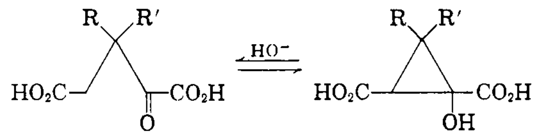
Communications TO THE EDITOR

On the Ring-Chain Tautomerism of α-Ketoglutaric Acids[1]

Sir:

One of the classic examples of the effect of *gem*-dialkyl groups on the stability of small ring compounds is the ring-chain tautomerism of the α-ketoglutaric acids which was investigated by Thorpe and his co-workers[2]:



The size of the alkyl group was reported to have a marked effect on the position of equilibrium, the larger groups giving predominately the cyclic isomer.

In view of the interest in these compounds,[3] and the known instability of cyclopropanol,[4] the structure of the compounds in which R and R′ were ethyl have been reinvestigated. Both acids (the "keto" form, herein designated as *A*, and the "cyclic" form, herein designated as *B*) gave dimethyl esters on treatment with diazomethane. (Ester *A*: liquid, b.p. 112–114 at 0.5 mm., *Anal.* Calcd. for $C_{11}H_{18}O_5$: C, 57.4; H, 7.9. Found: C, 57.4; H, 8.1. ester *B:* m.p. 58–60°, *Anal.* Calcd.: C, 57.4; H, 7.9. Found: C, 57.6; H, 7.6.). Each ester could be converted back to the corresponding acid by basic hydrolysis. The absence of a hydroxy band in the infrared for either ester indicates that the cyclic structure is incorrect.

The further observations that neither acid will react with lead tetraacetate[5] or with 2,4-dinitrophenylhydrazine, even with prolonged reaction times show that neither is an α-keto acid. The semicarbazone reported[1] for *A* has now been shown to be a semicarbazonium salt (Calcd. for $C_{10}H_{19}O_6N_3$: C, 43.3; H, 6.9; N, 15.2. Found: C, 43.6; H, 6.9; N, 15.3.)

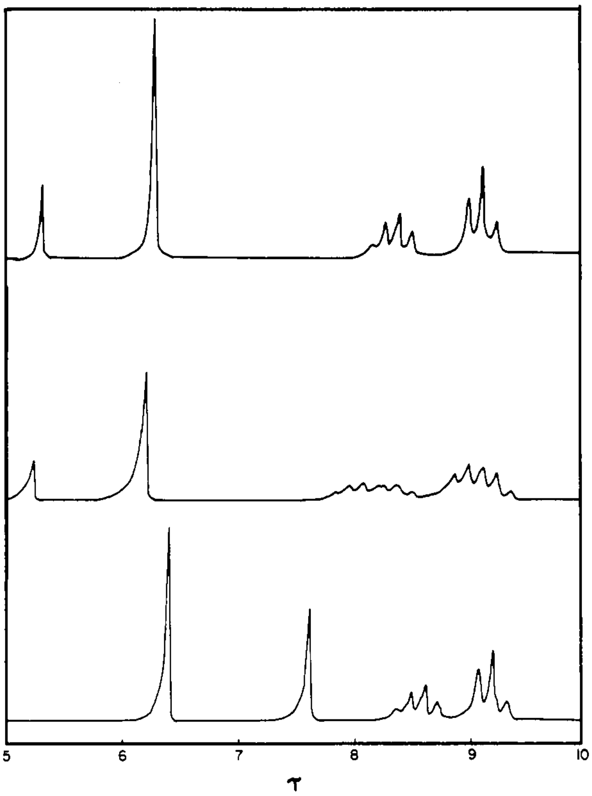


Fig. 1. NMR spectra: upper curve, ester *B*; middle curve, ester *A*; bottom curve, dimethyl β,β-diethylglutarate. The values are in p.p.m. referred to tetramethylsilane as the internal reference (τ values).

The correct structures are indicated by the NMR spectra (Fig. 1). The bands at 9.1–9.2[6] arise from the methyl of the ethyl group, and the methylene contributes the bands at 8.1–8.7. The band at 6.2–6.4 is due to the methyl of the ester, and the band at 7.64 of dimethyl β,β-diethylglutarate is attributed to the methylene groups attached to the carboxylate groups.

Both of the unknown esters have a band at 5.3, which must arise from a proton attached to a carbon bearing two electron withdrawing groups. (Formals have a band at 5.4 whereas a methylene attached to a single oxygen leads to a band at 5.8.) Furthermore, the two protons which are responsible for this band show no spin-spin splitting and therefore the adjacent carbons probably do not bear

---

[1] This work was supported by the Office of Ordnance Research, U. S. Army.

[2] S. S. Deshapanda and J. F. Thorpe, *J. Chem. Soc.*, **121**, 1430 (1922); E. W. Lanfear and J. F. Thorpe, *J. Chem. Soc.*, **123**, 1683 (1923). See however, K. C. Bhattacharyya, *Current Sci.* (*India*), **21**, 312 (1952).

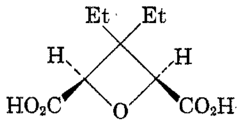
[3] *Cf.* G. S. Hammond in *Steric Effects in Organic Chemistry*, M. Newman, Ed., John Wiley & Sons, New York, 1956, pp. 463–464; E. A. Royals, *Advanced Organic Chemistry*, Prentice-Hall, New York, 1954, p. 178.

[4] J. D. Roberts and V. C. Chambers, *J. Am. Chem. Soc.*, **73**, 3176 (1951).

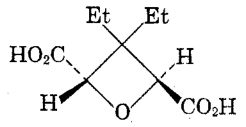
[5] It is improbable that steric effects prevented reaction with lead tetraacetate since α-methyl-β,β-diethyl-α′-ketoglutaric acid reacts with lead dioxide under conditions similar to those used here: J. Cologne and D. Joly, *Ann. chim.*, **18**, 286 (1943).

[6] Observed shift in ppm referred to tetramethylsilane (10.0) as the internal standard in dilute carbon tetrachloride solution in accord with the suggestion of G. V. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

other protons. Only structures Ia and Ib will accommodate this spectrum.



Ia



Ib

The spectrum also permits assignment of configuration, for in the ester of *B*, the methyl bands at 9.1 have the normal three components, whereas the corresponding band of *A* has five components of which part must originate from a chemical shift. Thus, the ethyl groups of *B* have the same environment and those of *A* have different environments, and correspondingly, *A* must be the *cis* isomer and *B* the *trans* isomer. This assignment is also in agreement with the ratio of ionization constants ($K_1/K_2 = 40$ for *A*, and 9 for *B*).

A consideration of the factors which favor the formation of a keto acid or a trimethylene oxide in the reaction by which the acids Ia and Ib are formed (the reaction of the α,α'-dibromoglutaric esters with strong base) will be postponed until the structures of all of the compounds in Thorpe's series have been reinvestigated.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WASHINGTON
SEATTLE 15, WASH.

KENNETH B. WIBERG
HOWARD W. HOLMQUIST

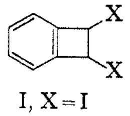
Received February 23, 1959

1,2-Bisdimethylaminobenzocyclobutene and its Rearrangement to α-Dimethylamino-*o*-Tolualdehyde

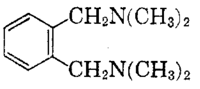
Sir:

Recently derivatives of benzocyclobutene have been studied by several groups of workers.[1-4] 1,2-Diiodobenzocyclobutene (I) has been prepared by Cava and co-workers[1,2] and has been shown to exist as *cis* and *trans* isomers.[3] It has been stated that I is inert to nucleophilic attack.[2]

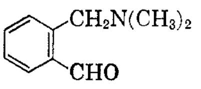
Treatment of pure *trans* I with excess dimethylamine yielded two equivalents of dimethylammonium iodide and a highly reactive liquid, b.p. 100–102°/2.5 mm., n_D^{25} 1.5094, for which we suggest the 1,2-bisdimethylaminobenzocyclobutene structure (II). The liquid II began to decompose within 15 minutes after distillation, making it impossible to obtain direct analytical data. Reduction of II with Raney nickel in dry petroleum ether yielded α,α'-dimethylamino-*o*-xylene (III), b.p. 80–82/4.2 mm., n_D^{25} 1.5024, which when treated with picric acid yielded a dipicrate, m.p. 192.6–194.1°. *Anal.* Calcd. for $C_{24}H_{26}N_8O_{14}$ ($C_{12}H_{20}N_2$ + $2C_6H_3N_3O_7$): C, 44.31; H, 4.03; N, 17.23. Found: C, 44.61; H, 4.09; N, 16.93. The infrared spectrum of III was identical to that of an authentic sample of α,α'-dimethylamino-*o*-xylene prepared by the method of von Braun and Cahn,[5] and a mixture melting point of the two dipicrates showed no depression.



I, X = I
II, X = N(CH₃)₂



III



IV

Treatment of II with dilute acid followed by isolation of the basic material yielded α-dimethylamino-*o*-tolualdehyde (IV), b.p. 84–86°/2.5 mm., n_D^{23} 1.5356. *Anal.* Calcd. for $C_{10}H_{13}NO$: C, 73.59; H, 8.03. Found C, 73.65; H, 8.13. The infrared spectrum of IV contained a conjugated carbonyl band at 1690 cm.$^{-1}$ and a band characteristic of *ortho* disubstitution at 760 cm.$^{-1}$ The ultraviolet spectrum is similar to that of other aromatic aldehydes $\lambda_{max}^{isooctane}$ 284 mμ (log ϵ = 3.11), 243 mμ (log ϵ = 4.05). The compound IV reduced Tollen's reagent and formed a *2,4-dinitrophenylhydrazone*, m.p. 175–176°. *Anal.* Calcd. for $C_{16}H_{17}N_5O_4$: C, 55.97; H, 4.99; N, 20.40. Found: C, 55.94; H, 4.96; N, 20.34. A *picrate* was also formed, m.p. 148–149°. *Anal.* Calcd. for $C_{16}H_{16}N_4O_8$: C, 48.98; H, 4.11; N, 14.28. Found: C, 49.22; H, 4.19; N, 14.31.

That dimethylamine was lost in the reaction of II to form IV was shown by treatment of II with picric acid in 95% alcohol. After five recrystallizations, analytically pure dimethylamine picrate was isolated. A mixture melting point of this picrate with that of an authentic sample of dimethylamine picrate showed no depression.

Cava has suggested that in the conversion of 1,2-dibromobenzocyclobutene to I there is elimination of bromine to form benzocyclobutadiene, followed by addition of iodine to the highly reactive double bond.[2] The possibility of a nucleophilic displacement of bromine by iodide ion was ruled out. The present results can be rationalized by a similar mechanism by postulating a *cis* elimination of hydrogen iodide followed by addition of dimethylamine to the benzocyclobutadiene intermediate. This would have to be followed by a second elimination and addition to give II. An alternative mechanism involving direct nucleophilic displacement of the iodine atoms is also possible.

---

[1] M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **78**, 500 (1956).

[2] M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **79**, 1701 (1957).

[3] W. E. Coleman and F. R. Jensen, *J. Org. Chem.*, **23**, 869 (1958).

[4] W. E. Coleman and F. R. Jensen, *J. Am. Chem. Soc.*, **80**, 6149 (1958).

[5] J. von Braun and R. S. Cahn, *Ann.*, **436**, 262 (1924).