 3.24 and 3.23, due to the aromatic methyl group at $\delta$ 2.3 and 2.05, due to the C-8 methyl group at $\delta$ 1.44 and 1.42 and due to the C-1 methyl group at $\delta$ 0.86 and 0.85 ppm for the

major and minor isomers, respectively. As in the other isomer, the high-temperature $^1$H NMR spectrum of **5** in DMSO-$d_6$ at 373 K showed only one set of resonances.

### Rate constant and free energy of activation for 4 and 5

The rate constant for the dynamic process detected for the ketone **4** at coalescence temperature (298 K) was calculated using the equation[8] $k = 2.22\ \Delta\nu$ with $\Delta\nu$ ($^1$H) for the aromatic methyl group at 253 K of 64 Hz. Hence $k_c = 142\ s^{-1}$.

The free energy of activation for **4** at coalescence temperature (298 K) then follows from the Eyring equation:[8]

$$\Delta G^{\ddagger} = 1.914 \times 10^{-2} T[10.319 + \log(T/k_c)]\ \text{kJ mol}^{-1}$$
$$= 1.914 \times 10^{-2} \times 298[10.319 + \log(298/142)]$$
$$= 60.7\ \text{kJ mol}^{-1}$$

The rate constant for **5** at coalescence temperature (298 K) was 163 $s^{-1}$ with $\Delta\nu$ ($^1$H) for the aromatic methyl group at 253 K of 74 Hz. This yields $\Delta G^{\ddagger} = 60.3$ kJ mol$^{-1}$.

## EXPERIMENTAL

Compounds **2**–**5** were prepared as described earlier.[3] $^1$H NMR spectra were recorded on a Bruker WH-270 spectrometer and the $^{13}$C NMR spectra on a JEOL FX-90Q spectrometer using a 5 mm probe and standard programs. The chemical shifts ($\delta$ ppm) and coupling constants (Hz) were given in standard fashion using either tetramethylsilane (for $^1$H NMR) or the central line (77.2 ppm) of $CDCl_3$ (for $^{13}$C) as reference. Probe temperatures were measured using a built-in thermocouple. Solutions of 5–10 mg ml$^{-1}$ were used for recording the $^1$H NMR spectra (both normal and variable temperature) and solutions of 60–80 mg ml$^{-1}$ for recording the $^{13}$C NMR spectra.

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## REFERENCES

1. B. J. Burreson, P. J. Scheuer, J. Finer and J. Clardy, *J. Am. Chem. Soc.* **97**, 4763 (1975); M. R. Hagadone, B. J. Burreson, P. J. Scheuer, F. S. Finer and J. Clardy, *Helv. Chim. Acta* **62**, 2484 (1979).
2. A. Srikrishna, G. V. R. Sharma and P. Hemamalini, *J. Org. Chem.* **58**, 2509 (1993).
3. A. Srikrishna, G. V. R. Sharma, S. Danieldoss and P. Hemamalini, *J. Chem. Soc., Perkin Trans. 1* 1305 (1996).
4. G. Büchi and B. Egger, *J. Org. Chem.* **36**, 2021 (1971).
5. L. L. Adams and F. A. Luzzio, *J. Org. Chem.* **54**, 5387 (1989).
6. J. Rodriguez and J.-P. Dulcere, *Synthesis* 1177 (1993).
7. A. Srikrishna and P. Hemamalini, *Indian J. Chem., Sect. B* **29**, 201 (1990).
8. J. Sandström, *Dynamic NMR Spectroscopy*. Academic Press, London (1982).