

CONTRIBUTION TO THE CORRELATION OF STERIC STRUCTURE WITH DISSOCIATION CONSTANTS IN ORGANIC COMPOUNDS.

III. CARBOXYLIC ACIDS

By L. ÖTVÖS, F. SIROKMÁN and Ö. GAÁL

Institute of Organic Chemistry, The University, Szeged

(Received September 20, 1958)

A new synthesis to prepare neopentyl carboxylic acid is described. By determining the dissociation constant of that compound it was possible to demonstrate the influence of the steric effect of β -substituents of aliphatic carboxylic acids on the dissociation constant.

In our foregoing two communications we studied, on one hand, the correlation of the steric effect of the ortho substituents of aromatic amines and the β -substituents of aliphatic amines with basicity, and, on the other hand, the interrelations of the dissociation constants and steric structures of carboxylic acids [1, 2]. HAMMOTH found [3] in the case of α -substituted carboxylic acids that dissociation constants gradually decrease with the rise of the space requirement of substituents. This means in essence that the strength of acids is reduced by the primary steric effect. In a former paper [2] we succeeded in proving exactly that the decrease of dissociation constants of α -substituted carboxylic acids is due, in addition to changes in the inductive effect, also to the primary steric hindrance caused by the entrance of the third substituent. This was proved by the observation that, on introducing the third substituent, dissociation constants decreased in the case of dimethyl and trimethyl acetic acid, respectively, to greater extent than expected on the basis of the changes in inductive effect.

At the time when our former papers was prepared, the dissociation constant of neopentyl carboxylic acid was not determined yet. Thus, it was not possible to examine the correlation of steric effects with dissociation constants in the case of β -substituted carboxylic acids. It was, however, expected that the primary steric effect causes also in the case of β -substituents decreases in the values of dissociation constants of carboxylic acids. This can be readily observed of necessity, namely, substituents of the carbon atom and the carboxyl group possess appreciably weaker inductive effects [4].

On purpose to investigate whether the mentioned decreases in dissociation constants actually exist with aliphatic acids containing one, two or three β -substituents, respectively, tert.-butyl-malonic diethylate was prepared by the DOX and BYWATER method [5], then neopentyl carboxylic acid obtain-

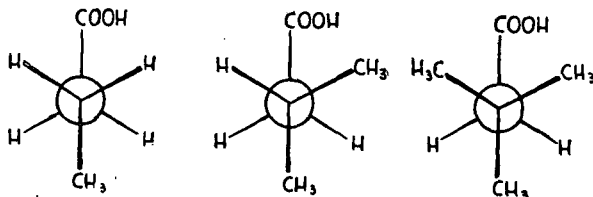
ed by the hydrolysis and decarboxylation of the product. The sodium salt of neopentyl carboxylic acid was prepared as well. SZEPESSY [6] established by measurements of conductivity of a dilution series of the pure acid and of the sodium salt the conductivity of the sodium salt obeys the OMSAGER equation [7]. Accordingly, it was possible to extrapolate to zero concentration. By this way, the value of λ_0 could be calculated, and, in the knowledge of this value, also the conductivity of the neopentylate anion could be calculated, using the Kohlrausch rule. Subsequently, the λ_0 value of the acid was calculated by measurements of conductivity of the hydrogen ion. Then, measuring the conductivity values of the acid in various concentrations, the mean value of data of K determined in various dilutions according to the Ostwald dilution law gave the dissociation constant of neopentyl carboxylic acid ($K = 1,0255 \cdot 10^{-5}$).

The dissociation constants of n-butyric acid, isovaleric acid and neopentyl carboxylic acid are disclosed by Table I.

Table I
Dissociation constants of β -substituted aliphatic carboxylic acids in water at 25°

	$10^5 K$	pK_a
n-butyric acid (8)	1,50	4,82
isovaleric acid (8)	1,67	4,78
neopentyl carboxylic acid . . .	1,025	4,998

It appears from the data of Table I that the introduction of the third methyl group in the β -carbon atom caused an appreciable decrease in the value of the dissociation constant which cannot be interpreted by the inductive effect. The decrease of dissociation constant is attributed to the primary steric effect of the three substituents of the β -carbon atom. In each of the three conformations, carboxyl group is surrounded by methyl groups as shown by the following figure:



leading thus to a reduction in the values of dissociation constant. In the case of isovaleric acid also a type of conformation is possible where the carboxyl group in the β -carbon atom is surrounded by a hydrogen atom and a methyl group. Consequently, the steric effect cannot prevail and thus, higher dissociation constant may exist. A similar observation was made in the case of butyric acid, although certain anomaly occurs.

*Experimental**Tertiary butyl malonic diethylate*

Malonic diethylate (477 g, 2,99 moles) is added to a solution of 60 g (2,6 moles) of sodium in 1300 ml of anhydrous ethanol, the mixture cooled below 5°, and 358 g (2,6 moles) of butyl bromide added within an hour. On allowing the mixture to stand at room temperature for a week, it was refluxed for an hour, ethanol removed by distillation and the salt dissolved in water. The diethylate was extracted with 4 × 50 ml of ether, dried over magnesium sulphate, ether removed by distillation and the residue subjected to fractionation under atmospheric pressure, applying a Widmer-column attachment. B. p. 202—203°. Weight: 90 g.

Neopentyl carboxylic acid

The obtained 90 g of diethylate were refluxed, under stirring, with 140 ml of 50% potassium hydroxide until the mixture becomes homogeneous (in about 30 minutes). On diluting with 50 ml of water, the aqueous azeotrope of the alcohol formed by hydrolysis was distilled, the alkaline solution acidified to pH 1 by concentrated hydrochloric acid and the precipitated potassium chloride filtered. Extracting the solution with 3 × 50 ml, the salt with 50 ml of ether, the combined ethereal solutions were dried over magnesium sulphate and ether removed by distillation. Owing to contamination by malonic acid, the residue solidified at room temperature. The repeated fractionation of the substance afforded 8,7 g of neopentyl carboxylic acid, b. p. 188—190°.

Analysis. Found: C 62,12; H 10,34. Calculated for $C_6H_{12}O_2$ (mol. wt. 116,156; C 62,04; H 10,41).

The sodium salt can be prepared from 1,16 g of neopentyl acid by treatment with the calculated quantity of 0,1 N sodium hydroxide. On evaporating under reduced pressure, traces of water are removed by distillation of the benzene azeotrope, and the residue recrystallized from a mixture of ethanol and ethylacetate.

* * *

Thanks are due to Mrs. K. L. LÁNG for carrying out the microanalyses.

References

- [1] Ötvös, L., F. Sirokmán: *Acta Phys. et Chem. Szeged* **2**, 118 (1956).
- [2] Sirokmán, F., L. Ötvös: *Ibid.* **2**, 127 (1956).
- [3] Hammonh, G. S., D. H. Hogle: *J. Amer. Chem. Soc.* **77**, 338 (1955).
- [4] Alexander, E. R.: *Principles of Ionic Organic Reactions* (John Wiley, New-York, 1950), p. 8.
- [5] Dox, A. W., W. G. Bywater: *J. Amer. Chem. Soc.* **58**, 731 (1936).
- [6] Szepessy, G.: unpublished communication.
- [7] Omsager, L.: *Phys. Z.* **28**, 277 (1927), **27**, 386 (1926).
- [8] Grunwald, E., E. B. J. Berkowitz: *J. Amer. Chem. Soc.* **73**, 4939 (1951).