The photodimerization of 3-phenyl-2-cyclohexenone

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Received June 5, 1967

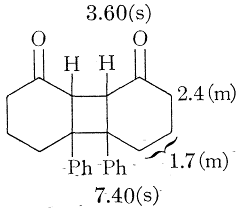
Ultraviolet irradiation of 3-phenyl-2-cyclohexenone has been found to give a single photodimer, whose structure has been established as the *cis–anti–cis* head-to-head cyclobutane derivative X.

Canadian Journal of Chemistry. Volume **45**, 2927 (1967)

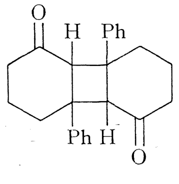
Although α,β-unsaturated carbonyl compounds have been known for many years to undergo photodimerization (cf. ref. 1), detailed studies of the structure and stereochemistry of such photodimers have rarely been carried out until recently. These investigations have shown that in most cases the products are cyclobutane derivatives. However, these dimers have been found to correspond to a number of different orientational and stereochemical types (cf., for example, ref. 2). It has become clear that the course of the dimerization may depend upon the structure of the monomer, the mode of its excitation, and the medium (cf., for example, ref. 3). In an investigation directed towards the clarification of the influence of the first of these factors, we have established the structures of the photodimers formed from three 3-aryl-2-cyclohexenones; in this paper we discuss the elucidation of the structure of the photodimer of 3-phenyl-2-cyclohexenone; in the next paper the structures of the photodimers of 3-(*p*-anisyl)-2-cyclohexenone and 3-(*p*-nitrophenyl)-2-cyclohexenone are discussed.

Irradiation of 3-phenyl-2-cyclohexenone in methanol, benzene, or cyclohexane in Pyrex vessels with a medium-pressure mercury arc lamp gave a single dimer in a good yield. The gross structure of this dimer was established as I by its spectroscopic properties and degradation.

Its infrared spectrum (λ_{max} ($CHCl_3$) 5.87 μ) is in accord with the presence of unconjugated carbonyl groups, and its nuclear magnetic resonance (n.m.r.) spectrum can be interpreted as shown in structure I (the chemical shift values are recorded on the δ scale). It may be noted that the signal assigned to the two tertiary, cyclobutyl protons appears as a singlet, thus preventing the immediate distinction of I from the head-to-tail structure II.



I



II

The photodimer was found to revert to the monomer in concentrated sulfuric acid, indicating that the structural integrity of the monomer units is retained. It was degraded as shown in Scheme 1. Treatment with *m*-chloroperbenzoic acid gave the dilactone III in a high yield. The dilactone showed a band in its infrared spectrum at 5.69 μ, attributable to the lactone groups, and its n.m.r. spectrum included a singlet at δ 5.62 p.p.m., assigned to the tertiary, cyclobutyl protons which

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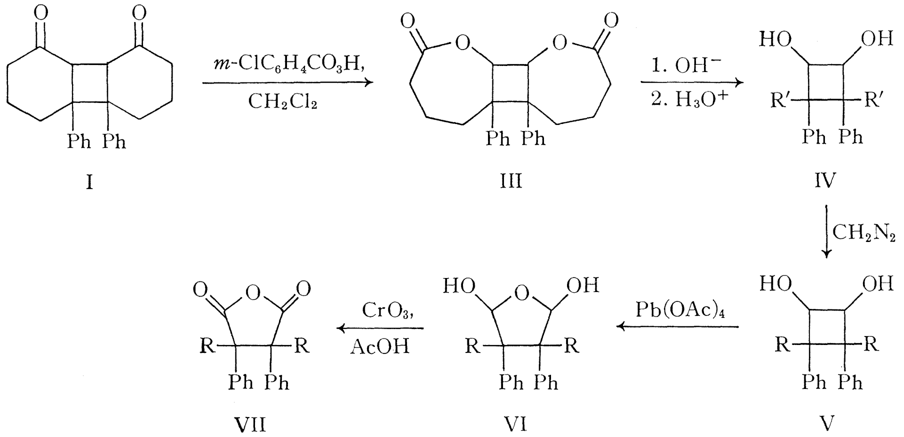


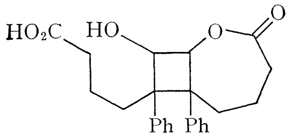
SCHEME 1. $R = (CH_2)_3CO_2CH_3$, $R' = (CH_2)_3CO_2H$.

now are situated on carbon atoms bearing an oxygen.

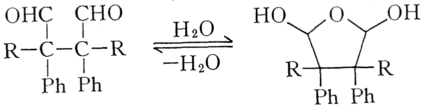
Hydrolysis of dilactone III with aqueous base gave the dicarboxylic acid IV, which was converted into the diester V by treatment with diazomethane. The diester showed bands in its infrared spectrum at 2.90 and 5.82 μ, confirming the presence of hydroxyl and ester functions. Its n.m.r. spectrum included a singlet at δ 3.56 p.p.m., assigned to the methoxyl protons of the ester groups, and two doublets (each with $J = 9$ c.p.s.) at δ 3.99 and 4.79 p.p.m. Treatment with D_2O led to the disappearance of the former doublet and collapse of the latter to a singlet. The higher field doublet can therefore be assigned to the hydroxyl protons, with the splitting attributed to coupling with the cyclobutyl protons, which give rise to the signal at δ 4.79. This coupling and the position of the carbonyl stretching band suggest strong intramolecular hydrogen bonding between the hydroxyl and ester groups in V.

Hydrolysis of dilactone III with dilute methanolic postassium hydroxide gave a product considered to be the lactone acid VIII. This product was also obtained together with the dilactone III when the Baeyer–Villiger oxidation of the photodimer was carried out with perbenzoic acid in the presence of p-toluenesulfonic acid. Compound VIII gave the dicarboxylic acid IV on further hydrolysis with aqueous base.

The dihydroxy diester V was oxidized by lead tetraacetate, as expected for a 1,2-diol. This reaction gave a compound, $C_{26}H_{32}O_7$, which showed bands in its infrared spectrum at 2.80 and 5.80 μ. Its n.m.r. spectrum included doublets ($J = 9$ c.p.s.) at δ 2.70 and 6.00 p.p.m. and showed no signal with $\delta > 7.5$ p.p.m. Treatment with D_2O led to the disappearance of the high-field doublet and the collapse of the other to a singlet. These data led to the assignment of structure VI to the oxidation product. This is considered to arise via hydration of the dialdehyde IX, the expected primary product from the cleavage of V with lead tetraacetate. This view was corroborated by the observation that dehydration of VI in carbon tetrachloride by azeotropic removal of water gave a solution whose n.m.r. spectrum lacked



VIII



IX VI

$R = (CH_2)_3\,CO_2CH_3$

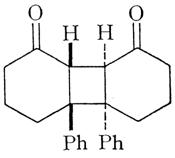
signals at δ 2.70 and 6.00 p.p.m., and showed a singlet at δ 9.95 p.p.m., attributable to aldehydic protons. Its infrared spectrum confirmed the presence of an aldehydic group in that it showed a new band at 3.65 μ. Although the product was not isolated, it clearly represents the aldehydic parent (IX) of the hydrate VI. Addition of water to the carbon tetrachloride solution caused immediate crystallization of the hydrate.

The hydrate VI was oxidized with chromic acid in acetic acid to give the anhydride VII. The infrared spectrum of this product had bands at 5.40, 5.60, and 5.78 μ, showing it to be a substituted succinic anhydride. This establishes the presence of the cyclobutane ring in the photodimer, and confirms that the hydroxyl groups in V are adjacent and thus that the dimer has a head-to-head orientation as in I.

We will now discuss the stereochemistry of the photodimer. Since the formation of products with *trans*-fused four- and six-membered rings has been observed in photoaddition reactions (2*e*, 4), it is necessary to establish both the nature of the ring fusions of the four- and six-membered rings and the *syn* or *anti* relationship of the six-membered rings with respect to the four-membered ring in order to define completely the stereochemistry of I.

Treatment of the photodimer with hot methanolic sodium methoxide failed to bring about any change. This demonstrates that both of the six-membered rings must be *cis* fused to the four-membered ring. Had a *trans*-fused system been present, such treatment would have been expected to lead to conversion into the corresponding *cis*-fused system via an enolate ion (4*b*).

After treatment of the dihydroxy dicarboxylic acid IV with sodium periodate in aqueous methanol for 2 h at room temperature, IV could be recovered unchanged to the extent of 86%. Even after treatment with this reagent at 48° for 20 h, it was not completely consumed. These observations show that the two hydroxyl groups of IV must have a *trans* relationship, since it would be anticipated that the corresponding *cis*-diol would be oxidized rapidly by periodate (5). This conclusion was corroborated by the very slow rate of oxidation of the dihydroxy diester V by lead tetraacetate; the second-order rate constant at 24° was found to be 0.072 ± 0.011 l mole^{-1} min^{-1} (cf. ref. 6). Since the Baeyer–Villiger oxidation is known to proceed with retention of configuration (7), and the hydrolysis of the lactone rings should not affect the stereochemistry of the molecule, it follows that the relationship of the two six-membered rings of the photodimer with respect to the four-membered ring must be *anti*. The dimer is thus defined as X, the *cis–anti–cis* isomer of the head-to-head structure I.



X

The product from the photodimerization of 3-phenyl-2-cyclohexenone may be compared with the photodimers obtained from other cyclohexenones. Eaton[2] has found that neat 2-cyclohexenone gives a good yield of two major dimeric products, formed in approximately equal amounts, together with a third, minor product. The major products were shown to be the *cis–anti–cis* isomers of the head-to-head and head-to-tail cyclobutane derivatives. Irradiation of piperitone (3-methyl-6-isopropyl-2-cyclohexenone) in aqueous ethanol gives a low yield of a photodimer which has been assigned a *cis–anti–cis* head-to-head cyclobutane structure (2*e*); a second product was considered to be the corresponding *anti* head-to-head cyclobutane derivative with at least one *trans* ring junction. The course of the photodimerization of isophorone (3,5,5-trimethyl-2-cyclohexenone) in solution has been found to be affected greatly by the polarity of the solvent; polar solvents strongly favor the formation of a head-to-head dimer, whereas

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[2] P. E. Eaton, private communication (cf. ref. 10).

nonpolar solvents favor the formation of a mixture of two head-to-tail dimers (3*a*).

Thus the photodimerization of 3-phenyl-2-cyclohexenone is distinguished by the fact that a single product, the nature of which is unaffected by variation in the polarity of the solvent, is formed in a high yield. Whether this circumstance reflects a fundamental difference in the nature of the photochemical process as a result of the phenyl substituent remains to be determined. However, it may be noted that $\pi \longrightarrow \pi^*$ singlet excitation is possible in Pyrex vessels with 3-phenyl-2-cyclohexenone, but not with 2-cyclohexenone, piperitone, and isophorone.

A further interesting feature of the photodimerization of 3-phenyl-2-cyclohexenone is its reversibility. Irradiation of a dilute solution of the photodimer in benzene gave a mixture of monomer and dimer in which the former was predominant. Such a reversibility of the photodimerization process does not appear to have been observed with simple cycloalkenones. Indeed, with cyclopentenone Eaton (2*b*) found that no photochemical interconversion of the head-to-head and head-to-tail photodimers occurs, indicating that photochemical reversion to monomer does not take place. However, it has long been known that reversion of the photodimers of cinnamic acid to monomer occurs under the influence of ultraviolet radiation (cf. ref. 8), and it is thus probable that reversibility is associated with the presence of phenyl substituents on the cyclobutane rings.[3]

EXPERIMENTAL

Melting points were determined on a Fisher–Johns hot stage and are uncorrected. Infrared spectra were recorded on Beckman IR-5 and IR-8 spectrophotometers, and were calibrated with the 6.24 μ band of polystyrene. Ultraviolet spectra were recorded on a Bausch and Lomb Spectronic 505 spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer; tetramethylsilane was used as an internal standard.

3-Phenyl-2-cyclohexenone

3-Phenyl-2-cyclohexenone, prepared by the method of Walker (9), was obtained as needles, m.p. 64–65°, λ_{max} (CCl_4) 5.98 μ, λ_{max} (EtOH) 222 (ϵ 14 200) and 284 mμ (ϵ 17 200); δ (CCl_4) 2.3 (m), 2.7 (m), 6.29 (t, J = 1 c.p.s.), and 7.4 (m) p.p.m.[4]

Photodimer of 3-Phenyl-2-cyclohexenone (I)

3-Phenyl-2-cyclohexenone was irradiated in methanol, benzene, and cyclohexane. In all experiments the same product was formed. In a typical run 3-phenyl-2-cyclohexenone (2 g) in benzene (60 ml) was irradiated for 40 h in a Pyrex tube with a 450 W Hanovia medium-pressure mercury arc lamp. Removal of the solvent gave a crystalline solid, from which the pure photodimer could be obtained in a 60–70% yield by recrystallization from methanol or ethyl acetate. The mother liquors contained mixtures of the monomer and dimer. The photodimer crystallized from ethyl acetate as prisms, m.p. 204–205°, λ_{max} ($CHCl_3$) 5.87 μ, λ_{max} (EtOH) 260 (ϵ 610)[5] and 296 mμ (ϵ 60) (ϵ_{220} 10 000); δ ($CDCl_3$) 1.7 (m), 2.4 (m), 3.60 (s), and 7.40 (s) p.p.m.

Anal. Calcd. for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02; mol. wt. 344. Found: C, 83.69; H, 7.04; mol. wt. (Rast) 311.

Reaction of I with Sulfuric Acid

The photodimer was dissolved in concentrated sulfuric acid. The solution was left at room temperature for 18 h, diluted with water, and extracted with ether. The monomer (50%) was isolated from the ethereal extract and identified as its 2,4-dinitrophenylhydrazone, m.p. 226.5–227° (lit. m.p. 226–228° (9)).

Baeyer–Villiger Oxidation of I; Formation of Dilactone III

A solution of the photodimer (4.30 g, 0.0125 mole) and *m*-chloroperbenzoic acid (FMC Corporation, 85% peracid, 6.80 g, 0.0336 mole) in methylene chloride (270 ml) was boiled under reflux for 12 h and left overnight. The reaction mixture was diluted with ether, and washed four times with aqueous 5% sodium hydroxide and four times with water. The organic layer was dried over magnesium sulfate. Removal of the solvent gave the crystalline dilactone III (96%). This could be recrystallized from benzene–hexane (with benzene of crystallization) or from carbon tetrachloride. The recrystallized product had m.p. 267.5–268°, λ_{max} (CCl_4) 5.69 and 8.80 μ; δ ($CDCl_3$) 1.4 (m), 2.1 (m), 5.62 (s), and 7.4 (m) p.p.m.

Anal. Calcd. for $C_{24}H_{24}O_4$: C, 76.57; H, 6.43. Found: C, 76.30, 76.84; H, 6.53, 6.58.

Dilactone III (58%) could also be obtained by the oxidation of the dimer with perbenzoic acid in

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[3] The possibility that photoequilibration determines the nature of the photodimer is discussed in the next paper.

[4] Abbreviations used: s, singlet; d, doublet; t, triplet; and m, multiplet.

[5] The most intense component of a band system with the vibrational fine structure characteristic of simple benzenoid systems.

benzene in the presence of *p*-toluenesulfonic acid for 3 days. A second product (17%) precipitated from solution during the reaction; after crystallization from carbon tetrachloride, it had m.p. 161–165°; λ_{max} (KBr) 2.94, 5.77, and 5.85 μ. It is considered to be the lactone acid VIII.

Hydrolysis of Diliactone III; Formation of Dicarboxylic Acid IV

Dilactone III (containing benzene of crystallization, 5.44 g) and a mixture of saturated aqueous sodium bicarbonate (250 ml) and aqueous 5% sodium hydroxide (50 ml) were heated under reflux for 4.5 h. The hot solution was decanted from a small amount of undissolved material, cooled in ice, and acidified with concentrated hydrochloric acid. The thick, gelatinous precipitate was crystallized twice from benzene–acetone to yield dicarboxylic acid IV (2.45 g) as needles, m.p. 194–196°, λ_{max} (KBr) 2.94 and 5.85 μ.

Anal. Calcd. for $C_{24}H_{28}O_6$: C, 69.88; H, 6.84. Found: C, 69.96; H, 6.90.

Treatment of dilactone III with dilute methanolic potassium hydroxide gave the lactone acid VIII, m.p. 161–165°, after crystallization from carbon tetrachloride. This, on reaction with hot aqueous sodium bicarbonate, was converted into IV.

Dimethyl Ester (V) of Dicarboxylic Acid IV

Treatment of dicarboxylic acid IV with ethereal diazomethane yielded the diester V, which crystallized from methanol as prisms, m.p. 172–174°, λ_{max} ($CHCl_3$) 2.90 and 5.82 μ; δ ($CDCl_3$) 1.5 (m), 2.0 (m), 3.56 (s), 3.99 (d, J = 9 c.p.s., absent after D_2O treatment), 4.79 (d, J = 9 c.p.s., singlet after D_2O treatment), and 7.5 (m) p.p.m.

Anal. Calcd. for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32. Found: C, 70.86; H, 7.39.

Oxidation of Diester V with Lead Tetraacetate; Formation of the Dialdehyde Hydrate VI

A solution of diester V (1.00 g) in glacial acetic acid (120 ml) which had been saturated with lead tetraacetate was left in the dark at room temperature for 24 h. Titration indicated that 97% of the theoretical amount of lead tetraacetate was consumed in that time. A solution of potassium iodide (2.5 g) and crystalline sodium acetate (60 g) in water (125 ml) was added, followed by solid sodium thiosulfate to destroy the iodine. The mixture was extracted with ether, and the extract was washed with water, with aqueous sodium carbonate, and again with water. The solution was dried over magnesium sulfate and the ether removed to give a thick, pale-yellow oil (800 mg), which was crystallized from carbon tetrachloride. Compound VI was obtained as fine needles, m.p. 142–144°, λ_{max} ($CHCl_3$) 2.80 and 5.80 μ; δ ($CDCl_3$) 1.2 (m), 2.1 (m), 2.70 (d, J = 9 c.p.s., absent after D_2O treatment), 3.56 (s), 6.00 (d, J = 9 c.p.s., singlet after D_2O treatment), and 7.5 (m) p.p.m.

Anal. Calcd. for $C_{26}H_{32}O_7 \cdot \frac{1}{4}H_2O$: C, 67.75; H, 7.11. Found: C, 67.86, 67.72; H, 6.94, 6.90.

The concentrated carbon tetrachloride mother liquors gave further crystals only after the addition of a drop of water. The n.m.r. spectrum of one such mother liquor showed no signals with δ 2.70 and 6.00 p.p.m. and a new singlet at δ 9.95 p.p.m. Its infrared spectrum had a band at 3.65 μ.

Oxidation of the Dialdehyde Hydrate VI; Formation of the Anhydride VII

A saturated solution of chromium trioxide in glacial acetic acid was added dropwise to a solution of crude VI in hot glacial acetic acid until the brown color persisted for 10 min of further heating. The cooled solution was diluted with water and extracted with ether. The ethereal extract was washed twice with water, once with aqueous 5% sodium hydroxide, and twice again with water, and was dried over magnesium sulfate. Removal of the ether gave a semicrystalline oil which crystallized completely when stirred with fresh ether. The anhydride VII crystallized from carbon tetrachloride as prisms, m.p. 184–185°; λ_{max} ($CHCl_3$) 5.40, 5.60, and 5.78 μ; δ ($CDCl_3$) 1.6 (m), 2.2 (m), 3.55 (s), and 7.4 (m) p.p.m.

Anal. Calcd. for $C_{26}H_{28}O_7$: C, 69.01; H, 6.24. Found: C, 69.27; H, 6.16.

Treatment of Dimer I with Base

Dimer I (100 mg) was refluxed for 2 h with a solution prepared by reaction of sodium (0.5 g) with methanol (25 ml). The solution was cooled, acidified with dilute acetic acid, and further diluted with water. The white precipitate was recrystallized from ethyl acetate and melted at 200–205° before and after admixture with pure I. The infrared spectra of the crude precipitate and the recrystallized material were identical with that of the photodimer.

Treatment of Dicarboxylic Acid IV with Sodium Periodate

Compound IV (0.300 g, 0.72 mmole) and sodium periodate (0.405 g, 1.53 mmoles) were dissolved in aqueous 40% methanol (13 ml), and the solution was left at room temperature for 2 h. It was then concentrated to one-half of its volume under reduced pressure, when 0.258 g (86%) of compound IV precipitated. A similar reaction mixture heated at 48° for 20 h also gave a small amount of compound IV.

Rate of Oxidation of Diester V with Lead Tetraacetate

The rate of oxidation of the dihydroxy diester V with lead tetraacetate was determined according to the directions of Criegee *et al.* (6*b*). The second-order rate constant at 24° was found to be 0.072 ± 0.011 l mole^{-1} min^{-1}.

Photochemical Reversion of Dimer I to Monomer

A solution of the photodimer (72 mg) in benzene (20 ml) was irradiated in a Pyrex tube with a 450 W Hanovia lamp for 24 h. Removal of the benzene gave an oily solid, from which the monomer, 3-phenyl-2-cyclohexenone (50 mg), was isolated by carbon tetrachloride extraction. The monomer was identified by its infrared and n.m.r. spectra. The rest of the material was unchanged dimer.

ACKNOWLEDGMENTS

Grateful acknowledgment is made to the National Research Council of Canada and to the United States National Institutes of Health for their generous support of this work.

REFERENCES

1. P. de Mayo. Advances in organic chemistry: methods and results. Vol. 2. *Edited* by R. A. Raphael, E. C. Taylor, and H. Wynberg. Interscience Publishers, Inc., New York. 1960. p. 367.
2. (*a*) P. Yates and M. J. Jorgenson. J. Am. Chem. Soc. **85**, 2956 (1963).
   (b) P. E. Eaton. J. Am. Chem. Soc. **84**, 2344 (1962).
   (*c*) R. C. Cookson, D. A. Cox, and J. Hudec. J. Chem. Soc. 4499 (1961).
   (*d*) R. C. Cookson, J. J. Frankel, and J. Hudec. Chem. Commun. 16 (1965).
   (*e*) H. Ziffer, N. E. Sharpless, and R. O. Kan. Tetrahedron, **22**, 3011 (1966).
3. (*a*) D. J. Trecker, A. A. Griswold, and O. L. Chapman. 152nd Meeting, American Chemical Society, New York. 1966. Abstr. Papers. p. S28. O. L. Chapman. 20th National Organic Chemistry Symposium, American Chemical Society, Burlington, Vermont. 1967. Abstr. Papers. p. 111.
   (*b*) H. Morrison, H. Curtis, and T. McDowell. J. Am. Chem. Soc. **88**, 5415 (1966).
   (*c*) P. E. Eaton and W. S. Hurt. J. Am. Chem. Soc. **88**, 5038 (1966). J. L. Ruhlen and P. A. Leermakers. J. Am. Chem. Soc. **88**, 5671 (1966); **89**, 4944 (1967).
4. (*a*) J. Corse, B. J. Finkle, and R. E. Lundin. Tetrahedron Letters, 1 (1961).
   (*b*) E. J. Corey, J. D. Bass, R. LeMahieu, and R. B. Mitra. J. Am. Chem. Soc. **86**, 5570 (1964).
5. V. C. Bulgrin and G. Dahlgren, Jr. J. Am. Chem. Soc. **80**, 3883 (1958). J. Honeyman and C. J. G. Shaw. J. Chem. Soc. 2454 (1959).
6. (*a*) R. Criegee, E. Büchner, and W. Walther. Ber. **73**, 571 (1940).
   (*b*) R. Criegee, E. Höger, G. Huber, P. Kruck, F. Marktscheffel, and H. Schellenberger. Ann. **599**, 81 (1956).
   (*c*) E. J. Moriconi, W. F. O'Connor, E. A. Keneally, and F. T. Wallenberger. J. Am. Chem. Soc. **82**, 3122 (1960).
7. P. A. S. Smith. Molecular rearrangements. *Edited by* P. de Mayo. Interscience Publishers, Inc., New York. 1963. Pt. 1. p. 588.
8. A. Schönberg. Präparative Organische Photochemie. Springer-Verlag, Berlin. 1958. p. 31.
9. G. N. Walker. J. Am. Chem. Soc. **77**, 3664 (1955).
10. E. Y. Y. Lam, D. Valentine, and G. S. Hammond. J. Am. Chem. Soc. **89**, 3482 (1967) (*added in proof*).