928. *Stereochemistry of the Diels–Alder Reaction with Ethylenic Sulphoxides. Part VI.*[1] *Acidity Constants of Carboxylic Acids.*

By H. Hogeveen and F. Montanari.

The apparent acidity constants of some 3-phenylthio-, 3-phenylsulphinyl-, and 3-phenylsulphonyl-bicyclo[2,2,1]hept-5-ene-2-carboxylic acids have been measured in 50% v/v ethanol–water. In the *trans*-series these constants follow the normal order of the inductive effects transmitted through a saturated chain of two carbon atoms, *i.e.*, $Ph{\cdot}SO_2 > Ph{\cdot}SO > PhS > H$, but in the *cis*-series the order is $Ph{\cdot}SO > Ph{\cdot}SO_2 > PhS > H$. The results are discussed in terms of direct effects transmitted through space in the rigid bicyclic systems: field effects, intramolecular hydrogen bonds, and steric hindrance to solvation. On the same basis the minor differences in acidity between sulphoxides isomeric at the sulphur atom are tentatively explained; the experimental values agree with previous assignments of configuration.

The acidity constants of β-substituted propionic acids $R{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ ($R = Ph{\cdot}SO_2$, $Ph{\cdot}SO$, PhS, H) have also been measured. They parallel those of *trans*-bicylic, not those of *cis*-bicyclic, compounds.

In the reaction between cyclopentadiene and β-phenylsulphinyl acrylic acids one may predict the formation of eight isomers (four *cis* and four *trans*), instead of the four obtained in the usual diene syntheses, on account of the asymmetry at the sulphur atom.[1,2] Six of these isomers have been isolated, and the *syn*- or *anti*-configurations at the sulphur atom have been assigned[1] to some of them. Although the means employed for such assignments (formation of iodohydrins and iodolactones, stereospecific reductions and oxidations at the sulphur atom, infrared and proton magnetic resonance spectra) led to consistent conclusions, further evidence is now presented, based on the acidities of the isomeric sulphoxides and the corresponding sulphones and sulphides.

The apparent acidity constants were measured potentiometrically in 50% v/v ethanol–water at 25°, and are reported in Table 1.

In the *trans*-series the acidities of compounds (V)—(VIII), and (XVI) follow the normal order of the inductive effect of the substituents, transmitted through a saturated chain of two carbon atoms, *i.e.*, $Ph{\cdot}SO_2 > Ph{\cdot}SO > PhS > H$ [the minor difference between the isomeric sulphoxides will be discussed below]. As shown in Fig. 1, a linear free-energy relation exists between the pK_a values of the bicyclic acids (V)—(VIII), (XVI) and those of β-substituted propionic acids $R{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ ($R = Ph{\cdot}SO_2$, $Ph{\cdot}SO$, PhS, H;

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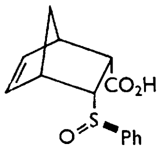
[1] Part V, Ghersetti, Hogeveen, Maccagnani, Montanari, and Taddei, *J.*, 1963, 3718.

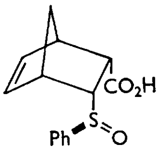
[2] Albera, Bonincontro, and Montanari, *Gazzetta*, 1960, **90**, 709.

TABLE 1.

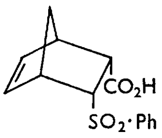
Apparent acidity constants (pK_a) of bicyclic carboxylic acids in 50% v/v ethanol–water at 25°.



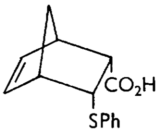
(I) 5·47



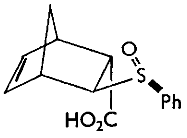
(II) 5·74



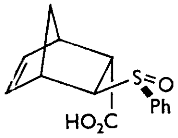
(III) 6·23



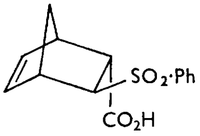
(IV) 6·41



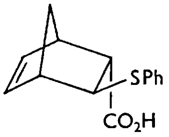
(V) 5·50



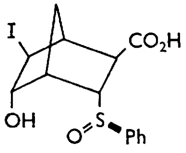
(VI) 5·65



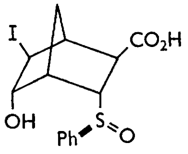
(VII) 5·36



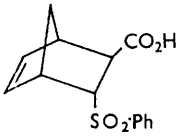
(VIII) 5·93



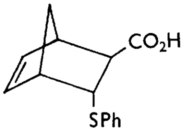
(IX) 5·10



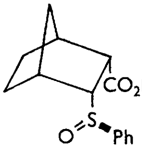
(X) 5·27



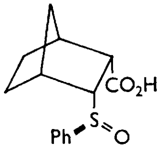
(XI) 5·25



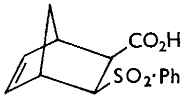
(XII) 5·93



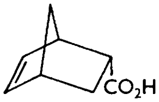
(XIII) 5·44



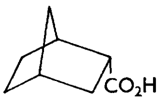
(XIV) 5·76



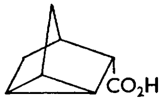
(XV) 6·03



(XVI) 6·51



(XVII) 6·62



(XVIII) 6·25

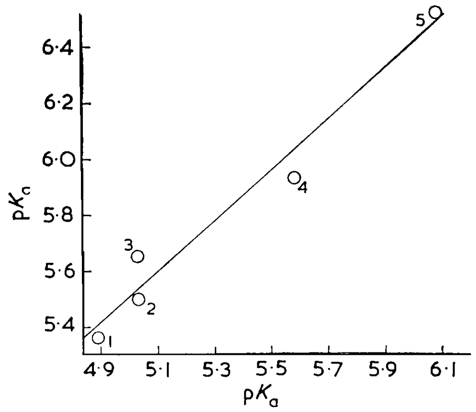


FIG. 1.

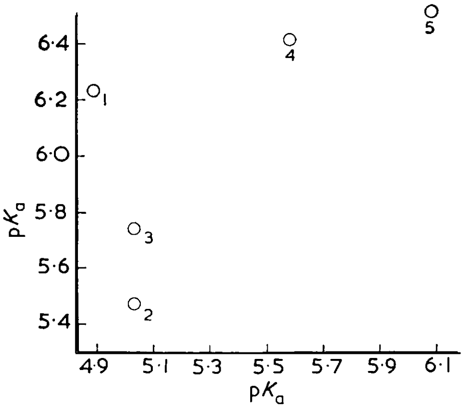


FIG. 2.

FIG. 1. Free-energy relation between pK_a's for acids $R\cdot CH_2\cdot CH_2\cdot CO_2H$ (horizontal axis) and 3-*exo*-R-bicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acids (vertical axis) (V—VIII) and (XVI).

R = (1) $Ph\cdot SO_2$, (2) *syn*-Ph·SO, (3) *anti*-Ph·SO, (4) PhS, (5) H.

FIG. 2. Plot as Fig. 1 for the *cis*-*endo*-series.

Table 2). The correlation coefficient $r = 0{\cdot}983$ is satisfactory.[3] The slope of the straight line is 0·90 ± 0·10 (standard deviation), which is close to unity, as it should be if the substituent effects on the acidities are the same in both systems.

TABLE 2.

Apparent acidity constants of β-substituted propionic acids, $R{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ in 50% v/v ethanol–water at 25°.

R	H	PhS	Ph·SO	$Ph{\cdot}SO_2$
pK_a	6·08	5·58	5·03	4·89

The *cis*-series does not afford a similar relation between the pK_a values of compounds (I)—(IV), (XVI) and those of propionic acids (Fig. 2). Acidity constants are lower than in the *trans*-series, particularly for the sulphone. The acidity order is: $Ph{\cdot}SO > Ph{\cdot}SO_2 > PhS > H$. A similar behaviour is shown by the *exo*-carboxy-sulphones, *trans* (XI) and *cis* (XV), whose pK_a values are near to those of sulphones *trans* (VII) and *cis* (III), respectively. The pK_a values of the *trans*-sulphides (XII) and (VIII) are identical.

The anomalous behaviour of the *cis*-derivatives indicates factors other than the normal inductive effects transmitted through the carbon chain. On account of the rigid structure and the proximity of the substituent to the reaction centre, interactions through space will be effective. These will be negligible in the propionic acids, because of the flexibility of the carbon chain which allows the molecules to reach the most favourable conformation; and in the *trans*-series the relation of the acidities to the inductive effect indicates a distance between the involved groups sufficient to make action through space very small.

In addition to inductive effects, the following interactions may be considered: (i) destabilization of the anion by a direct effect, through space, of the electronegative substituent, rigidly fixed in the neighbourhood of CO_2^- (field effect);[4,5] (ii) stabilization of the undissociated acid by formation of an intramolecular hydrogen-bond between the carboxyl group and the vicinal substituent; and (iii) destabilization of the anion by a steric effect of the vicinal group, which leads to removal of solvent molecules from around the carboxylate ion (steric hindrance to solvation).[6,7] All these will be most pronounced in the *cis*-compounds, whose acidities will, as a result, be lower than those in the *trans*-series.

In the *cis*-sulphones the occurrence of an intramolecular hydrogen bond between the carboxyl and the sulphonyl group seems improbable on account of the polarity of the solvent.* In the sulphide (IV), where hydrogen-bonding does not occur,* an appreciable steric hindrance to solvation seems also to be excluded, at least on the basis of molecular models. It is reasonable to assume that the non-bonding electrons of sulphur will destabilize the anion. In the sulphone (III), removal of solvent molecules from the space between CO_2^- and the bulky sulphonyl group would decrease the dielectric constant of the medium. Consequently the electrostatic repulsion between the two groups would increase, destabilizing the anion, in accord with the effect caused by steric hindrance to solvation.

The above discussion may be tentatively extended to the sulphoxides. As shown in

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* In the alcohols corresponding to the sulphone (III) and the sulphide (IV) the infrared spectra showed an intramolecular hydrogen bond only for the sulphone in an aprotic solvent (CCl_4).[1]

[3] Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[4] Ingold, " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, New York, 1953, p. 727.

[5] Meyers, *Tetrahedron Letters*, 1962, 1125.

[6] Hammond, in " Steric Effects in Organic Chemistry," ed. Newman, Wiley, New York, 1956, pp. 426, 428.

[7] Gold, in "Progress in Stereochemistry," Vol. III, eds. de la Mare and Klyne, Butterworths, London, 1962, pp. 186, 189.

Table 1, there is a difference of 0·27 between the pK_a's of *cis*-isomers (I), (II), and of 0·15—0·17 between those of *trans*-isomers (V), (VI), and (IX), (X). It was supposed,[2] and then confirmed by proton magnetic resonance spectroscopy,[1] that the most probable conformation of the Ph·SO group in the bicyclic sulphoxides is one in which the sulphur–phenyl bond is outward from the bicyclic system, and roughly parallel to the C:C bond. In these conditions, where the phenyl group has maximum rotational freedom around the sulphur–phenyl axis, the negative oxygen atom of the sulphinyl group lies close to the oxygen atoms of the carboxyl group in the *anti*-isomer; in the *syn*-isomer the distance is greater. Therefore, it may be expected that *anti*- will be less acidic than *syn*-sulphoxides, although, on account of the dipolar * character of the sulphinyl group, the resulting field effect on the carboxyl anion ought to be limited. In addition, the positive sulphur atom of the sulphoxides can get closer to the negative oxygen atoms of the anion than what is sterically allowed to the sulphur atom in the sulphones.

The experimental results are in agreement with the predictions and correspond to previous configurational assignments (*syn, anti*).[1] When the dipole S:O is oriented towards the C:C bond (*syn*-isomers) its effect is negligible, as shown by the almost identical pK_a values of the *cis*- (I) and *trans*-sulphoxide (V). The opposite orientation (*anti*-isomers) results in a more appreciable difference between compounds (II) and (VI). The smaller differences in pK_a's of *syn*- and *anti*-*trans*-isomers (V), (VI), and (IX), (X) than for the *cis*-compounds (I) and (II) are related to a greater distance, in the *trans*-series, between the sulphinyl and the carboxyl group. Finally it can be observed that hydrogen bonding and steric hindrance to solvation would cause more appreciable differences between pK_a's of the sulphoxides, so that an explanation in terms of simple field effects seems to fit the experimental results better.

The acidity constants of the isomers (I) and (II) have also been measured in ethanol–water mixtures and the results are reported in Table 3. The pK_a's increase with the percentage of ethanol in the solvent, owing to lower solvation of the anion than of the acid, and consequent increase in the free energy of ionization. The results show that the *syn*- (I) remains more acidic than the *anti*-isomer (II), although it is difficult to explain, on a qualitative basis, why the difference is smallest in 50% v/v ethanol–water.

TABLE 3.

Apparent acidity constants of 3-*endo*-phenylsulphinylbicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acids (I) and (II) in ethanol–water at 25°.

EtOH (wt. %)	18·1	42·5 (= 50% v/v)	79·7
pK_a of compound (I)	4·54	5·47	6·62
pK_a of compound (II)	4·92	5·74	6·99

Further, the apparent acidity constants of some saturated bicyclic compounds have been measured in 50% (v/v) ethanol–water (Table 1). In the sulphoxides, the double bond of the bicyclic ring has a negligible influence on the acidities, as shown by comparison between the pK_a's of the saturated compounds (XIII) and (XIV) with the unsaturated analogues (I) and (II). It is interesting that the *endo*-nortricyclenecarboxylic acid (XVIII) is more acidic than the *endo*-norbornene (XVI) and the *endo*-norbornane acid (XVII). This may be correlated with the " unsaturation " of the cyclopropane ring.[9]

EXPERIMENTAL

Determination of Acidity Constants.—The pK_a values were determined potentiometrically with a Beckman model G pH-meter at 25° ± 1°. 0·1 mmole of acid in carbon dioxide-free

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* This statement is independent of the detailed charge distribution between sulphur and oxygen.[8]

[8] Mangini, *Boll. sci. Fac. Chim. ind. Bologna*, 1960, **18**, 191; Szmant, in " Organic Sulfur Compounds," Vol. I, ed. Kharash, Pergamon Press, Oxford, 1961, p. 154; Price and Oae, " Sulfur Bonding," Ronald Press, New York, 1962, p. 129.

[9] Fuchs, Kaplan, Bloomfield, and Haban, *J. Org. Chem.*, 1962, **27**, 233.

1 : 1 ethanol–water (50 ml.) was titrated with 0·01N-sodium hydroxide in the same solvent. In duplicate or triplicate measurements the variation was not more than ± 0·02 pK_a unit. The pK_a values were taken as the pH at half-neutralization point, when above 5. Below this value the extensive Henderson equation [10] was applied.

Compounds.—The syntheses have been reported elsewhere,[1,2,11,12] except for the following.

β-*Phenylthiopropionic acid.* Acrylic acid (7·2 g.) was heated for 20 hr. on a steam-bath with thiophenol (22 g.). The solid product was dissolved again in aqueous sodium hydrogen carbonate. Extraction with chloroform to eliminate thiophenol, and acidification, yielded the sulphide (9·2 g.), m. p. 59·5—61° (lit.,[13] 60—61°) (from light petroleum).

β-*Phenylsulphinylpropionic acid.* β-Phenylthiopropionic acid (1·0 g.) was heated for 2 hr. on a steam-bath with peracetic acid (2 equiv.). Evaporation gave a quantitative yield of the sulphoxide, m. p. 100—101·5° (lit.,[13] 97—99°) (from ethyl acetate).

β-*Phenylsulphonylpropionic acid.* β-Phenylthiopropionic acid (1·0 g.) was heated for 2 hr. on a steam-bath with an excess of peracetic acid. Evaporation gave the sulphone, m. p. 124—125° (lit.,[14] 123—124°) (from benzene).

The configurations of 3-*exo*-*syn*-phenylsulphinylbicyclo[2,2,1]hept-5-ene-2-endo-carboxylic acid (V),[2] m. p. 183—194°, and of 2-*exo*-*anti*-phenylsulphinylbicyclo[2,2,1]hept-5-ene-2-endo-carboxylic acid (VI),[2] m. p. 204—205°, have not been previously [1] assigned.

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V GRUPPO DI RICERCA, BOLOGNA, ITALY. [*Received, April 16th*, 1963.]

[10] Glasstone, " Textbook of Physical Chemistry," Van Nostrand, New York, 1947, p. 1003.

[11] Albera, Luciani, and Montanari, *Boll. sci. Fac. Chim. ind. Bologna*, 1960, **18**, 52.

[12] Luciani, Montanari, and Tramontini, *Gazzetta*, 1960, **90**, 731.

[13] Holmberg and Schjänberg, *Arkiv Kemi, Min., Geol.*, 1942, *A*, **15**, No. 20; *Chem. Zentr.*, 1943, I, 388.

[14] Otto, *Ber.*, 1888, **21**, 89.