Novel Photochemical Synthesis of 2-Aryl-1,3-cyclohexanediones

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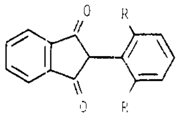
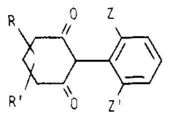
Benzophenone-sensitized photolysis of cyclic 2-diazo 1,3-diketones in aromatic solvents affords moderate yields of 2-aryl-1,3-cyclohexanediones. The reaction, which appears to involve electrophilic attack of a triplet diketocarbene on electron-rich aromatics, is particularly useful for preparing 2-aryl-1,3-cycloalkanediones with ortho substituents. The reaction is general and has been applied to the synthesis of over 20 2-aryl-1,3-cyclohexanediones. The scope and limitations of the reaction are discussed.

Potentially useful biocidal activity has been observed[1] for 2-aryl-1,3-indandiones in which the aromatic ring bears one or, preferably, two ortho substituents (e.g., 1). These compounds are easily synthesized using the Shapiro method, i.e., base-promoted condensation of phthalide and aromatic aldehydes.[2] For structure-biological activity studies of the 2-aryl-1,3-cyclohexanediones (2), a direct synthesis of these compounds was highly desirable.



1, R = CH_3, Cl



2

Z, Z' = alkyl, halogen, etc.

R, R' = H, alkyl, aromatic, etc.

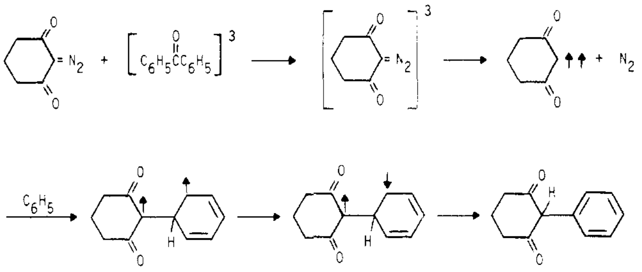
None of the several synthetic routes to 2-aryl-1,3-cycloalkanediones reported in the literature[3] appeared to be applicable to the synthesis of the desired bis ortho substituted 2-aryl-1,3-cycloalkanediones. The most versatile literature route to 2-aryl-1,3-cycloalkanediones is base condensation of phenylacetonitriles with glutarate esters to give 6-aryl-6-cyano-5-ketohexanoate esters which, in some cases, may be directly cyclized under acid hydrolysis conditions to 2-aryl-1,3-cyclohexanediones. Generally the 6-aryl-6-cyano-5-ketohexanoate esters must be hydrolyzed and decarboxylated to the 6-aryl-5-ketohexanoic acid, which is then esterified and cyclized under basic conditions. This route has several disadvantages: (1) the starting materials are relatively inaccessible; (2) the yields for bis ortho substituted 2-aryl-1,3-cycloalkanediones are very low; and (3) the procedure is lengthy and involves intermediates which are difficult to purify.

In this paper we wish to report a novel, direct photochemical synthesis of variously substituted 2-aryl-1,3-cyclohexanediones in yields ranging from 7 to 57%.

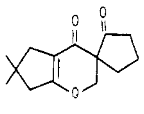
Synthesis

Scheme I depicts a possible mechanism for the photochemical synthesis of 2-phenyl-1,3-cyclohexanedione.

Scheme I



The primary reaction process for singlet ketocarbenes is the Wolff rearrangement.[4] Direct photolysis of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione in carbon tetrachloride gives primarily the ketene dimer 3[5] or, in aqueous solution, the ring-contracted ketoacid 4 as the only product.[6] However, Jones and Ando[7] demonstrated that triplet bis(carbomethoxy)carbene generated by the benzophenone-sensitized irradiation of methyl diazomalonate added to carbon-carbon double bonds to form cyclopropanes with loss of stereochemistry. These workers also found that the photosensitized irradiation of methyl diazomalonate in benzene gave a 1.6:1 ratio of 7,7-bis(carbomethoxy)cycloheptatriene and dimethyl phenylmalonate.[7] These results indicate that triplet ketocarbenes do not undergo facile Wolff rearrangement and are sufficiently electrophilic to add to aromatic rings.



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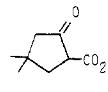

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Two facts provide evidence that it is the triplet diazo ketone (hence triplet ketocarbene) that is generated in the benzophenone-sensitized photolysis of 2-diazo-1,3-cycloalkanediones: (1) direct phytolysis of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione through a Pyrex filter for 48 h produced no change in the diazoketone; and (2) the relative extinction coefficients of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione and benzophenone in the region >3000 Å allows >98% of the light to be absorbed by the benzophenone.

Results

The first test of Scheme I was to photolyze, through Pyrex, 2-diazo-1,3-cyclohexanedione in benzene, using benzophenone as the triplet sensitizer. After chromatography and recrystallization, a 52% yield of 2-phenyl-1,3-cyclohexanedione (5) was isolated as a somewhat unstable

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(1) J. Maas, "Proceedings of the 4th International Symposium on Medicinal Chemistry, Noordwijkerhout, The Netherlands, September 9-13, 1974". Elsevier, New York, 1974, pp 143-172.

(2) S. L. Shapiro, K. Geiger, J. Youlus, and L. Freedman, *J. Org. Chem.*, **25**, 1860 (1960); S. L. Shapiro, K. Geiger, and L. Freedman, *ibid.*, **26**, 3580 (1961).

(3) H. Born, R. Pappo, and J. Szmuszkovicz, *J. Chem. Soc.*, 1779 (1953); B. E. Betts and W. Davey, *J. Chem. Soc.*, 3336 (1961); F. M. Beringer, P. S. Forgione, and M. D. Hudis, *Tetrahedron*, **8**, 49-63 (1960).

(4) M. Jones, Jr., and R. A. Moss, Eds., "Carbenes", Vol. I, Wiley-Interscience, New York, 1973, pp 107-114 and 117-125.

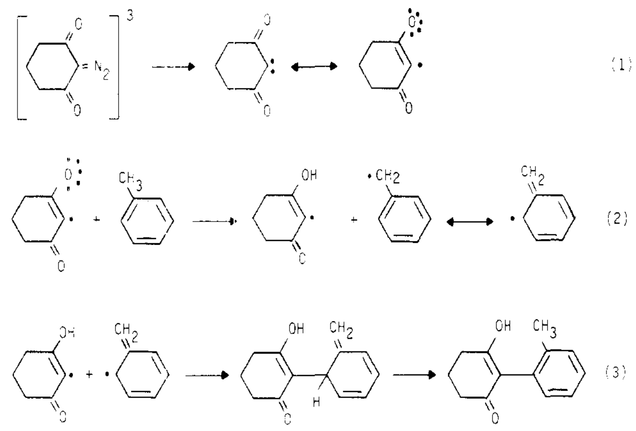
(5) H. Veschambre and D. Vocelle, *Can. J. Chem.*, **47**, 1981-1988 (1969).

(6) I. K. Korobitsyna and V. A. Nikolaev, *Zh. Org. Khim.*, **12** (6), 1251-60 (1976).

(7) M. Jones, Jr., W. Ando, M. E. Hendrick, A. Kulczycki, Jr., P. M. Howley, K. F. Hummel, and D. S. Malament, *J. Am. Chem. Soc.*, **94**, 7469 (1972).

0022-3263/79/1944-4906$01.00/0

Scheme II



crystalline solid, which decomposed rapidly upon exposure to air. IR, NMR, and UV spectral data are in agreement with the literature values[8] (see Experimental Section).

The results of the sensitized phytolysis of 2-diazo-1,3-cyclohexanediones in a variety of aromatic solvents are summarized in Table I. Aromatic solvents substituted only with electron-withdrawing groups were unreactive. Thus the benzophenone-sensitized photolysis of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione in chlorobenzene gave no acidic products containing an aromatic ring. Photolysis of the same diazo ketone in a 3:1 mixture of chlorobenzene–mesitylene gave only **10** in 22% yield.

Alkyl substituents on the aromatic nucleus produced a surprising orientation effect. With alkyl groups present, the attacking ketocarbene was directed effectively to the ortho position(s). For example, the sensitized photolysis of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione in toluene gave a 23% yield of **11** as the only product containing an aromatic ring. The structure of **11** was confirmed by comparison with the authentic material prepared by literature methods.[9] Authentic samples of 2-(3′-methylphenyl)-5,5-dimethyl-1,3-cyclohexanedione and 2-(4′-methylphenyl)-5,5-dimethyl-1,3-cyclohexanedione were also prepared by using these methods. The TLC of the crude photolysis mixture showed trace components which could be these two isomers.

In those cases (*m*-xylene, *m*-chlorotoluene, and *m*-tolunitrile) where the ortho-directing effect of an aryl alkyl group could produce two isomers, these were obtained, and in most cases, each isomer was isolated free of the other by column chromatography. No particular steric effect was observed. Thus in the sensitized photolysis of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione in *m*-xylene, the crude product afforded 12% of **15** and 11% of **16**.

One possible rationale for the ortho-directing effect of alkyl substituents is shown in Scheme II. The radicals formed in step 2 are viewed as existing as a tight pair in a solvent cage. Collapse of the radical pair occurs at the ortho position before the benzyl radical has time to diffuse away from the dione radical and undergo reorientation.

Scheme II correctly predicts the products in all cases which were studied (see Table I). Trace amounts of other isomers were, however, usually present but in quantities too small to isolate and determine their structure. One exception is the result obtained with *m*-methylanisole. In this case in addition to the two expected isomers **19** and **20** a third dione was isolated and its structure characterized as 2-(2′-methoxy-4′-methylphenyl)-5,5-dimethyl-1,3-cyclohexanedione (**21**). This product is a relatively minor component in the photolysis mixture.

As additional tests of Scheme II, the photolysis of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione was carried out in *tert*-butylbenzene and in anisole. Purification of each of the crude photosylates from these two experiments gave white, crystalline solids with broad melting points. The solids could not be further resolved either by low-pressure liquid chromatography or TLC. The IR and NMR spectral data on these solids indicated they were each isomeric mixtures of 2-aryl-5,5-dimethyl-1,3-cyclohexanediones. The elemental analysis of each solid was also consistent with the structure of a 2-aryl-5,5-dimethyl-1,3-cyclohexanedione.

The data given in Table I indicate that the photosensitized decomposition of cyclic 2-diazo 1,3-diketones in aromatic solvents is a versatile procedure for the synthesis of 2-(polysubstituted phenyl)-1,3-cyclohexanediones. However, this procedure is not applicable to open-chain or heterocyclic 2-diazo 1,3-diketones. The photolysis of 3-diazo-2,4-pentanedione, 3-diazo-1,1,1-trifluoro-2,4-pentanedione, or 2-diazo-1,3-diphenyl-1,3-propanedione in mesitylene containing benzophenone gave no acidic products in the reaction mixture. One possible explanation for the failure of the open-chain diazo diketones to undergo the desired reaction is the availability of intramolecular reaction pathways for the open-chain systems which are not possible in the cyclic cases.

Attempts to carry out the sensitized photolysis with heterocyclic 2-diazo 1,3-diketones were also unsuccessful. When 5-diazo-2,2-dimethyl-*m*-dioxane-4,6-dione (prepared from Meldrum's acid) was photolyzed in mesitylene containing benzophenone, there was obtained a small quantity of a crude product which showed no aromatic protons in the NMR and appeared to be a complex mixture by TLC. This negative result is particularly surprising in light of the fact that the triplet carbene from this diazo compound has been successfully added to carbon–carbon double bonds.[7] In another example the benzophenone-sensitized photolysis of 1,2-diphenyl-4-diazo-3,5-pyrazolidinedione in mesitylene gave 1,2-diphenyl-3,5-pyrazolidinedione as the only major product.

Conclusions

Existing synthetic methodology for obtaining 2-aryl-1,3-cyclohexanediones requires multi-step procedures and is not suitable for the preparation of bis ortho substituted 2-aryl-1,3-cyclohexanediones. We have described a general, direct procedure for the preparation of 2-(polysubstituted phenyl)-1,3-cyclohexanediones by the photosensitized decomposition of 2-diazo-1,3-cyclohexanediones in aromatic solvents. The starting materials are readily available, and the products are obtained, in modest yield, in a single step. This synthetic method has been used to prepare a variety of biologically active 2-aryl-1,3-cyclohexanediones.[10]

Experimental Section

General. Melting points are uncorrected. IR spectra (listed in Table II for all compounds) were taken on a Perkin-Elmer Model 137 spectrometer. NMR spectra (listed in Table II for all compounds) were obtained on a Varian A-60 spectrometer at 60 MHz, using $(CH_3)_4Si$ as an internal standard. Elemental analyses[10]

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(8) T. S. Gore and V. K. Yadav, *Indian J. Chem.*, 1, 321 (1963); see also Born and Betts in ref 3.

(9) The method used to prepare the authentic dione samples consisted of condensing the appropriate phenylacetonitrile with diethyl 3,3-dimethylglutarate to give ethyl 6-aryl-6-cyano-5-keto-3,3-dimethylhexanoate which was hydrolyzed, decarboxylated, and cyclized to the 2-aryl-1,3-cycloalkanedione. Refer to the Experimental Section for the synthesis of 2-(2′-methylphenyl)-5,5-dimethyl-1,3-cyclohexanedione by this method.

(10) Structure–activity relationships and the biocidal activity of these compounds will be reported elsewhere. Satisfactory elemental analyses have been obtained for all compounds.

Table I. Photolysis Products[a] of 2-Diazo-1,3-cyclohexanediones in Aromatic Solvents

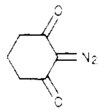
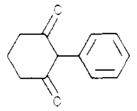
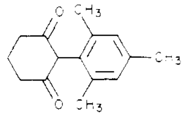
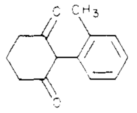
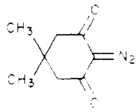
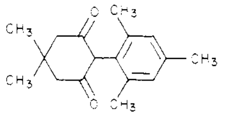
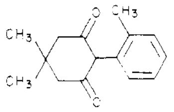
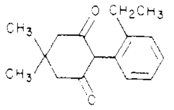
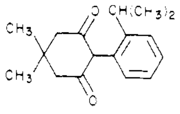
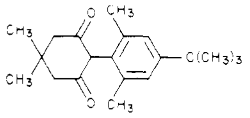
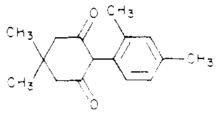
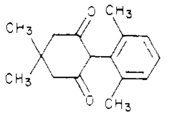
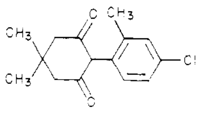
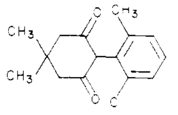
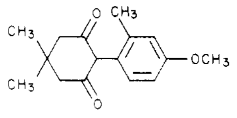
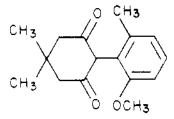
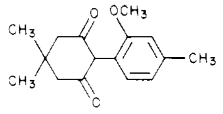
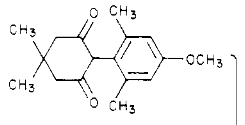
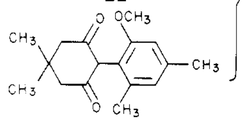
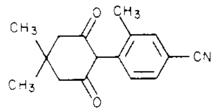
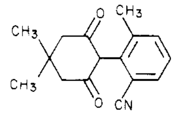
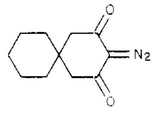
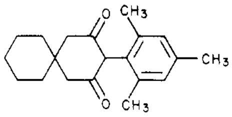
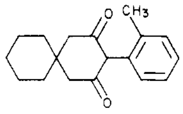
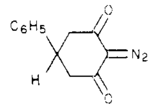
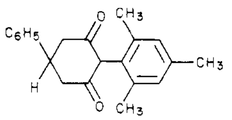
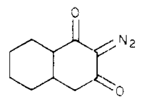
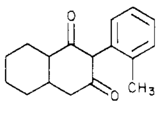
diazo ketone	solvent	product(s)	yield,[b] %	mp, °C
 5	benzene	 6	52	154-55
5	mesitylene	 7	31	196-98
5	toluene	 8	40	140-43
 9	mesitylene	 10	25	215-17
9	toluene	 11	23	179-81
9	ethylbenzene	 12	10	118-21
9	cumene	 13	10	161-64
9	3,5-dimethyl-*tert*-butylbenzene	 14	22	244-49
9	*m*-xylene	 15	12	167-69
		 16	11	183-86
9	*m*-chlorotoluene	 17	11	190-92
		 18	7	188-91

Table I *(continued)*

diazo ketones	solvent	product(s)	yield,[b] %	mp, °C
9	*m*-methylanisole	 **19**	17	165-66
		 **20**	12	119-24
		 **21**	3	172-74
9	3,5-dimethylanisole	 **22**  **23**	23[c]	155-59
		 **24**	12	241-43
9	*m*-tolunitrile	 **25**	11	193-95
 **26**	mesitylene	 **27**	24	196-202
26	toluene	 **28**	22	143-45
 **29**	mesitylene	 **30**	57	215-16
 **31**	toluene	 **32**	20	165-67

[a] In all cases the parent dione corresponding to the diazo ketone was observed as a major product. [b] Isolated yield based on diazo ketone. [c] Isolated as a mixture of isomers not separable by column chromatography or TLC.

were performed by the Technical Center Analytical Group. All photochemical reactions were carried out using a 200-W Hanovia, medium-pressure, quartz, mercury-vapor immersion lamp through a Pyrex filter. All compounds listed in Table I were synthesized and isolated using methods identical with those detailed for the specific examples presented below.

Chromatography. Analytical thin-layer chromatography (TLC) was performed using 5 × 20 cm MN precoated silica gel plates (0.25 mm thickness) with UV 254 indicator. Open-column chromatography was carried out using Woelm silica gel (63–200 μm) and commercial distilled-in-glass solvents. Column eluent was collected in 10-mL fractions on a Buchler Fractomette Alpha

Table II. IR and NMR Data on 2-Aryl-1,3-cyclohexanediones

compd no.	IR[a]	NMR[b]
6	2.9–3.9 (enolic OH), 6.23 (C=O), 13.2, 14.4 (aromatic)[c]	2.07 (m, 2 H, CH_2), 2.5 (t, 4 H, CH_2CO), 7.25 (s, 5 H, aromatic)
7[d]	2.9 (enolic OH), 6.2 (C=O), 12.38 (aromatic)	2.03 (s, 6 H, 2′,6′-CH_3), 2.25 (s, 3 H, 4′-CH_3), 2.0–2.7 (m, 6 H, ring CH_2), 6.91 (s, 2 H, aromatic)
8[d]	2.8 (enolic OH), 6.1 (C=O)	2.08 (s, 3 H, 2′-CH_3), 1.8–2.6 (m, 6 H, ring CH_2), 7.1 (m, 4 H, aromatic)
10[d]	2.9 (enolic OH), 6.15 (C=O)	1.15 (s, 6 H, 5,5-CH_3), 2.03 (s, 6 H, 2′,6′-CH_3), 2.28 (s, 3 H, 4′-CH_3), 2.36 (s, 4 H, ring CH_2), 6.90 (s, 2 H, aromatic)
11[d]	2.8 (enolic OH), 6.10 (C=O)	1.13 (s, 6 H, 5,5-CH_3), 2.10 (s, 3 H, 2′-CH_3), 2.34 (s, 4 H, ring CH_2). 7.10 (m, 4 H, aromatic)
12[d]	2.9 (enolic OH), 6.13 (C=O)	1.08 (s, 6 H, 5,5-CH_3), 1.08 (t, 3 H, CH_2CH_3), 2.28 (s, 4 H, ring CH_2), 2.28 (q, 2 H, CH_2CH_3), 7.10 (m, 4 H, aromatic)
13[d]	2.9 (enolic OH), 6.20 (C=O), 7.30, 7.35 (gem CH_3)	1.15 (s, 6 H, 5,5-CH_3), 1.15 (d.,6 H, CH-$(CH_3)_2$), 2.37 (s, 4 H, ring CH_2), 7.10 (m, 4 H, aromatic)
14[d]	2.9 (enolic OH), 6.15 (C=O)	1.20 (s, 6 H, 5,5-CH_3), 1.30 (s, 9 H, C-$(CH_3)_3$), 2.10 (s, 6 H, 2′,6′-CH_3), 2.39 (s, 2 H, ring CH_2), 2.47 (s, 2 H, ring CH_2), 7.12 (s, 2 H, aromatic)
15[d]	2.9 (enolic OH), 6.15 (C=O)	1.15 (s, 6 H, 5,5-CH_3), 2.10 (s, 3 H, 2′-CH_3), 2.31 (s, 3 H, 4′-CH_3), 2.39 (s, 4 H, ring CH_2), 7.10 (m, 3 H, aromatic)
16[d]	2.9 (enolic OH), 6.15 (C=O)	1.15 (s, 6 H, 5,5-CH_3), 2.05 (s, 6 H, 2′,6′-CH_3), 2.36 (s, 4 H, ring CH_2). 7.08 (s, 3 H, aromatic)
17[d]	2.9 (enolic OH), 6.15 (C=O)	1.10 (s, 6 H, 5,5-CH_3), 2.05 (s, 3 H, 2′-CH_3), 2.38 (s, 4 H, ring CH_2). 7.10 (m, 3 H, aromatic)[d]
18[d]	2.9 (enolic OH), 6.13 (C=O)	1.15 (pair of singlets, 6 H, 5,5-CH_3), 2.10 (s, 3 H, 2′-CH_3), 2.38 (s, 4 H, ring CH_2), 7.15 (m, 3 H, aromatic)
19[d]	2.8–3.9 (enolic OH), 6.3 (C=O), 11.23 (isolated aromatic H), 11.52 (2 adjacent aromatic H's)[c]	1.10 (s, 6 H, 5,5-CH_3), 2.07 (s, 3 H, 2′-CH_3), 2.35 (s, 4 H, ring CH_2), 3.80 (s, 3 H, OCH_3), 6.85 (m, 4 H, aromatic and enolic OH)
20[d]	2.9 (enolic OH), 6.33 (C=O), 12.95 (aromatic)[c]	1.18 (s, 6 H, 5,5-CH_3), 2.11 (s, 3 H, 2′-CH_3), 2.41 (s, 4 H, ring CH_2), 3.71 (s, 3 H, OCH_3), 7.00 (m, 3 H, aromatic)
21[d]	2.9 (enolic OH), 6.15 (C=O)	1.15 (s, 6 H, 5,5-CH_3), 2.35 (broad singlet, 7 H, 4′-CH_3 and ring CH_2), 3.75 (s, 3 H, OCH_3), 6.80 (m, 3 H, aromatic)
22[d,e] 23	2.9 (enolic OH), 6.20 (C=O)	1.15 (s, 6 H, 5,5-CH_3), 2.05 (s, 2′,6′-CH_3), 2.30 (s, 4′-CH_3), 2.35 (s, 4 H, ring CH_2), 3.67 (s, OCH_3), 3.75 (s, OCH_3), 6.65 (m, 2 H, aromatic)
24[d]	2.9–3.7 (enolic OH), 4.55 (CN), 6.25 (C=O), 11.3, 11.9	1.12 (s, 6 H, 5,5-CH_3), 2.10 (s, 3 H, 2′-CH_3), 2.42 (s, 4 H, ring CH_2), 7.35 (m, 3 H, aromatic)
25[d]	2.9–3.8 (enolic OH), 4.50 (CN), 6.20 (C=O)[c]	1.15 (pair of singlets, 6 H, 5,5-CH_3), 2.10 (s, 3 H, 2′-CH_3), 2.40 (broad s, 4 H, ring CH_2), 7.05 (m, 3 H, aromatic)[d]
27[d]	2.9 (enolic OH), 6.15 (C=O)	1.50 (broad s, 10 H, spiro ring CH_2), 2.03 (s, 6 H, 2′,6′-CH_3), 2.25 (s, 3 H, 4′-CH_3), 2.40 (s, 4 H, ring CH_2), 6.98 (s, 2 H, aromatic)
28[d]	2.9 (enolic OH), 6.18 (C=O)	1.48 (broad s, 10 H, spiro ring CH_2), 2.10 (s, 3 H, 2′-CH_3), 2.45 (s, 4 H, ring CH_2), 7.10 (m, 4 H, aromatic)
30[d]	2.9 (enolic OH), 6.15 (C=O)	2.00 (s, 2′- or 6′-CH_3), 2.10 (s, 2′- or 6′-CH_3), 2.29 (s, 3 H, 4′-CH_3), 2.78 (m, 4 H, ring CH_2), 3.40 (m, 1 H, CHC_6H_5), 6.91 (s, 2 H, 2-aryl ring H), 7.35 (s, 5 H, 5-aryl ring)
32[d]	2.95 (enolic OH), 6.22 (C=O)	1.0–2.5 (m, 10 H, ring CH_2 and CH), 2.05 (s, 3 H, 2′-CH_3), 7.10 (m, 4 H, aromatic)

[a] Microns. Principal peaks only. Run in $CHCl_3$ unless otherwise indicated. [b] δ in deuteriochloroform (unless otherwise indicated) with tetramethylsilane as the internal standard. Enolic OH usually not recorded. [c] Run in KBr. [d] Satisfactory combustion analytical data for C,H (±0.4%) were provided for these compounds. [e] Isolated and analyzed as the isomeric mixture.

200 Linear Fraction collector. Selected fractions were stripped on a Buchler Rotary Evapo-mix and examined by TLC prior to combining fractions.

Materials. Aromatic solvents used in the photochemical reactions were reagent grade and were used without further purification. Commercially available benzophenone was used as the triplet sensitizer. Some of the diazo ketones used are known compounds and were prepared by the literature methods. Syntheses for the novel 2-diazo-1,3-cyclohexanediones used in this study are presented in the examples below.

2-Phenyl-1,3-cyclohexanedione (6). A solution of 1.50 g (0.0109 mol) of 2-diazo-1,3-cyclohexanedione[11] in 350 mL of dry benzene containing 7.50 g (0.0412 mol) of benzophenone was degassed with N_2 for 1 h and irradiated until an aliquot showed no diazo peak (4.68 μm) in the IR. The irradiation required 3 h. The benzene was removed on the rotary evaporator, and the residue was triturated (3 × 25 mL) with CCl_4 and filtered under N_2 to give 1.06 g (52%) of a white powder. A TLC (70:30 hexane-ethyl acetate) of this material showed one major spot at R_f 0.40 and a trace component at R_f 0.18 (1,3-cyclohexanedione). This material was purified by preparative TLC (2.0 mm thick precoated MN silica gel plates developed with 70:30 benzene-ethyl acetate) followed by recrystallization from benzene to give 600 mg of a white, crystalline solid, mp 154–155 °C [lit.[8] mp 158–159 °C], which showed one spot on TLC at R_f 0.40 (70:30 hexane-ethyl acetate): UV (95% EtOH) λ_{max} 230 (6640), 280 nm (12 307) [lit.[8] λ_{max} 229 (4450), 279 nm (9800)]. When exposed to air for a short period, this compound decomposed to a bright yellow solid.

2-(2′,4′,6′-Trimethylphenyl)-1,3-cyclohexanedione (7). A solution of 5.00 g (0.036 mol) of 2-diazo-1,3-cyclohexanedione[11] in 500 mL of mesitylene containing 32.8 g (0.18 mol) of benzophenone was degassed with N_2 for 1 h and irradiated until an aliquot showed no diazo absorption (4.68 μm) in the IR and TLC (9:1 benzene-ethyl acetate) showed no diazo ketone at R_f 0.31. The irradiation required 11 h. The reaction mixture was extracted with 0.25 N NaOH (4 × 100 mL). The combined base extracts were washed with ether (2 × 200 mL), acidified with 1 N HCl, and extracted into $CHCl_3$ (3 × 75 mL). The $CHCl_3$ extract was dried ($MgSO_4$) and filtered and the solvent removed under reduced pressure to leave 5.06 g of a light-brown solid. A TLC (4:1 benzene-ethyl acetate) of this solid showed major spots at R_f 0.46 and 0.18[12] and minor spots at R_f 0.61, 0.56, and 0.25. This material was chromatographed through 250 g of silica gel, eluting with a gradient from pure benzene to 4:1 benzene-ethyl acetate. All fractions showing a single spot at R_f 0.46 were combined and the solvent removed to leave 2.60 g (31%) of a white solid. This was recrystallized from diisopropyl ether to afford an analytical sample, mp 196–198 °C.

2-(2′,4′-Dimethylphenyl)-5,5-dimethyl-1,3-cyclohexanedione (15) and 2-(2′,6′-Dimethylphenyl)-5,5-dimethyl-1,3-cyclohexanedione (16). A solution of 5.00 g (0.0301 mol) of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione[13] in 500 mL of *m*-xylene containing 27.4 g (0.15 mol) of benzophenone was degassed with N_2 for 1 h and irradiated overnight. The photosylate was extracted with 0.25 N NaOH (4 × 100 mL) and the combined base extracts washed with ether (2 × 75 mL) and acidified with 1 N HCl. The acidified aqueous layer was extracted with $CHCl_3$ (3 × 100 mL), the $CHCl_3$ extracts dried ($MgSO_4$) and filtered, and the solvent removed to give 3.61 g of a tan solid. The synthesis was repeated using 7.00 g (0.042 mol) of diazo ketone and 38.38 g (0.21 mol) of benzophenone in 500 mL of *m*-xylene. The workup described above gave 5.48 g of tan solid. TLC (4:1 benzene-ethyl acetate) of this solid showed a major spot at R_f 0.48 with trace components at R_f 0.60, 0.55, and 0.22 and a moderately intense spot at R_f 0.18. The combined crude product (9.09 g) was chromatographed through 300 g of Woelm silica gel and eluted with 500 mL of benzene, 500 mL of 95:5 benzene-ethyl acetate, 1000 mL of 9:1 benzene-ethyl acetate, and 2000 mL of 4:1 benzene-ethyl acetate. The eluent was collected in 10-mL fractions. Fractions 1–94 contained <0.5 g of a yellow oil which was not characterized. Fractions 95–150 contained a pale yellow solid (2.18 g) which showed one spot at R_f 0.55 (1:1 hexane-ethyl acetate). An analytical sample was prepared by recrystallization from benzene to give a white solid, mp 167–169 °C. This compound was assigned structure **15** on the basis of its NMR.[14] Fractions 151–230 were combined to give 2.0 g of a white solid which analyzed for one spot at R_f 0.57 on TLC (1:1 hexane-ethyl acetate). An analytical sample of this material was obtained by recrystallization from benzene to give white crystals, mp 183–186 °C. This component was assigned structure **16** on the basis of its NMR.

2-Diazo-5-phenyl-1,3-cyclohexanedione (29). A solution of 20.0 g (0.106 mol) of 5-phenyl-1,3-cyclohexanedione[15] in 75 mL of ethanol was cooled to −10 °C and stirred magnetically under N_2. To the mixture was added 10.75 g (0.106 mol) of triethylamine. Tosyl azide (20.95 g, 0.106 mol) was added all at once, and the mixture was stirred for 1 h at 0–5 °C. The solvent was removed on the rotary evaporator (<40 °C), and the residue was taken up in 200 mL of ether. The ether was extracted with a solution of 3.1 g of KOH in 200 mL of water and dried ($MgSO_4$) and the solvent removed to leave a yellow solid. This was recrystallized from hexane-ethanol to give 8.38 g (32%) of a yellow, crystalline solid: mp 122–124 °C; IR ($CHCl_3$) 4.41, 4.54 ($=N_2$), 6.01 μm (C=O).

2-(2′,4′,6′-Trimethylphenyl)-5-phenyl-1,3-cyclohexanedione (30). A solution of 7.0 g (0.0327 mol) of 2-diazo-5-phenyl-1,3-cyclohexanedione and 29.77 g (0.163 mol) of benzophenone in 500 mL of mesitylene was degassed for 1 h with N_2 and irradiated overnight. The photolysis mixture was extracted with 0.25 N NaOH (4 × 100 mL) and the combined base extracts washed with ether (2 × 75 mL), acidified with 1 N HCl, and extracted with $CHCl_3$ (4 × 100 mL). The combined $CHCl_3$ extracts were dried ($MgSO_4$), and the solvent was removed to give 7.5 g of a tan solid. After chromatography through silica gel with benzene-ethyl acetate, 5.7 g (57%) of a white solid was obtained. An analytical sample was prepared by recrystallization from benzene-ethyl acetate to give a white, crystalline solid, mp 215–216 °C.

2-Diazodecalin-1,3-dione (31). A solution of 10.0 g (0.0768 mol) of decalin-1,3-dione[16] in 50 mL of ethanol was magnetically stirred under nitrogen and cooled to −10 °C. To this solution was added 7.77 g (0.0768 mol) of triethylamine followed by 15.14 g (0.0768 mol) of tosyl azide added all at once. The mixture was stirred for 1 h at 0 °C and the solvent removed (<40 °C). The residue was taken up in 200 mL of ether and the ether washed with a solution of 8.0 g of KOH/400 mL of water, dried ($MgSO_4$), filtered, and removed to yield a yellow solid. This was recrystallized from ethanol to give 5.23 g (35%) of a yellow, crystalline solid: mp 81–83 °C; IR ($CHCl_3$) 4.65 ($=N_2$), 6.06 μm (C=O).

2-(2′-Methylphenyl)decalin-1,3-dione (32). A solution of 7.0 g (0.0364 mol) of 2-diazodecalin-1,3-dione and 33.18 g (0.182 mol) of benzophenone in 500 mL of toluene was degassed for 1 h with N_2 and irradiated overnight. The photolysis mixture was extracted with 0.25 N NaOH (4 × 100 mL), acidified with 1 N HCl, and extracted with chloroform. The $CHCl_3$ extracts were combined and dried ($MgSO_4$) and the solvent removed to give 4.56 g of an amorphous yellow solid. This was purified by column chromatography through silica gel, using a benzene-ethyl acetate elution gradient. The solid obtained (3.2 g, 34%) was recrystallized from benzene to give an analytical sample, mp 165–167 °C.

2-(2′-Methylphenyl)-5,5-dimethyl-1,3-cyclohexanedione (11). An authentic sample of this compound was prepared for structure confirmation, using the following procedure. To a solution of sodium ethoxide in ethanol (prepared by adding 45.45 g, 1.98 g-atom, of sodium to 560 mL of anhydrous ethanol) was added, dropwise, a solution of 440.0 g (2.037 mol) of diethyl

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[11] H. Stetter and K. Kiehs, *Chem. Ber.*, **98**, 1181 (1965).

[12] The material at R_f 0.18 was isolated by preparative TLC of the crude photolysis mixture. The physical properties (mp, IR, NMR, TLC) indicated this component to be 5,5-dimethyl-1,3-cyclohexanedione.

[13] M. Regitz and D. Stadler, *Justus Liebigs Ann. Chem.*, **687**, 214 (1967).

[14] The structure of this compound was confirmed by independent synthesis. Ethyl 3,3-dimethylglutarate was condensed with 2,4-dimethylphenylacetonitrile to give ethyl 6-(2′,4′-dimethylphenyl)-6-cyano-5-keto-3,3-dimethylhexanoate which was hydrolyzed, decarboxylated, and cyclized to give 2-(2′,4′-dimethylphenyl)-5,5-dimethyl-1,3-cyclohexanedione. This material was identical in all respects (mp, IR, NMR, TLC) with the photochemically synthesized material.

[15] K. W. Rosenmund, H. Herzberg, and H. Schutt, *Chem. Ber.*, **87**, 1258 (1954).

[16] C. K. Chuang and Y. L. Tien, *Chem. Ber.*, **69**, 27 (1936).

3,3-dimethylglutarate and 200.0 g (1.52 mol) of 2-methylphenylacetonitrile. The reaction mixture was stirred and refluxed under N_2 with slow removal of the ethanol until 80% of the ethanol had been removed. The mixture was cooled to 25 °C, poured into ice water, and extracted with ether (3 × 300 mL). The basic aqueous solution was acidified with cold 6 N HCl and the resulting oil extracted into ether. The combined ether extracts of the acidified aqueous layer were washed with water, dried ($MgSO_4$), and filtered and the ether removed to leave 309.1 g (67%) of a light yellow viscous oil. Spectral data indicate this to be ethyl 6-(2′-methylphenyl)-6-cyano-5-keto-3,3-dimethylhexanoate: IR (neat) 3.17–3.66 (enolic OH), 4.54 (CN), 5.68 (ester C=O), 5.95 (ketone C=O), 6.10, 6.21 μm (enolic C=C); NMR ($CDCl_3$) δ 0.75–1.43 (m, $CO_2CH_2C\mathbf{H}_3$), 1.22 (s, 3,3-CH_3), 2.32 (s, 2′-CH_3), 2.36 (s, $C\mathbf{H}_2CO_2Et$), 2.73 (s, $C\mathbf{H}_2CO$), 4.23 (q, $CO_2C\mathbf{H}_2CH_3$), 4.93 and 12.3 (s, CHCN and enolic OH), 7.23 (m, aromatic).

A solution of 296.1 g (0.982 mol) of ethyl 6-(2′-methylphenyl)-6-cyano-5-keto-3,3-dimethylhexanoate, 880 mL of glacial acetic acid, 310 mL of water, and 310 mL of concentrated sulfuric acid was refluxed for 48 h. The mixture was cooled to room temperature, and 600 mL of water and 300 mL of isopropyl ether were added. The mixture was stirred and cooled in an ice bath and filtered and the white solid washed several times with water and several times with isopropyl ether. This solid was dried overnight in a vacuum oven to give a white powder, mp 179.5–180.5 °C.

The mixed melting point of this material and the product obtained from the photolysis of 2-diazo-5,5-dimethyl-1,3-cyclohexanedione in toluene is 179–180 °C. The IR, NMR, and TLC of **11** prepared by photolysis and **11** prepared by the above method are identical.

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Registry No. **5**, 1460-08-8; **6**, 56964-05-7; **7**, 68427-45-2; **8**, 71871-65-3; **9**, 1807-68-7; **10**, 71885-47-7; **11**, 724-40-3; **12**, 71871-66-4; **13**, 71871-67-5; **14**, 68427-50-9; **15**, 68427-46-3; **16**, 68427-47-4; **17**, 71871-68-6; **18**, 71871-69-7; **19**, 71871-70-0; **20**, 71871-71-1; **21**, 71871-72-2; **22**, 71871-73-3; **23**, 71871-74-4; **24**, 71871-75-5; **25**, 71871-76-6; **26**, 7230-19-5; **27**, 71871-77-7; **28**, 71871-78-8; **29**, 68427-48-5; **30**, 68427-49-6; **31**, 68427-51-0; **32**, 68427-52-1; benzene, 71-43-2; mesitylene, 108-67-8; toluene, 108-88-3; ethylbenzene, 100-41-4; cumene, 98-82-8; 3,5-dimethyl-*tert*-butylbenzene, 98-19-1; *m*-xylene, 108-38-3; *m*-chlorotoluene, 108-41-8; *m*-methylanisole, 100-84-5; 3,5-dimethylanisole, 874-63-5; *m*-tolunitrile, 620-22-4; ethyl 3,3-dimethylglutarate, 71885-49-9; 2,4-dimethylphenylacetonitrile, 68429-53-8; ethyl 6-(2′,4′-dimethylphenyl)-6-cyano-5-keto-3,3-dimethylhexanoate, 68427-53-2; 5-phenyl-1,3-cyclohexanedione, 493-72-1; tosyl azide, 941-55-9; decalin-1,3-dione, 68429-52-7; diethyl 3,3-dimethylglutarate, 17804-59-0; 2-methylphenylacetonitrile, 22364-68-7; ethyl 6-(2-methylphenyl)-6-cyano-5-keto-3,3-dimethylhexanoate, 71871-79-9.

Photoisomerizations of Protonated Phenols. Extension of the Photochemistry of Cyclohexa-2,5-dienones

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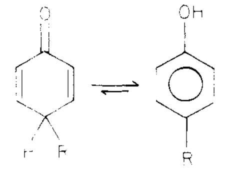
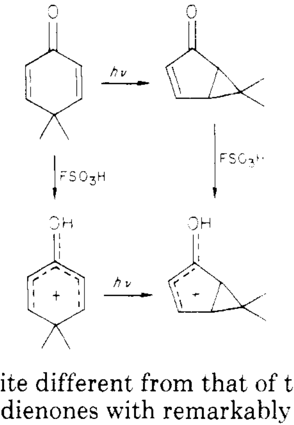
Protonated methyl-substituted phenols have been found to undergo a variety of photoisomerizations when irradiated at a low temperature in FSO_3H. The products obtained depend upon the wavelength of the light used. The general sequence of reactions was shown to be the photochemical transformation of the para-protonated form of a phenol ($\lambda_{max} \sim 310$ nm) to the corresponding protonated bicyclo[3.1.0]hex-3-en-2-one, a reaction which is directly comparable to the photoisomerization observed with cross-conjugated cyclohexadienones. Several bicyclo[3.1.0]hex-3-en-2-ones were recovered by neutralization of the acid solutions. The second step in the overall photoisomerization sequence involved the transformation of the protonated bicyclohexenones ($\lambda_{max} \sim 330$ nm) to protonated phenols. The extent of the photoreaction of the starting protonated phenol was governed by the wavelength of the light used for the irradiation; light of wavelength 300 nm drove only the first step of the sequence, while with broad band irradiation ($\lambda > 320$ nm) both steps occurred. One exception to this general behavior was found with protonated 2,4,6-trimethylphenol. In this case a meta-protonated isomer ($\lambda_{max} \sim 373$ nm) was converted to protonated 1,3,5-trimethylbicyclohex-3-en-2-one on irradiation with light of wavelength greater than 360 nm. With shorter wavelength light, photoisomerizations of the para-protonated form of 2,4,6-trimethylphenol were also observed.

While the photochemical reactions of a large variety of cross-conjugated cyclohexadienones have been examined,[1] these studies have not been extended to molecules having less than two substituents at C_4. The reason for this apparent neglect is not hard to find. Such compounds are difficult to prepare and readily revert to their more stable phenolic tautomers, eq 1. The photochemical behavior of phenols is quite different from that of the cross-conjugated cyclohexadienones with remarkably few isomerization reactions being reported.[2,3]



(1)

Scheme I



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[1] For reviews see: D. I. Schuster, *Acc. Chem. Res.*, 11, 65 (1978); P. J. Kropp, *Org. Photochem.*, 1, 1 (1967); K. Schaffner, *Adv. Photochem.*, 4, 81 (1966); H. E. Zimmerman, *ibid.*, 1, 183 (1963).