

A reasonable reaction path compatible with the large rate enhancement caused by the *ortho*-benzamido group, the acid catalysis (compare runs 3 and 5 in Table I) and the fact that cleavage

TABLE I
HYDROLYSIS OF AMIDES IN 6.9 M ACETIC ACID, IN WATER

Amide	T, ° C.	Time, hr.	Acidity, M ^a	Cleavage, % ^b
I	80	5	0.89	87
II	80	168	0.89	<0.5
I	112	0.5	0.89	89
II	112	168	0.89	^c
I	111	0.5	0.089	44

^a Molarity of sulfuric acid. In all runs except the last the acid was present in large excess over the reactants. In the last run, sulfuric acid was present at the start to the extent of two equivalents to one of amide. ^b Based on isolated carboxylic acid. In all cases the yield of amine hydrochloride was within 2% of that of the acid. ^c A different reaction occurred; see text.

occurs at the more crowded of the two carbonyl groups is shown in Fig. 1. The proposal involves nucleophilic attack of the benzoyl oxygen on the carbon atom of the protonated *tert.* amide carbonyl group with consequent displacement of the dicyclohexylamine and rapid hydrolysis of the resulting six-member ring intermediate.⁵

Some support for this mechanism has been obtained by the isolation in 80% yield of the proposed intermediate benzoylanthranil (III)⁶ from a cleavage reaction of I carried out for twenty hours at 80° in a solution of dry dioxane saturated with hydrogen chloride. It was further shown that under the reaction conditions which caused the cleavage of I to the extent of 87% in five hours, III was hydrolyzed to IV to an extent greater than 96% at the end of twenty minutes.

Because amide groups are the most prominent functionality of proteolytic enzymes, the general type of assisted hydrolysis observed here should be considered along with other mechanistic proposals which have been put forth to explain enzymatic hydrolysis.⁷ A number of variations of this general scheme can be envisioned and we plan to investigate several of these.

(5) Of the other possible mechanisms which we have considered, the most likely involves general acid catalysis by the protonated benzamido group as in *i*. However, this type of electrophilic assistance is expected to be much less effective than that afforded by direct protonation of the carbonyl group undergoing reaction, a protonation which appears to be at least as favorable as that of the benzoyl oxygen. The complex *i* would also be destabilized by powerful non-bonded repulsions. Further studies which might provide evidence concerning this mechanism are planned.

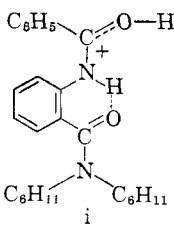
(6) P. R. Levy and H. Stephen, *J. Chem. Soc.*, 985 (1956).

(7) In a recent review,⁸ Bender has discussed the possibility that enzymatic amide groups might assist in the hydrolysis of carboxylic acid derivatives. He has also suggested the use of acylated anthranilic acid derivatives as model systems and has even anticipated the possible involvement of intermediates such as III.

(8) M. L. Bender, G. R. Schonbaum, and G. A. Hamilton, *J. Polymer Sci.*, 49, 75 (1961).

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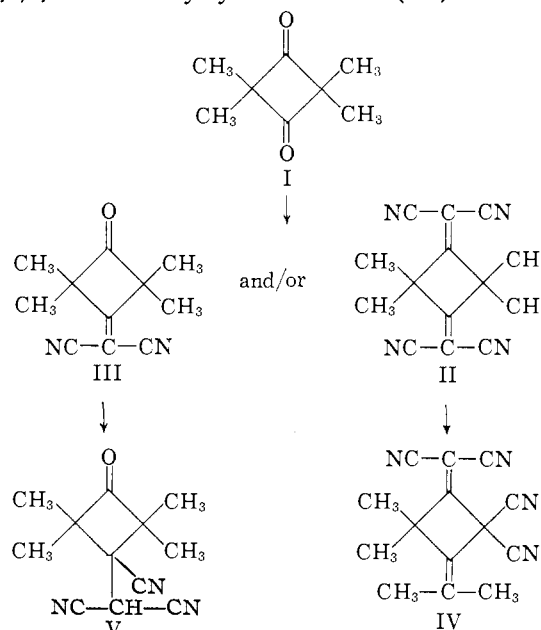
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1,3 π -INTERACTION IN A CYCLOBUTANE SYSTEM Sir:

Although 1,3 π -interaction has been invoked in the cyclobutane ring system to explain various chemical phenomena,^{1,2} no experimental proof of its existence has appeared despite attempts³ to provide such evidence by the examination of the ultraviolet spectra of 1,3-dioxocyclic unsaturated cyclobutanes. We wish to report that, using this approach, evidence indicating 1,3 π -interaction⁴ in the cyclobutanes I-IV has been obtained.

The dione I with malononitrile (1:2.4 molar ratio) in pyridine solution at 25° for one week gave bis - (dicyanomethylene) - 2,2,4,4 - tetramethylcyclobutane (II) in 97% yield, m.p. (sinters 250°) 305-310° (dec.); $\lambda_{\text{max}}^{\text{KBr}}$ 4.48 and 6.14 μ . (*Anal.* Calcd. for C₁₄H₁₂N₄: C, 71.17; N, 5.12; N, 23.71. Found: C, 71.39; H, 5.25; N, 23.85). By lowering the amount of malononitrile (1:1.1) and decreasing the reaction time (three days) dicyanomethylene-2,2,4,4-tetramethylcyclobutanone (III) was ob-



tained as the major product (46%) along with the bis-dicyanomethylene compound II (21%). The cyclobutanone (III) had m.p. 108-108.5°; $\lambda_{\text{max}}^{\text{KBr}}$ 4.48, 5.55, and 6.14 μ ; (*Anal.* Calcd. for C₁₁H₁₂-

(1) E. F. Silversmith and J. D. Roberts, *J. Am. Chem. Soc.*, 80, 4083 (1958).

(2) E. J. Smutny, M. C. Caserio and J. D. Roberts, *ibid.*, 82, 1793 (1960).

(3) 1,3-Dimethylenecyclobutane failed to show absorption in the ultraviolet attributable to 1,3 π -interaction (F. F. Caserio, Jr., S. H. Parker, R. Piccolini and J. D. Roberts, *ibid.*, 80, 5507 (1958)). 3-Methylenecyclobutanone was synthesized but no conclusions could be drawn regarding 1,3 interaction because of the presence of 3-methylcyclobutanone (F. F. Caserio, Jr., and J. D. Roberts, *ibid.*, 80, 5837 (1958)).

(4) (a) Recently, the ultraviolet and infrared absorption spectra of 3-thiacyclobutanone were found to be "anomalous," and possible transannular sulfur-carbonyl interaction was considered (J. C. Martin, Abstracts of 139th A.C.S. meeting, St. Louis, Missouri, March, 1961, p. 31-0). Previously the possibility of 1,3 bonding was raised in the case of 3-methylenetrimethylene oxide (D. E. Applequist and J. D. Roberts, *J. Am. Chem. Soc.*, 78, 4012 (1956)). (a) An analogous 1,4 π -interaction has been observed in exomethylene derivatives of a boat 1,4-cyclohexanedione derived from quinone and cyclopentadiene (S. Winstein, L. DeVries, and R. Orloski, *ibid.*, 83, 2020 (1961)).

TABLE I
ULTRAVIOLET SPECTRA OF CYCLOBUTANES I-V

	Isobutane		Ethanol		Acetonitrile	
	λ_{\max} m μ	ϵ	λ_{\max} m μ	ϵ	λ_{\max} m μ	ϵ
I ^a	227	168	227	173		
	302	32.4	302	30		
	308	39.4	307	30		
II					232	30,000
					239	26,900
III	236	11,000	237	10,450	237	11,000
	319	120.5	318	120.5	316	120
IV			228	11,600		
			240	7,360		
			275	643		
V			223	207		
			290	30		

(a) The dione I shows additional absorption at 271 ($\epsilon = 10.2$), 282 ($\epsilon = 25.4$), 296 ($\epsilon = 28$), and 348 m μ ($\epsilon = 18.4$) in isobutane and at 282 ($\epsilon = 24$) and 345 m μ ($\epsilon = 18$) in ethanol.

N₂O: C, 70.18; H, 6.42; N, 14.89. Found: C, 70.24; H, 6.62; N, 14.80).

Evidence for the retention of the four-membered ring in both II and III was afforded by the chemical analyses, as well as by the presence of a single peak in the proton n.m.r. spectra; τ values⁴: I, 8.69; II, 8.24; III, 8.49.

Upon treating compound II with methyltriphenylphosphonium iodide or triethylamine, a remarkable rearrangement leading to formal exchange of two cyano groups with two methyl groups was observed to yield an isomeric product identified as IV, m.p. 158–159; (*Anal.* Calcd. for C₁₄H₁₂N₄: C, 71.17; H, 5.12; N, 23.71; mol. wt., 236. Found: C, 70.70; H, 5.22; N, 23.83; mol. wt., 245). The structure assignment of IV is based on (a) $\lambda_{\max}^{\text{KBr}}$ 4.45 μ (CN), 5.98 μ (isopropylidene group), 6.08 μ (C=C(CN)₂), 7.16 μ and 7.28 μ (*gem* dimethyl); (b) the proton n.m.r. spectrum of CDCl₃ solution shows signals at $\tau^4 = 7.82$, 7.96, and 8.37 in a 1:1:2 intensity ratio in accord with the two different (isopropylidene) and two similar (ring *gem* dimethyl) methyl groups; (c) ozonolysis gave acetone, which was identified as the 2,4-dinitrophenylhydrazone derivative; (d) in tetrahydrofuran solution the product gave no e.p.r. signal at 25 or 50°. A nucleophile-catalyzed ring opening-ring closure sequence is proposed for conversion of II to IV.

The cyclobutanone V was prepared by acidification of the salt obtained in 60% yield by reaction of the cyclobutanone (III) with tetraethylammonium cyanide. Compound V has m.p. 155.5–156.5° (dec.); $\lambda_{\max}^{\text{KBr}}$ 4.45, 5.55, 7.2 and 7.25 μ ; (*Anal.* Calcd. for C₁₂H₁₀N₂O: C, 66.95; H, 6.08; N, 19.53. Found: C, 66.89; H, 5.99; N, 19.40).

The existence of non-bonded interaction of the π -orbitals at the 1,3 positions of compounds I–IV is suggested from the ultraviolet absorption data summarized in Table I.

For compound III the absorption at 237 m μ in ethanol is attributed to the dicyanomethylene group⁵ and that at 318 m μ to the carbonyl group.⁶

(4) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(5) The wave length and intensity of this band is that expected for a cycloalkylidenemalononitrile; e.g., cyclopentylidenemalononitrile has $\lambda_{\max}^{\text{EtOH}}$ 238.5 m μ (ϵ 12,000) (unpublished results of Dr. J. K. Williams).

With V as a model, the bathochromic shift of 28 m μ (290–318 m μ) together with a four-fold increase in ϵ is strongly indicative of interaction.

Transannular interaction in II causes the appearance of a doublet at 232 and 239 m μ with an ϵ greater than the twofold increase expected from comparison with compound III. For IV, two new maxima appear at 228 and 275 m μ , in addition to the expected absorption at 240 m μ attributable to the dicyanomethylene function.

Evidence establishing 1,3-interaction in the dione I is less definitive. The spectra exhibit considerable fine structure. Assuming that the $n \rightarrow \pi^*$ transition at 302–307 m μ corresponds to that at 290 m μ for V, a bathochromic shift in the range of 12–17 m μ is observed, however, without an increase in ϵ . Whether this shift arises from intramolecular charge transfer^{7,8} between the two carbonyl groups or whether, because of the known sensitivity of $n \rightarrow \pi$ transition to polar environment,⁹ it is due to the influence of the electrons of one carbonyl group on the $n \rightarrow \pi$ transition¹⁰ of the other is also unresolved.

These data will be discussed more fully in a forthcoming publication, and evidence will be presented indicating that 1,3-interactions of these compounds are not of significant importance in the ground state.

(6) The absorption in the 300 m μ region for compounds I and III is regarded as an $n \rightarrow \pi^*$ transition of the carbonyl group since a hypsochromic shift is observed in changing to more polar solvents (see H. McConnell, *J. Chem. Phys.*, **20**, 700 (1952), for leading references). These shifts are small in agreement with the observations of Kosower and Wu, who found that cyclobutanones give unusually low solvent-dependent shifts (E. M. Kosower and G.-S. Wu, *J. Am. Chem. Soc.*, **83**, 3142 (1961)).

(7) J. Tanaka and S. Nagakura, *J. Chem. Phys.*, **24**, 311 (1956).

(8) S. Nagakura, *ibid.*, **23**, 1441 (1955).

(9) L. Goodman and H. Shull, *ibid.*, **22**, 1138 (1954).

(10) H. L. McMurry, *ibid.*, **9**, 231 (1941).

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THE REACTIVITY OF HYDROGEN ATOMS IN ALKALINE SOLUTIONS

Sir:

Recent radiation chemical investigations of aqueous solutions yield chemical evidence for the transient formation of e_{aq} (or H₂O⁻), and the reactivity of this species with specific scavengers. The pH dependence, the effects of scavenger concentration and isotope effects in aqueous solutions of organic^{1,2} and inorganic^{3–7} solutes indicate that the entity e_{aq} is of considerable kinetic importance. The radiation stability of H₂O₂^{3,4,8} and N₂O^{6,7} in acid solutions is interpreted by assuming that these solutes act as efficient scavengers for solvated elec-

(1) D. Armstrong, E. Collinson, F. S. Dainton, D. M. Donaldson, E. Hayon, M. Miller and J. Weiss, *Proc. Int. Conference Peaceful Uses of Atomic Energy*, **29**, 80 (1958).

(2) J. T. Allan and G. Scholes, *Nature*, **187**, 218 (1960).

(3) N. F. Barr and A. O. Allen, *J. Phys. Chem.*, **63**, 928 (1959).

(4) G. Czapski, J. Jortner and G. Stein, *ibid.*, **65**, 984 (1961).

(5) A. R. Anderson and E. J. Hart, *ibid.*, **65**, 804 (1961).

(6) F. S. Dainton and D. B. Peterson, *Nature*, **186**, 878 (1960).

(7) G. Czapski and J. Jortner, *ibid.*, **188**, 4744 (1960).

(8) J. T. Sworski, *J. Am. Chem. Soc.*, **76**, 4687 (1954).