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THE RATES OF DEPROTONATION OF SOME CYCLOPROPYLTOLUENE DERIVATIVES IN SEARCH FOR THE EFFECT OF THE CONFORMATION OF CYCLOPROPYL GROUPS ON THE STABILIZATION OF THE CARBANIONIC CENTRES

M. JOHN PERKINS*†
Department of Chemistry, Chelsea College, Manresa Road, London SW3 6LX, England

and

N. BEKIR PEYNIRCIOGLU*
Department of Chemistry, Middle East Technical University, Ankara, Turkey

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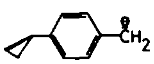
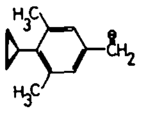
Abstract—*p*-Cyclopropyltoluene and 2-cyclopropylmesitylene have been prepared and the rates of base-catalyzed H–D exchange of the benzylic hydrogen atoms, *para* positioned with respect to the cyclopropyl group, have been compared with those of suitable model compounds. The results are in accord with earlier findings, where a cyclopropyl group exerts more stabilization to the carbanionic centres than do other alkyl groups. The present results suggest that this stabilization is independent of the conformation of the cyclopropyl group (perpendicular or bisected) with respect to the carbanionic centre.

It is well known that a cyclopropyl group, which is attached to a positively charged carbon atom, stabilizes the carbonium ion centre, when the three-membered ring is in the bisected conformation.[1–4] In contrast, to our knowledge there is no experimental study which investigates the effect of the conformation of the cyclopropyl group on carbanionic centres, indeed, there is little quantitative experimental information on the effect of this group on the stability of an adjacent carbanionic centre, although it has been shown that the kinetic effect of a 3-membered ring on a base-catalyzed hydrogen–deuterium exchange at a carbon atom to which it is attached is rate-enhancing.[5]

Carbanions of the types **1** and **2** have now been generated as intermediates in base-catalyzed hydrogen isotope exchange studies, and the rates of exchange have been compared with those of model compounds. The effect of the three-membered ring is through the aromatic ring in these compounds; in **1** the cyclopropyl ring can assume any conformation, whereas in **2** it is locked in the perpendicular conformation with respect to the developing carbanionic centre.[2]





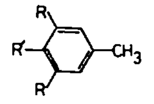
The hydrocarbons **3–9** were prepared and used for this investigation (see Table 1).

RESULTS AND DISCUSSION

The base-catalyzed deuterium exchange of the benzylic hydrogens, *para* positioned with respect to R′ (Table 1) was followed by NMR spectroscopy. It has been suggested[6] that kinetic acidities can give only a rough measure of the carbanion stabilities; however,

Table 1. Pseudo first order rate constants (k) for base-catalyzed methyl-proton exchange in the hydrocarbons[a]

Hydrocarbons



Compound	R	R′	k (10^4) sec^{-1}	Rel. rate
3	H	isopropyl	0.22 ± 0.025	1.00
4	H	cyclopropyl	0.50 ± 0.03	2.30
5	methyl	cyclopropyl	0.056 ± 0.004	0.26
6	H	methyl	0.38 ± 0.04	1.74
7	methyl	H	0.64 ± 0.03	2.91
8	H	H	6.9 ± 0.9	31.8
9	H	vinyl	very fast	very fast

[a] See Experimental for reaction conditions.

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† Present address: Department of Chemistry, Royal Holloway and Bedford Colleges, Egham Hill, Egham, Surrey TW20 0EX, U.K.

when the kinetic acidities of similar and closely related compounds are compared, this criticism is not serious.

Potassium *t*-butoxide (4.46 M) in DMSO-d_6 (4.00 ml) was used to effect the exchange and a standardized general procedure[7] was followed. Exchange was assumed to be effectively irreversible during the initial stages and to follow pseudo first order kinetics. The NMR integral amplitudes (I) for the exchanging protons were measured for each compound, and log I values were plotted against time. The slopes of the straight lines obtained were proportional to the rates of exchange of each compound. Rate data for individual hydrocarbons were reproducible within about ±10% (Table 1). The figures in Table 1 result from at least three determinations on each hydrocarbon.

There was no evidence from the spectra that the vinylic, aromatic, or cyclopropyl hydrogens of compounds **3**–**9** are exchanged under the conditions employed, and the integral amplitudes for the aromatic protons were used as internal standards in the measurements to find the corrected integral amplitude for the benzylic protons. Exchange was followed to between 5% and 20% completion. Carrying out the reactions to low conversion minimized the influence of kinetic isotope effects, but resulted in relatively large error limits, since only a small change in integral signal was being monitored.

The kinetic data are converted into relative rates (CH_3 in *p*-cymene (**3**) = 1) in the last column of Table 1. In view of the complex nature of concentrated solutions of alkoxide in DMSO-d_6, we emphasize the relative, rather than the absolute rates. Care was taken to carry out all experiments under strictly comparable conditions, but a satisfactory check on the relative rate data by reacting two hydrocarbons together in a single experiment was precluded by the very small chemical shift differences between the methyl protons of the different substrates.

Compounds **3**–**7** exchange more slowly than toluene (**8**), whereas *p*-methylstyrene (**9**) exchanges too rapidly to be compared with other members of the series. *p*-Cyclopropyltoluene (**4**) exchanges faster than both *p*-cymene (**3**) and *p*-xylene (**6**). These results indicate that the cyclopropyl group assists formation of carbanion **1** more than do other alkyl groups, but that the stabilization is very much less than that afforded by the vinyl group, in accord with previous observations.[5]

Compound **4** is expected to have the three-membered ring in the bisected conformation due to the "conjugation" of the cyclopropyl group with the aromatic ring. This has been shown to be the case in the overwhelming majority of studies on arylcyclopropanes; for example Closs and Klinger[8] reached this conclusion on the basis of NMR evidence, and although one later study[9] led to the conclusion that little conjugation exists between the π orbitals of the aromatic ring and the cyclopropyl group, which may be in a non-bisected conformation, more recent work does support the bisected conformation and the conjugative interaction.[10] Since the kinetic effect of the cyclopropyl group is so small, the effect which controls the conformation of the developing *p*-cyclopropylbenzyl anion (**1**) is almost certainly the same as that in *p*-cyclopropyltoluene itself, i.e. an interaction of cyclopropane orbitals with the π orbitals of the aromatic ring.

When the exchange rate of toluene (**8**) is compared with that of mesitylene (**7**), it can be assumed that the two *meta* methyl groups slow the rate of exchange by a factor of 10.9. If there were no interaction between the methyl groups and the cyclopropyl substituent in 2-cyclopropylmesitylene (**5**), the relative rate of exchange of the remaining methyl at C-5 would be expected to be 0.21. The observed value is 0.26, only slightly higher than the expected value, and indeed within its experimental error. It may therefore be concluded that under our experimental conditions the cyclopropyl ring, which in **5** is locked in the perpendicular conformation, can stabilize the developing carbanionic centre created at the benzylic position *para* to itself to an extent similar to that due to the three-membered ring in compound **4**, where the cyclopropyl group is in the bisected conformation.[10]

The cyclopropyl group might be expected to stabilize an adjacent carbanionic centre due both to its low-lying vacant molecular orbitals[5,11] (conjugative stabilization) and because of the high s character of the bond joining the 3-membered ring to the anionic centre (inductive stabilization). Previous studies[3,4] mentioning cyclopropylcarbinyl anion predict some preference for the perpendicular geometry. Although the preference for this conformation seems to be slight,[4] similar conclusions have been drawn regarding the preferred geometry of cyclopropylamine.[12]

According to our results it seems unrealistic to ascribe the small effects to conjugative stabilization. Perhaps the greater stabilizing effect of the 3-membered ring compared to that of the other alkyl groups is due only to an inductive effect resulting from the high s character of bonds attached to the cyclopropane ring.

EXPERIMENTAL

NMR spectra were recorded on a Perkin–Elmer R-32 (90 MHz) instrument, and IR spectra on a Perkin–Elmer 257 grating spectrophotometer. GLC analyses were performed with a Pye series 105 chromatograph. Solvents were dried and purified by standard techniques prior to use. In the kinetic measurements potassium *t*-butoxide and DMSO-d_6 were obtained from Aldrich Chemical Co. and Rose Chemicals Ltd., respectively, and were used as supplied.

Preparation of materials

Compounds **3** and **6**–**9** were commercially available, and were distilled and checked for purity (GLC). *p*-Cyclopropyltoluene (**4**) was prepared by a slightly modified Simmons–Smith[13] procedure, by means of the reaction of CH_2I_2 and Zn–Cu couple with *p*-methylstyrene (**9**). The addition of CH_2I_2 and **9** to a stirred ethereal suspension of Zn–Cu couple was carried out slowly and simultaneously to avoid polymerization of **9**. The product (**4**) had b.p. 46–48°/2.5 mm (lit.[14] 67–68°/8 mm). 2-Vinylmesitylene was similarly cyclopropanated to obtain 2-cyclopropylmesitylene (**5**), b.p. 80–81°/0.8 mm (lit.[15] 78–80°/0.6 mm).

Kinetic measurements

Potassium *t*-butoxide (2.00 g) was dissolved in DMSO-d_6 (4.00 ml) under a nitrogen atmosphere in a serum-capped vial to form a 4.46 M solution. The vial was then placed in a constant temp bath (38.0±0.50°) together with another serum-capped vial containing the hydrocarbon. After thermal equilibration, 200 μl of the hydrocarbon was injected into the base solution and the vial was shaken for a few seconds. Aliquots (30–40 μl) were taken at appropriate time intervals and quenched by injection into 5 ml of cold water. Each sample was then extracted with pentane and dried ($MgSO_4$). The extracts were then stripped from the solvent and redissolved in CCl_4 for NMR spectroscopy.

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