ORGANIC AND BIOLOGICAL CHEMISTRY

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Structure and Properties of Cyclic Compounds. III.[1] Dissociation Constants of Simple α,β-Unsaturated Cyclic Acids

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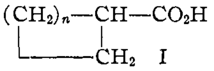
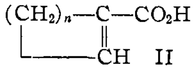
The dissociation constants of a number of simple α,β-unsaturated acids with endo- and exocyclic double bonds have been measured and the results interpreted in terms of strain and steric effects in the rings.

Roberts and Chambers[2a] measured the dissociation constants of the cycloalkyl carboxylic acids (I, $n = 1$–4), and found that the cyclopropyl- and cyclobutylcarboxylic acids (I, $n = 1, 2$) were considerably stronger than the cyclopentyl- and cyclohexylcarboxylic acids (I, $n = 3, 4$).[2b] They interpreted these results as due to the fact that the external bonds of the smaller rings have more *s*-character,[3] as a result of the angle deformations, and this leads to a general electron-attracting ($-I$) effect by the ring atoms, and hence a greater dissociation constant. The "strain energies" of cyclopentane and cyclohexane rings are negligible,[4] and as a result acid strengthening does not occur in these two cases.

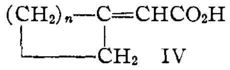
The presence of a double bond, however, in or near a 5- or 6-carbon ring greatly affects the stability of the system.[5] It seemed of interest to determine whether this would be reflected in the dissociation constants of the cycloalkenyl carboxylic acids (II, $n = 2$–5), and the cycloalkylidene acetic acids (IV, $n = 3$–5), since strain or steric effects might be greater in the anion than in the carboxylic acid. The dissociation constants of these acids as well as their acyclic analogs *cis*-α,β-dimethylacylic acid (tiglic acid) (III) and β,β-dimethylacrylic acid (V), are given in Table I.



$(CH_2)_n{-}CH(CO_2H){-}CH_2$ (ring) I



$(CH_2)_n{-}C(CO_2H){=}CH$ (ring) II



$(CH_2)_n{-}C(=CHCO_2H){-}CH_2$ (ring) IV

TABLE I

TABLE OF DISSOCIATION CONSTANTS[a]

n	I[b]	II	IV
1	0.62	..	..
2	.62	7.2	..
3	.33	0.78	0.21
4	.32	.38	.33
5	..	.23	.19
Acyclic	..	.38 (III)	.39 (V)

[a] $K_a \times 10^7$ in 50% aqueous ethanol at 25.0°. [b] Ref. 2a.

The presence of a double bond in a 5-membered ring leads to strain in the system[5]; this will be much greater in a 4-membered ring since both rings are planar and the internal angles of the latter are smaller. However, in a six-membered ring strain is relieved by folding of the ring and cyclohexene has a "half-chair" configuration.[6] Thus for the cyclobutenyl- and cyclopentenylcarboxylic acids (II, $n = 2, 3$) the unsaturated ring will exert a large $-I$ effect on the acid grouping, thus facilitating ionization and increasing the acid strength. It is found that these acids have higher dissociation constants than cyclohexenylcarboxylic acid (II, $n = 4$), which has the same value as tiglic acid (III). Cycloheptenylcarboxylic acid (II, $n = 5$) has a slightly lower dissociation constant than these last two acids, and this is probably due to the fact that the small amount of strain present in cyclohexenylcarboxylic acid and tiglic acid is absent in the larger 7-membered ring acid.

In general in an α,β-unsaturated carboxylic acid the inductive ($-I$) effect of the double bond increases the acid strength, since ionization is facilitated. The mesomeric effect, however, leads to a decrease in acid strength, since in the undissociated acid resonance interaction between the double bond and carboxyl-group stabilizes the acid, but in the anion resonance stabilization is primarily within the carboxylate ion itself, and the conjugate double bond has a smaller effect.[7a] If there is some steric hindrance to coplanarity then the mesomeric effect will be decreased since resonance interaction in the undissociated acid is more difficult. However there will be little change in the inductive effect, which will lead to an increase in the dissociation constant.[7b] For a double bond exocyclic to a six-membered ring there is interference with the ring α-hydrogen atoms,[5] and this is not present when the double bond is exocyclic to a cyclopentane ring. Thus cyclohexylideneacetic acid (IV, $n = 4$) should be a stronger acid than cyclopentylideneacetic acid (IV, $n = 3$), and this is found to be the case. Similarly for β,β-dimethylacrylic acid (V), steric interaction between the methyl and carboxyl groups leads to an increase in the dissociation constant, whereas for cycloheptylideneacetic acid (IV, $n = 5$) folding of the ring must relieve steric strain, since this acid has a lower dissociation constant.

It is interesting to compare the differences in the dissociation constants for the three series of acids.

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(1) *Chemistry & Industry*, 900 and 1020 (1954), are considered as Parts I and II.

(2) (a) J. D. Roberts and V. C. Chambers, THIS JOURNAL, **73**, 5030 (1951); (b) M. Kilpatrick and J. G. Morse, *ibid.*, **75**, 1854 (1953), found that values varied in different solvents, but the order was generally the same.

(3) A. D. Walsh, *Trans. Faraday Soc.*, **45**, 179 (1949).

(4) M. T. Rogers and J. D. Roberts, THIS JOURNAL, **68**, 843 (1946).

(5) H. C. Brown, J. H. Brewster and M. Schechter, *ibid.*, **76**, 467 (1954).

(6) D. H. R. Barton, R. C. Cookson, W. Klyne and C. W. Shoppee, *Chemistry & Industry*, 21 (1954).

(7) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953; (a) p. 77, (b) p. 744.

In the case of the cycloalkylideneacetic acids these differences are small, since the controlling factor is the small steric repulsions. The differences for the various cycloalkyl carboxylic acids are also small, since the strain effects are small, but for the cycloalkenyl carboxylic acids the large strain effects due to the endocyclic double bonds produce large changes in the dissociation constants.

Experimental

Preparations of the Acids.—Tiglic acid was prepared by the method of Buckles and Mock,[8] m.p. 64°, from water. β,β-Dimethylacrylic acid was prepared according to Smith,[9] m.p. 67°, from water. Cyclopentylidene,[10] cyclohexylidene-[11] and cycloheptylideneacetic[12] acids were prepared by a Reformatsky reaction with ethyl bromoacetate and the corresponding ketone, followed by saponification and dehydration of the resulting hydroxy ester. Their m.p.'s were 63° (lit. 64°[10]), 91° (lit. 91°[12]), 55° (lit. 54°[12]), respectively.

Cyclobutenecarboxylic acid was prepared from cyclobutanecarboxylic acid,[13] and had m.p. 72° (pentane).

Cyclopentenecarboxylic Acid.—Cyclopentanone (10 g.) and sodium cyanide (12 g., 100% excess) in water (50 ml.) was cooled in an ice–salt bath, and sodium bisulfite (25 g.) in water (60 ml.) added slowly with vigorous stirring during 0.5 hour. After stirring for a further 4 hr. the solution was filtered, and filtrate and residue extracted with ether. The ether solution was dried and the solvent removed under reduced pressure. The crude cyanohydrin in pyridine (25 ml.) and benzene (25 ml.) was treated with a mixture of phosphorus oxychloride (30 ml.) and pyridine (30 ml.). The mixture was warmed slowly and heated under reflux for 0.5 hour. The reaction mixture was cooled and poured onto ice and extracted with ether. The ethereal solution was washed with dilute hydrochloric acid and water, and then dried. Evaporation of the solvent and distillation of the residue gave 1-cyanocyclopentene (6 g.), b.p. 72° (15 mm.), $n^{20}{}_D$ 1.4690. The nitrile was hydrolyzed with 90% phosphoric acid at 130–140° for 5 hours.[14] The cooled mixture was diluted with an equal volume of water and extracted with ether. The ether was dried and evaporated and the residue crystallized from pentane to m.p. 121° (lit. 122°[15]).

Cyclohexenecarboxylic Acid.—Cyclohexanone cyanohydrin was prepared in like manner and dehydrated to 1-cyanocyclohexene, b.p. 86° (18 mm.), $n^{20}{}_D$ 1.4818. The nitrile was hydrolyzed as above to the acid, m.p. 38° from pentane (lit. 37°).[16]

Cycloheptenecarboxylic Acid.—Cyanocycloheptene, b.p. 54–55° (1 mm.), $n^{22}{}_D$ 1.4850, prepared from cycloheptanone as above, was hydrolyzed with phosphoric acid to the acid, m.p. 51° from pentane (lit. 49°[17]).

Determination of Dissociation Constants.—The dissociation constants were determined from the value of the *p*H at the half-neutralization point of a graph of *p*H *vs.* volume of sodium hydroxide solution. The solvent used was prepared by mixing equal volumes of purified dry ethanol and water and had $d^{25}{}_4$ 0.9272. Samples of the acids (0.05–0.10 g.) were dissolved in this solvent (50 ml.) in a beaker immersed in a constant temperature bath (at 25.0 ± 0.2°), and were titrated with carbonate-free sodium hydroxide (0.245 *N*) prepared in the same solvent. The *p*H determinations were with a model G Beckman *p*H meter, using glass and calomel electrodes with long leads, and frequent standardizations were made with buffer solutions of *p*H 4 and 7. The determinations were carried out in duplicate or triplicate. The values were not corrected for ionic strength, or liquid junction potential. The results are shown in the table. Under the same conditions benzoic acid had $K_a\,10^7 = 5.55$.

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[8] R. E. Buckles and G. V. Mock, *J. Org. Chem.*, **15**, 680 (1950).

[9] L. I. Smith, W. W. Prichard and L. J. Spillane, *Org. Syntheses*, **23**, 27 (1943).

[10] G. A. R. Kon and R. P. Linstead, *J. Chem. Soc.*, **127**, 616 (1925).

[11] M. Schmid and P. Karrer, *Helv. Chim. Acta*, **31**, 1067 (1948).

[12] G. A. R. Kon and C. J. May, *J. Chem. Soc.*, **129**, 1549 (1927).

[13] A. Campbell and H. N. Rydon, *ibid.*, 3002 (1953).

[14] W. S. Rapson and R. G. Shuttleworth, *ibid.*, 636 (1940).

[15] E. A. Braude and W. F. Forbes, *ibid.*, 1755 (1951).

[16] E. A. Braude and J. A. Coles, *ibid.*, 2014 (1950).

[17] E. A. Braude, W. F. Forbes and E. A. Evans, *ibid.*, 2202 (1953).

MEXICO 20, D. F., MEXICO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WASHINGTON]

Acid–Base Catalysis in Concentrated Acid Solution. Deuterium Isotope Effects in the Decarbonylation of Aromatic Aldehydes[1]

BY W. M. SCHUBERT AND HOWARD BURKETT[2]

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Isotope effects have been determined for (1) the decarbonylation of mesitaldehyde *vs.* deuteromesitaldehyde (MesCDO) in 60 to 100% sulfuric acid, and (2) the decarbonylation of mesitaldehyde in 60 to 100% sulfuric *vs.* deuterosulfuric acid. The observed isotope effects are not explained by a termolecular mechanism. With certain reasonable assumptions, a bimolecular mechanism of successive proton transfer steps, equations 2 and 3, is consistent with the isotope effects. All previous observations[5] are explainable on the basis of the bimolecular mechanism, including (1) the shapes of the plots of k_{obsd} *vs.* % sulfuric acid for 2,4,6-trimethyl-, triethyl- and triisopropylbenzaldehyde, and (2) the fact that for the mesitaldehyde decarbonylation, the change in k_{obsd} with sulfuric acid percentage is in apparent agreement with the unimolecular mechanism, 4, over part of the acid range.

Introduction

It was first suggested by Hammett, on the basis of the constancy of the sum,[3] $\log k_{\text{obsd}} + H_0$, that for many reactions catalyzed in concentrated acids the rate-controlling step is a unimolecular decomposition of a conjugate acid of the substrate (equation 4), or a proton transfer from the conjugate acid to solvent bases, this step being independent of the concentration or nature of the bases which receive the proton.[4] The acid-catalyzed decarbonylation of 2,4,6-trialkylbenzaldehydes has been shown not to proceed by this generalized mechanism, although for mesitaldehyde there is apparent agreement with the unimolecular mechanism over part of the range of sulfuric acid concentrations in which

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[2] On sabbatical leave from De Pauw University during 1953–1954.

[3] For substrates that are appreciably ionized, the more general equation, $\log k_{\text{obsd}} + H_0 - \log([\text{B}]/[\text{B}]_{\text{stoich}}) = \text{const.}$, applies; see, *e.g.*, reference 5.

[4] L. P. Hammett "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter IX.