Tetrahedron Letters No.19, pp. 2317-2320, 1968. Pergamon Press. Printed in Great Britain.

ACID-CATALYZED DEUTERIUM EXCHANGE IN CYCLOPROPYL ACETONE

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(Received in UK 1 February 1968; accepted for publication 8 February 1968)

The literature abounds with references to the ability of the cyclopropyl group to release charge through its pseudo p-π orbitals to centers of positive charge character (1). Recently, from a study of the shift parameters of the F^{19} nmr spectra of meta- and para- fluorophenylcyclopropane, Pews (2) has demonstrated the absence of ground state conjugative interaction between the phenyl and cyclopropyl moieties relative to fluoro- substituted toluene. In light of the many examples in which there is definitive interaction between a cyclopropyl group and centers of positive charge character, it was suggested that the degree of interaction is greatly dependant on the charge situation of the center with which interaction occurs.

In this paper we wish to report evidence supporting Pews' suggestion. Acid-catalyzed deuterium exchange in ketones proceeds via the same mechanism as bromination, which has been postulated to have a transition state close to enol in geometry (3). Thus, relative rates of deuterium exchange at the methyl and methylene groups in cyclopropyl acetone (4) should be a direct indication of the stabilizing effect of the cyclopropyl group in the 3-enol when contrasted with a similar ratio for the isopropyl analog, 4-methyl-2-pentanone (FIG I and TABLE I).

FIG. I

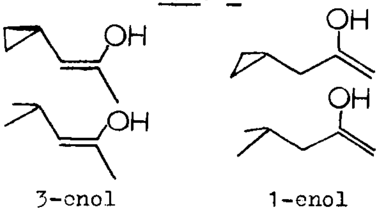


TABLE I.

Ketone	k_{CH_2}(sec^{-1}) x 10^6	k_{CH_3}(sec^{-1}) x 10^6	$K_D$$^{a)}$
Cyclopropyl acetone	16.0	7.5	2.1
4-Methyl-2-pentanone	4.9$^{b,c)}$	6.7	0.8
1-(1-Methylcyclopropyl)-2-propanone	6.3	7.1	0.9
4,4-Dimethyl-2-pentanone	2.4$^{c)}$	8.1	0.3

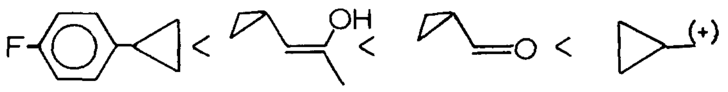
a) Rate constants have been calculated from the nmr spectra of the deuterating ketones (5). For a discussion of the treatment of primary data and the derivation of the reported rate constants, see refs 5b,c. $K_D = k_{CH_2}/k_{CH_3}$

b) Because of overlaping signals, these rates have been estimated by combining the total rate of deuteration with a value for K_D determined by bromination.

c) Ref 5c.

The results indicate a relative stabilizing factor of ca 3 for both cyclopropyl acetones studied, suggesting a common origin. Because of the similarity in the steric requirements of the cyclopropyl and isopropyl and the 1-methylcyclopropyl and t-butyl groups, the enhanced stability of the 3-enol in the cyclopropyl ketones is very likely due to conjugation between the cyclopropyl group and the unsaturated system of the 3-enol. Neglecting entropy differences, which should be small, the factor 3 gives a calculated energy of stabilization of ca 0.7 kcal/mole. This is intermediate to fluorophenylcyclopropane (zero) and the interaction of a cyclopropyl group with a carbonyl carbon (as manifested in the observed barrier to rotation (6) in cyclopropyl carboxaldehyde of >2.5 kcal/mole). Stabilization energies roughly calculated from rate ratios in solvolyses studies (1b) are even greater (ca 10 kcal/mole). Thus there appears to be a rough correlation between calculated stabilization energies and an intuitive ordering of the electronic demands of the system interacting with the cyclopropyl group. (FIG. II)

FIG. II



A correlation between experimental interaction energies and Hückel calculated charge distributions (7) might prove interesting, and such work is in progress.

Acknowledgements:

We would like to thank Professor Arne Fredga for all facilities placed at our disposal. Further thanks are due Dr. M. Vidal, Université de Grenoble, France, for a generous gift of 1-(1-methylcyclopropyl)-2-propanone. This investigation was supported by a grant from the Swedish Natural Science Research Council.

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Before the initiation of this study, we carried out an "extended" Hückel calculation on the 1- and 3-enols of cyclopropyl acetone to assess their relative stabilities. The 3-enol was calculated to be more stable by 5.5 kcal/mole; a qualitatively correct prediction.