Notes

Photochemical Reactions of 2,4-Diethyl-2,4-diphenyl-1,3-cyclobutanedione in Benzene and in Isopropyl Alcohol[1]

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Introduction

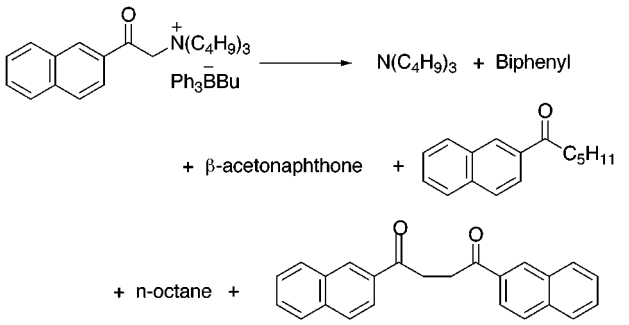
Our group has recently identified several new ways to photochemically alter polymeric thin films and surfaces.[2] Our most versatile strategy employs a tetraorganylborate, chromophore-containing ammonium salt,[3] activated by an intramolecular single electron transfer from the borate to the excited state of the chromophore releasing a radical and trisubstituted borane from the oxidized borate.

The reduced chromophore, under the appropriate circumstances, decomposes to a second radical often more stable than the first, by releasing free amine. For example, products from the photolysis of *N*,*N*,*N*-tributyl-*N*-acetonaphthone ammonium butyltriphenylborate arise from the 2-acetonaphthyl radical and butyl radical. These are shown, along with tributylamine, in Scheme 1.[4]

Each of the reaction intermediates produced in this intramolecular single electron-transfer process can be used for its own purpose. In the example given, the butyl radicals produced can be used to initiate vinyl polymerization,[5] while the tributylamine can be used to catalyze the thermal polymerization of epoxides.[2d] This salient chemistry predicted the use of these compounds, and close analogues, in imaging methodologies derived from the basic studies of the photochemistry of benzophenonemethyltri-*n*-butylammonium butyltriphenylborate.[6] Photoimaging phenylglyoxylate moieties in thin films[7] was similarly predicted from studies of model compounds.

1,3-Cyclobutanediones seemed attractive for modifying films since they are readily available precursors for photogeneration of cyclopropanones. Cyclopropanones, relatively reactive compounds, resisted synthesis by classical routes until the Turro group reported that tetramethyl-1,3-cyclobutanedione produced a stable cyclopropanone when irradiated in protic solvents.[8] Tetramethyl-1,3-cyclobutanedione also undergoes Norrish I α-cleavage upon UV irradiation in inert solvent, this being followed by decarbonylation and intramolecular radical coupling to afford tetramethylcyclopropanone as the primary product (70−80%), along with dimethyl ketene (20−30%).[9,10] Cyclobutanediones are stable compounds but, under mild conditions, easily form adducts with a wide range of compounds, such as alcohols, primary or secondary amines, olefins, and dienes when irradiated with UV light.[11] Thus, a set of such compounds could be coupled onto a surface that could be functionalized in a spatially specific manner by selective irradiation and further incubation. The chemistry of the cyclopropanone could thus serve as a link between the solid surface and the reactive compounds in solution.

Scheme 1



We chose **1** as a model compound from which to develop the idea. The initial plan was that the phenyl groups could be conveniently functionalized with acrylate or styrene moieties for facile conversion to a polymeric 1,3-cyclobutanedione. However, as it turns out, phenyl substitution causes the reaction pathways to vary from those observed with tetraalkylcyclobutanediones. This, in part, is reported in this paper.

Results and Discussion

Irradiation of either ***cis*-1** or ***trans*-1** at 350 nm in benzene gave isomeric indanones **2** and **3** in 70−80% yield. Stereochemical assignment is based on the ^{1}H NMR spectra in that the phenyl group on C1 has a

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Scheme 2

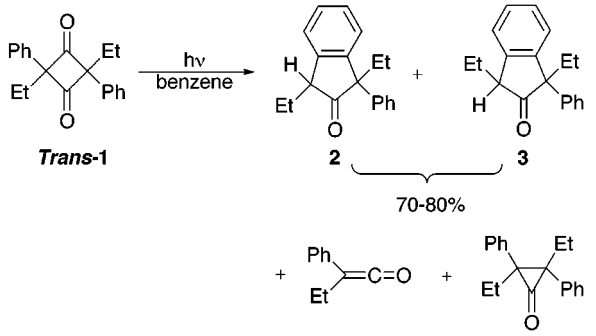

Table 1. Yields[a] and the Quantum Yields in the Photolysis[b]

		yield (%)							
	solvent	**2**	**3**	**4**	**5**	**6**	**7**	**8**	ϕ^c
***cis*-1**	benzene	50	17					12	0.1
***cis*-1**	isopropyl alcohol	30	20	28	7			8	0.95
***trans*-1**	benzene	50	32					10	0.1
***trans*-1**	isopropyl alcohol	35	15			20	15	5	0.9

[a] Yields were obtained from the ^{1}H NMR data of the crude photo product using mesitylene as the internal standard. [b] Yields and quantum yields were measured at ambient temperature. [c] Quantum yield of the disappearance of the starting material.

deshielding effect on the ethyl group at the 3 position. Reaction of ***trans*-1** is shown in Scheme 2. Formation of the ketene was detected by GC/MS, and the resulting spectrum was compared with that of an authentic sample. The infrared spectrum of the reaction mixture was measured immediately after photolysis. The existence of cyclopropanone was supported by the observation of a weak IR band at 1857 cm^{-1}. The yields and quantum yields are shown in Table 1.

Alcohol solvents had been used previously to trap the reactive intermediate ketene and cyclopropanone formed from the photolysis of tetramethyl 1,3-cyclobutanedione.[9] Unexpectedly, we found irradiation of ***cis*-1** or ***trans*-1** in isopropyl alcohol gave a stereoisomeric mixture of cyclic acetals **4/5** or **6/7** respectively, as well as the indanones and solvent trapped ketene **8**. The stereochemistry at the 2 and 4 positions of the starting cyclobutanedione remains intact throughout the reaction, and there is no attendant isomerization.

Acetal formation is well-known in the photochemistry of cyclobutanones,[12] but unprecedented for 1,3-cyclobutanediones. The mechanism suggested in the cyclobutanone photolysis case is that the 1,4 acyl alkyl biradical formed upon α-cleavage rearranges to cyclic oxacarbene through electronic reorganization.[13] Subsequent H−O bond insertion by the carbene in the solvent produces the cyclic acetal. Attempts to trap the oxacarbene formed using a variety of alkenes were unsuccessful, and in nonreactive solvents, the major product is the indanone. These results imply that the 1,4 biradical and oxacarbene interconvert, and product formation is driven by the relative reactivity of the carbene-trapping reagent. ^{1}H NMR data suggest acetals **4** and **6** bear acetal hydrogens on the same side of the adjacent phenyl group. The preference of formation of **4** and **6** over their epimers is attributed to the steric effect of the phenyl group on carbene insertion, especially when the two phenyls are

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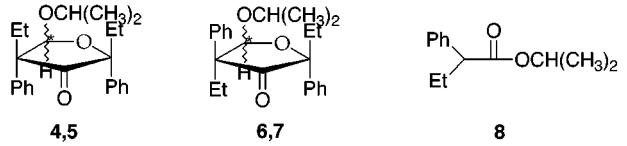
Scheme 3



cis to each other. They thus provide steric interference on one side of the ring that, under such circumstances, produces a high ratio of **4:5**, Scheme 3. The preferred formation of **4** from ***cis*-1** could be synthetically useful.

We suggest (Scheme 4) that irradiation of **1** leads through Norrish I α-cleavage to a 1,4-biradical that decays by three pathways: (i) cycloelimination to generate ketene, which could be trapped by alcoholic solvents; (ii) decarbonylation to produce the 1,3 diyl biradical, subsequent ring closure of which leads to the cyclopropanone (A major alternative process for the 1,3-biradical is attack on the phenyl ring at the ortho position by one of the radical sites. This forms intermediate **9**, a conjugated ketone. Rearomatization through a [1,3] hydrogen shift affords indanone as the final product, and the intermediacy of **9** allows no stereochemistry to be inherited from the starting compound.); (iii) ring expansion through electronic reorganization to oxacarbene **10**, which is trapped by alcohol (in inert solvent, regeneration of the 1,4-biradical from **10** prevails, and no product from oxacarbene was detected).

The quantum yield of the disappearance of **1** was larger in alcoholic solvent than in benzene. A similar phenomenon was observed for tetramethylcyclobutanedione, only it is less prominent. The high quantum yield in isopropyl alcohol is mainly attributed to the existence of oxacarbene intermediate **10**, and its further reaction with solvent to produce acetal in competition with the intramolecular coupling reaction of the 1,4-biradical to regenerate the starting material.

The photolysis of ***cis*-1** in methyl alcohol-*d* produced cyclic acetals **4** and **5** that were >95% (from ^{1}H NMR and MS analysis) deuterated at the methine site of the acetal carbon. This result supports the mechanism we proposed for the acetal generation in that the corresponding oxacarbene **10** is an intermediate in the deactivation process of the 1,4-biradical. Also, we observed indanones **2** and **3** to be 60% deuterated at the 3 position (calculated from the GC/MS data). This is attributed to the 1,3-hydrogen transfer during rearomatization from intermediate **9**. In this reaction, a hydrogen from the phenyl ring may exchange with deuterium from the solvent.

To prove the existence of the biradical intermediates, we synthesized 2,4-dicyclopropyl-2,4-diphenyl-1,3-cyclobutanedione (**11**), hoping the ring opening of the cyclopropylcarbinyl radical could compete with the original decay processes, Scheme 5. However, irradiation of **11** in C_6D_6 afforded no ring-opened product that could be detected on ^{1}H NMR, because the phenyl substituent on the radical site provides substantial thermodynamic stability. The ring-opening process is slowed, while the reverse reaction is favored.[14]

The photolysis of ***trans*-1** and ***cis*-1** in the presence of thiophenol revealed that trapping of the oxacarbene

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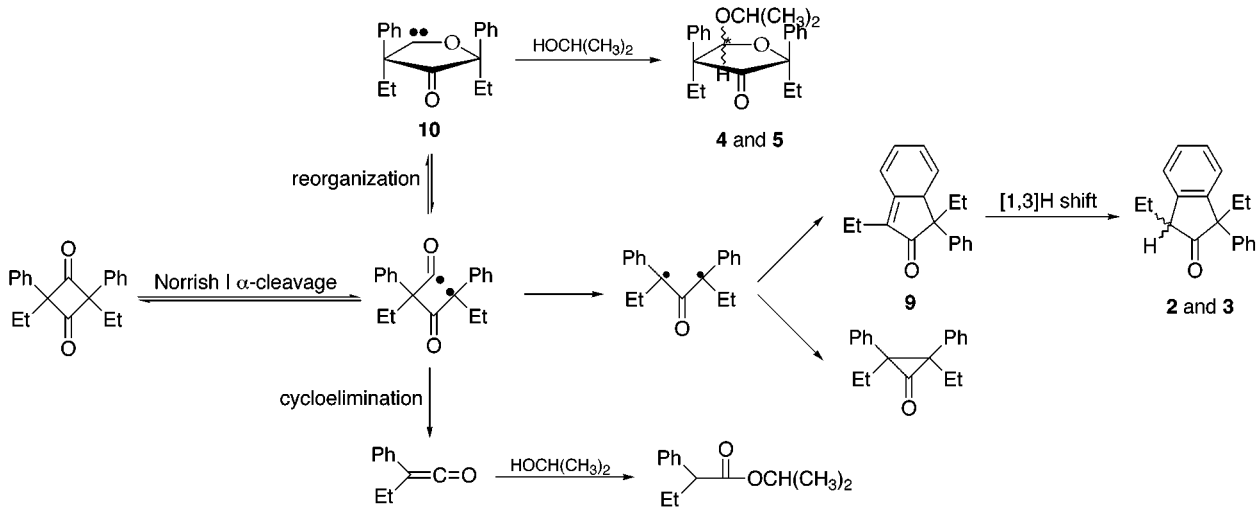
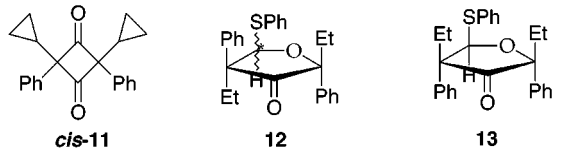
Scheme 4. Proposed Mechanism



Scheme 5



intermediate by thiophenol was more efficient than by alcohol. Mercaptal **12** was observed to form in as high as 85% yield from ***trans*-1**, and mercaptal **13** was formed in high yield from ***cis*-1**. No H-transfer to the biradical was observed, even though a high thiophenol concentration (2 mol/L) was used. Since alkyl substitution has little effect on the rate of atom transfer,[15] H-abstraction by the benzyl radical from thiophenol for which $k = 3.13 \times 10^5$ M^{-1} s^{-1} at 25 °C[16] could be a good model for our system. Assuming 5% of the radical trapping product could be detected on GC/MS, this experiment indicates that the upper limit for the biradical lifetime is around 80 ns.

Experimental Section

General Information. NMR spectra were recorded in $CDCl_3$ with TMS (0 ppm) as the internal reference for ^1H (200 or 400 MHz) or solvent (77.0 ppm) as the internal reference for ^{13}C (50MHz). Infrared spectra were recorded on a FTIR spectrometer in concentrated CCl_4 solution. UV−vis spectra were obtained using a Hewlett-Packard Diode Array spectrometer and were taken in benzene solution. GC measurements were carried out on a Hewlett-Packard 5890 instrument (FID detector), with a 30 m J&W DB-1 capillary column. GC/MS spectra were determined at an ionizing voltage of 70 eV. Flash chromatography was performed using silica gel 60 (70−270 mesh or 230−400 mesh). Thin-layer chromatography was conducted with Whatman silica 60 gel F_{254} plates, with thickness of 250 μm. HRMS were obtained from Mass Spectrometry Lab of the University of Illinois at Urbana−Champaign. All reagents were purchased from Aldrich Chemical Co. and used as received, unless otherwise noted. Benzene was distilled under Ar from sodium/benzephenone immediately prior to use.

General Procedures for Irradiation and Product Isolation. A Pyrex tube containing dilute (~0.01 M) solution of the 1,3-cyclobutanedione derivative was degassed with dry argon for 10−15 min. It was next sealed and irradiated at ambient temperature in Rayonet PRP-100 photoreactor equipped with 15 350 nm GEF8T5/BLB lamps and a circulating water jacket. Completion of the reaction was indicated by the disappearance of the starting material by GC/MS. After photolysis the ^1H NMR was compared with those of the separated products. Flash column chromatography was performed using hexanes and ethyl acetate as eluting solvents. Quantum yields were determined by GC using valerophenone as the actinometer and chlorobenzene as the internal standard. The absorption of the starting material was adjusted to a same value, and the conversion was controlled below 10%.

***cis*- and *trans*-2,4-Diethyl-2,4-diphenyl-1,3-cyclobutanedione (1).** The title compounds were synthesized from 2-phenylbutyryl chloride by a modification of the procedure described by Dehmlow.[17] Prior to heating to 100 °C to form the dimer, vacuum distillation was performed to purify the ketene. This resulted in superior yields. Flash chromatography was employed to purify the two stereoisomers, which were then be separated by preparative TLC using hexanes:ethyl acetate = 20:1 as developing solvents. ^1H NMR and ^{13}C NMR spectra were consistent with those in the literature. A difference in the UV−vis spectra of ***cis*-1** and ***trans*-1** was observed: for ***cis*-1**, the [n−π^*] transition had a $\lambda_{max} = 344$ nm with $\epsilon = 69$, while for ***trans*-1**, the same transition had a λ_{max} at 346 nm, with $\epsilon = 136$.

***(±)-(1R*,3R*)*-1,3-Diethyl-1-phenyl-2-indanone (2) and *(±)-(1R*,3S*)*-1,3-Diethyl-1-phenyl-2-indanone (3).** Flash column chromatography was performed after the photolysis of **1** in benzene. The isomers were characterized by their MS, high-resolution CIMS, and ^1H and ^{13}C NMR spectra. The MS fragmentation patterns were similar for the two isomers: 91, 115, 128, 129, 178, 179, 207(base), 235, 236, 264. Compounds **2** and **3** could thermally isomerize between themselves on the GC. HR-CIMS: calcd for (M + H) *m/z* 264.151415, found 264.151391.

For **2**: ^1H NMR ($CDCl_3$, 200 Hz) δ 7.42−7.37 (m, 3H), 7.30−7.17 (m, 6H), 3.37 (t, 1H, $J = 6.6$), 2.61−2.44 (m, 1H), 2.14−2.00 (m, 1H), 1.81−1.66 (m, 2H), 0.75 (t, 3H, $J = 7.2$), 0.68 (t, 3H, $J = 7.2$); ^{13}C NMR δ 219.8 (C), 143.0 (C), 141.7 (C), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.7 (CH), 127.3 (CH), 126.8 (CH), 124.6 (CH), 63.1 (C), 54.1 (CH), 32.1 (CH_2), 25.8 (CH_2), 11.3 (CH_3), 9.7 (CH_3); IR 3061, 3021, 2967, 2934, 2876, 1745, 1445, 1149 cm^{-1}.

For **3**: ^1H NMR ($CDCl_3$, 200 Hz) δ 7.42−7.36 (m, 3H), 7.27−7.16 (m, 6H), 3.45 (t, 1H, $J = 6.6$), 2.68−2.51 (m, 1H), 2.15−1.92 (m, 3H), 0.94 (t, 3H, $J = 7.2$), 0.68 (t, 3H, $J = 7.2$); ^{13}C NMR δ 218.4 (C), 142.6 (C), 141.7 (C), 141.0 (C), 128.4 (CH), 127.7 (CH), 127.5 (CH), 126.9 (CH), 125.8 (CH), 124.3 (CH), 63.1 (C), 51.2 (CH), 30.4 (CH_2), 21.8 (CH_2), 11.0 (CH_3), 10.3 (CH_3); IR 3064, 2936, 2878, 1745, 1440−1490 (multi), 908, 756 cm^{-1}.

2,4-Diethyl-2,4-diphenyl-5-isopropoxytetrahydrofuran-3-ones (4−7). For **4**: ^1H NMR ($CDCl_3$, 400 Hz) δ 7.27−7.22 (m,

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(17) Dehmlow, E. V.; Slopianka, M. *Liebigs Ann. Chem.* **1979**, 572−593.

2H), 7.12−7.02 (m, 8H), 5.80 (s, 1H), 4.27−4.05 (septet, 1H, J = 6.0), 2.14−2.09 (m, 1H), 2.10−1.99 (m, 1H), 1.98−1.87 (m, 1H), 1.33−1.31 (d, 3H, J = 6.0), 1.28−1.26 (d, 3H, J = 6.0), 0.74 (t, 3H, J = 7.0), 0.70 (t, 3H, J = 7.2); ^{13}C NMR δ 214.6 (C), 138.8 (C), 136.6 (C), 128.41 (CH), 127.6 (CH), 127.1 (CH), 126.8 (CH), 126.6 (CH), 124.8 (CH), 102.3 (CH), 85.9 (CH_2), 69.9 (CH), 60.0 (CH_2), 33.1 (CH_2), 25.2 (CH_2), 23.3 (CH_3), 21.4 (CH_3), 8.1 (CH_3), 7.43 (CH_2); IR 1757 cm^{-1} for C=O stretching; HRMS (CI) calcd for (M + H) m/z 351.196020, found 351.195900.

The other isomers were not separable and had similar MS fragmentation patterns: 77, 91, 105, 117, 133, 148(base), 190, 207, 235, 264, 293. The distinctive chemical shifts for the acetal hydrogens for the other isomers are δ 5.83, δ 5.41, and δ 5.39. According to the ^{1}H NMR analysis and molecular modeling, the stereochemistry of **4** is with acetal proton being *cis* to the two phenyl groups.

Trapping with Thiophenol. Compounds ***cis*-1** or ***trans*-1** (0.02 mol/L in benzene) along with 10% (v/v) thiophenol was placed in a Pyrex tube, degassed with Argon, sealed, and irradiated until the starting material disappeared. Only one racemic thioacetal **13** was formed from ***cis*-1** in 60% yield, while two racemic isomers in the ratio 1:2 were produced in 60% yield from ***trans*-1**. Phenylthiol-2-phenyl butyrate was produced, along with traces of **2** and **3** in both cases. The yield of acetal increased with increasing concentration of thiophenol.

2,4-Diethyl-2,4-diphenyl-5-phenylthiotetrahydrofuran-3-one (12). The stereoisomers of **12/13** could not be separated from the thiol ester by column chromatography. The isomers had similar MS patterns: 57, 77, 91 (base), 105, 118, 145, 219, 265, 293. The distinctive chemical shifts for the acetal hydrogens are δ = 5.735 (**13**) and δ = 5.509, 5.893 (**12**).

***cis*- and *trans*-2,4-Dicyclopropyl-2,4-diphenyl-1,3-cyclobutanedione (11).** The precursor, cyclopropyl phenyl ketene, was synthesized according to a five-step synthetic strategy described by Tidwell.[18] After vacuum distillation, the ketene was heated to 120 °C for 3 days. Subsequent column chromatography afforded pure ***trans*-11** and ***cis*-11**, which were characterized by ^{1}H NMR, ^{13}C NMR, MS, and HRMS. Identical MS patterns were observed for the two isomers: 77, 91, 102, 115, 129, 130, 158(base), 202, 215; HRMS calcd for M$^+$ m/z 316.146330, found 316.146026.

For ***trans*-11**: ^{1}H NMR ($CDCl_3$, 200 Hz) δ 7.62−7.57 (m, 4H), 7.44−7.32 (m, 6H), 1.21 (tt, 2H), 0.41−0.20 (m, 4H); ^{13}C NMR δ 206.7 (C), 133.5 (C), 128.8 (CH), 127.7 (CH), 125.8 (CH), 81.1 (C), 17.4 (CH), 1.9 (CH_2).

For ***cis*-11** ^{1}H NMR ($CDCl_3$, 200 Hz) δ 7.31−7.14 (m, 10H), 1.49 (tt, 2H), 0.61−0.58 (m, 8H); ^{13}C NMR δ 207.1 (C), 133.9 (C), 128.6 (CH), 127.6 (CH), 126.0 (CH), 82.1 (C), 15.5 (CH), 2.1 (CH_2).

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