J. Org. Chem. 1990, 55, 5165–5170

1 is a compound with considerable biological interest, which is further heightened by the observation that it is mutagenic.[8] The reactions of 1 with nucleophiles such as the nucleic acid bases[19c] and proteins[19d] have been reported. Our NMR observations suggest that at pH 7.4 ("physiological pH") 1 exists completely in the form of its sodium salt (see Table I and Figure 2). This conclusion is supported by UV studies, which show spectral changes from pH 2.8 to 6.5 but none above pH 6.5.[17] We believe these conclusions should also hold in biological systems and may be relevant to the reactivity of 1 in such systems.

Summary

The intramolecularly H-bonded cis enolic form of malondialdehyde in chloroform is converted to an intermolecularly H-bonded trans enol by methoxy compounds such as methanol and 3,3-dimethoxypropanal. "Polar impurities" such as acetone and dioxane do not induce this effect. In aqueous solution sodio-1 predominates at pH >6. Based upon ^{1}H NMR coupling constants, both 1 and sodio-1 have the trans configuration in aqueous solution.

Experimental Section

Caution. Malondialdehyde, 3,3-dimethoxypropanal, and especially β-methoxyacrolein have been reported to be mutagenic[8] and should be handled with utmost care.

Malondialdehyde (1) was prepared by either the acid-catalyzed hydrolysis of 1,1,3,3-tetramethoxypropane (2) or the protonation of sodio-1. The hydrolysis of 2 was carried out by using the procedures of Protopopova and Skoldinov (12 mmol of 2, 1 mmol of HCl/3.5 mL of water)[9a] or Bertz (10 mmol of 2, 10 mmol of HCl/10 mL of water)[7] and was followed by ^{1}H NMR spectroscopy with solvent suppression. The former procedure required 75 min at 25 °C followed by 10 min at 55 ± 5 °C. The latter was followed for 75 min at 25 °C; the amount of 1 became constant after 45 min. The aqueous solutions were extracted with equal volumes of deuteriochloroform, which were used for the NMR studies summarized in Tables I and III. To obtain NMR spectra in pure water, an internal capillary of acetone-d_6 was used for locking the spectrometer.

For the studies in which MeOH, 1,1-DME, or acetone was added, 1 was obtained by acidification (pH 1) of 1 M aqueous solutions of sodio-1.[9a,19] The solid sodio-1 had been dried for 6 days at 100 °C/0.1 mTorr. ^{13}C NMR (H_2O, pH 9.6): δ 193.9, 193.04 (shoulder), 193.0, 192.5, 109.5, 109.3 ppm. Minor peaks at δ 193.8, 193.7, 193.2, 192.8, 192.7, 192.5 (shoulder), 192.3, 191.9, 191.8, 191.7, 191.6 ppm. ^{13}C NMR (H_2O, pH 1): δ 186.1, 111.5 ppm. ^{13}C NMR ($CDCl_3$): δ 181.5, 103.5 ppm. Extraction with an equal volume of deuteriochloroform and drying over anhydrous sodium sulfate gave the material used for the addition of MeOH (Mallinckrodt anhydrous, 0.01% water actual lot analysis), 1,1-DME (stored over 5A molecular sieves), or acetone (dried over 5A molecular sieves). In one of the MeOH runs 1,4-dioxane (4 equiv), which had been added to the aqueous solution of sodio-1 as an internal standard, was also present (see text). Benzene (100 μL) was added to the deuteriochloroform solutions as an internal standard, or the residual $CHCl_3$ peak was used. Deuteriochloroform solutions were referenced with TMS; aqueous solutions with sodium 3-(trimethylsilyl)-1-propanesulfonate (DSS), which was also used as an internal standard for integration. NMR spectra were obtained with a Bruker AM 360; parameters were used that gave 0.1-Hz digital resolution.

Acknowledgment. S.H.B. wishes to thank Prof. H. Quast (Würzburg) for suggesting that we reinvestigate this problem, and we thank A. M. Mujsce (AT&T Bell Laboratories) for GC–MS analyses.

Supplementary Material Available: Table of data for the addition of acetone, 1,1-DME, or MeOH to 1 (1 page). Ordering information is given on any current masthead page.

Diaryl-Substituted Maleic Anhydrides

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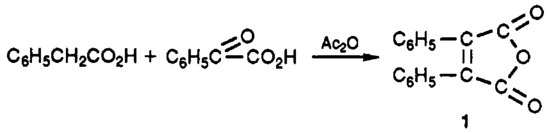
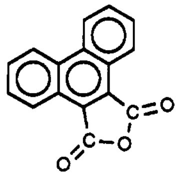
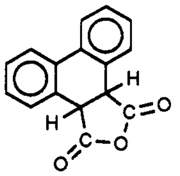
In previous work we have described the photodimerization of 1-cyclohexene-1,2-dicarboxylic anhydride[1] and the preparation and properties of polyimides derived from the photodimer as well as from the photodimer of dimethyl maleic anhydride.[2] Although these polyimides exhibited good thermal and hydrolytic stability, we wished to prepare fully aromatic analogues of dimethylmaleic anhydride and especially its photodimer for optimum physical and chemical properties.

A report by Fager that diphenylmaleic anhydride gave a photodimer[3] led us to investigate the aryl-substituted maleic anhydrides. Various routes to diphenylmaleic anhydride (1) were surveyed by Koelsch and Wawzonek[4] who concluded that the best synthesis by far was a Perkin condensation of benzoylformic acid as the mixed K–Na salt with phenylacetic acid by acetic anhydride. We prepared several hundred grams of diphenylmaleic anhydride this way and tried to duplicate Fager's photodimerization. Both NMR and mass spectrometry showed that the product of UV irradiation was a mixture of the phenanthrene dicarboxylic anhydride and its dihydro derivative.



1





When diphenyl anhydride was irradiated in solution with iodine and O_2, only the phenanthrene anhydride formed. Its physical properties were identical with the putative photodimer. A scale model shows that diphenylmaleic anhydride is crowded, and that explains its ready cyclization by loss of H_2 from the excited state.

Under electron impact diphenylmaleic anhydride shows a large peak for loss of CO, but only a small peak for loss of CO_2. This pattern constitutes a reversal of that characteristic of maleic and phthalic anhydrides and their derivatives generally.[5-9] The difference in behavior must be attributed to the phenyl substituents, presumably by

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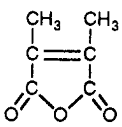
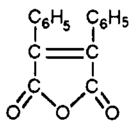
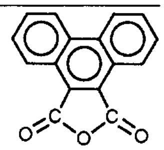
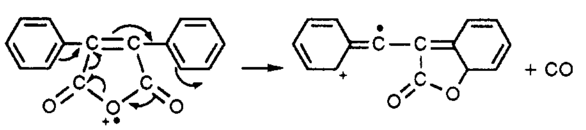
Table I. Relative Peak Intensities

			
$M^{\bullet+}$	22.3	70.6	93.4
$(M - CO)^{\bullet+}$	0.1	15.7	2.4
$(M - CO_2)^{\bullet+}$	69.8	0.6	36.0
$(M - CO, CO_2)^{\bullet+}$	100.0	100.0	100.0

virtue of their ability to function as sterically accessible electron-rich targets for electrophilic attack, thus:



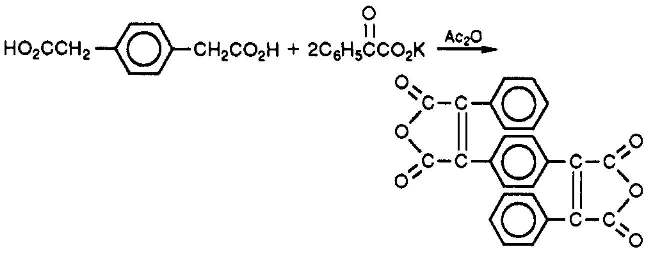
In effect, we view this as an internal ion/induced dipole interaction to close a new ring, binding the CO_2 group to the aromatic ring and thus preventing primary loss of CO_2. Other substituted maleic and phthalic anhydrides that do not fill the bill as well, as illustrated by the mass spectra of dimethylmaleic and phenanthrenedicarboxylic anhydrides (Table I), do not depart substantially from the behavior of their unsubstituted counterparts under electron impact. The product of the present reaction is pictured as a distonic ion[10,11] well-endowed for resonance stabilization of both the charge and the radical site.

We have found the method of Koelsch and Wawzonek, with some modifications, useful as a general synthesis of diaryl-substituted maleic anhydrides. Table II lists the substituted diphenylmaleic anhydrides we have prepared in this way.

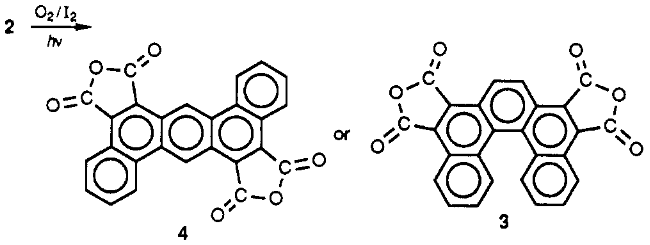
As diphenylmaleic anhydride does not give a photodimer, we had to discover another way to prepare a diaryl-substituted maleic dianhydride. Condensation of phenylenediacetic acid with 2 mol of benzoyl formate proceeds smoothly to give phenylenebis(phenylmaleic anhydride) in high yields.

The equation is written for the para isomer, and most of our work has been with that isomer, although *m*-phenylenediacetic acid also condenses readily with benzoylformate.

It was difficult at first to obtain a crystal structure of *p*-phenylbis(phenylmaleic anhydride) (**12**) to determine the orientation of the benzene rings because it crystallizes in flat, very thin plates. Evidence for the structure as written was found in the mass spectrum of the cyclized derivative. The mass spectrum is simple with three large peaks representing the molecular ion and fragments arising from loss of one and then both anhydride groups. Several doubly charged ions also are prominent—a characteristic of polycyclic aromatics. The spectra of the two isomers **3** and **4** would be similar. However, we would expect **3** to undergo ring closure readily by loss of H_2. This is evident in the spectrum of **2**:



2

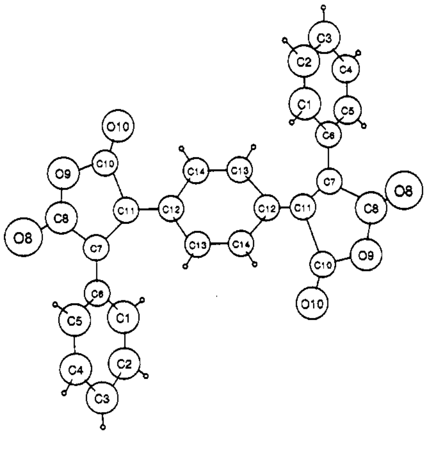


4 **3**

m/z	probable origin	relative intensity
422	$M^{\bullet+}$	100
350	$(M - C_2O_3)^{\bullet+}$	50.2
278	$(M - 2C_2O_3)^{\bullet+}$	98.6
276	$(m/z\ 278 - H_2)^{\bullet+}$	17.7
274	$(m/z\ 276 - H_2)^{\bullet+}$	4.9

No evidence for loss of H_2 appears in the fused-ring dianhydride, so we ascribe to its structure **4**.

Eventually structure **2** was confirmed by crystal structure determination. Errors are somewhat larger than usual because of the thin crystals.



2, 1,4-phenylenebis(phenylmaleic anhydride)

Diphenylmaleic anhydride and other aryl-substituted maleic anhydrides either fluoresce or lose hydrogen to ring close when irradiated, rather than dimerize. An exception is 3,4-dihydro-1,2-naphthalic anhydride (**5**) from ethyl 4-phenylbutyrate and ethyl oxalate.[12]

---

(1) Nimry, T. S.; Fields, E. K.; Meyerson, S.; Wright, M. E.; Hall, H. K., Jr. *J. Org. Chem.* **1983**, *48*, 4102. Winzenburg, M. L.; Fields, E. K.; Sinclair, D. P.; Ray, G. S.; Wright, M. E.; Hall, H. K., Jr. *Ibid.* **1988**, *53*, 2624.

(2) Fields, E. K.; Winzenburg, M. L.; Behrend, S. J. 1984 Intern. Chem. Congress Pacific Basin Soc., Abstr. 100110. Nimry, T. S.; Fields, E. K. U.S. 4,360,657; U.S. 4,413,115.

(3) Fager, J. H. U.S. 3,372,169.

(4) Koelsch, C. F.; Wawzonek, S. *J. Org. Chem.* **1941**, *6*, 684.

(5) McLafferty, F. W.; Gohlke, R. S. *Anal. Chem.* **1959**, *31*, 2076.

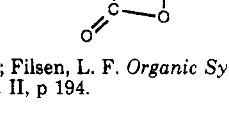
(6) Budzikiewicz, H.; Djarassi, C.; Williams, D. H. *Mass Spectrometry of Organic Compounds*; Holden-Day: San Francisco, 1967; p 224.

(7) Fields, E. K.; Meyerson, S. *Adv. Phys. Org. Chem.* **1968**, *6*, 1.

(8) Meyerson, S.; Puskas, I.; Fields, E. K. *J. Chem. Soc., Chem. Commun.* **1969**, 346.

(9) Hammerum, S. *Mass Spectrom. Rev.* 1988, *7*, 123.

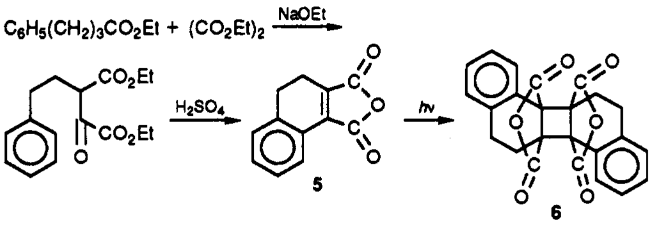
(10) The term "distonic" may not be strictly appropriate here because the resonance configurations that can be drawn for the product include also the carbene radical cation:



(11) Hershberg, E. B.; Filsen, L. F. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 194.

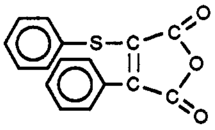
(12) Erlenmeyer, E. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2528.

(13) Rohmer, H. *Ibid.* **1898**, *31*, 281.



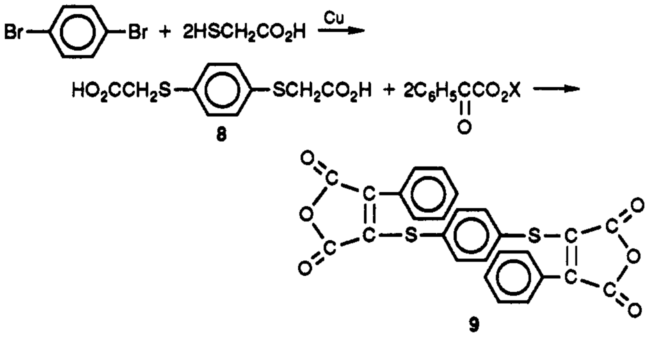
The dimer **6** cleaves to the monomer at 317–320 °C and under electron impact. There is no parent ion, but small peaks for loss of CO, CO + CO_2, and 2CO + CO_2. Phenylmaleic anhydride also gives a 2 + 2 photodimer, but the yield is only 2%.

Thioacetic acids do not condense with benzoyl formate unless activated by aryl nuclei. (Phenylthio)glycolic acid gave 80% phenyl(phenylthio)maleic anhydride (**7**).

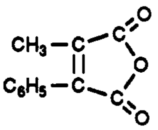


7

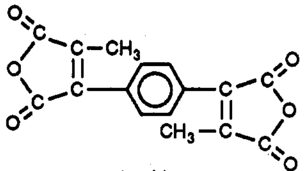
A high yield of dianhydride **9** resulted from benzoyl formate and *p*-phenylenebis(thioglycolic acid) (**8**).



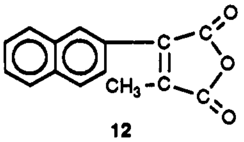
Pyruvic acid condenses with phenylacetic acid, *p*-phenylenediacetic acid, and β-naphthylacetic acid with alkali metal acetates and acetic anhydride to give methylarylmaleic anhydrides (**10**, **11**, and **12**).



10

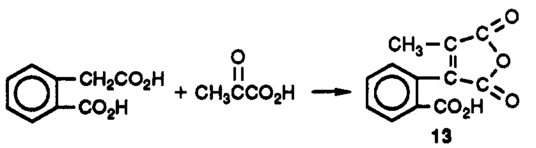


11



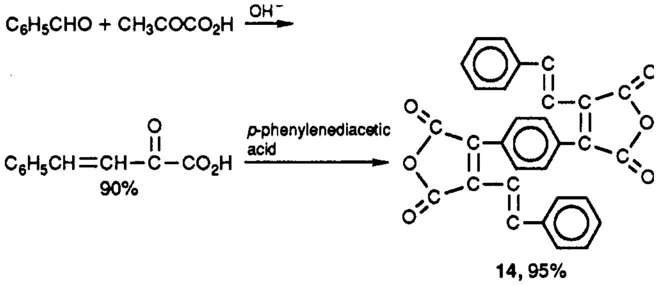
12

Yields generally are lower than with benzoylformic acid, although in one reaction with homophthalic acid, pyruvic acid gave a high yield, 92%.



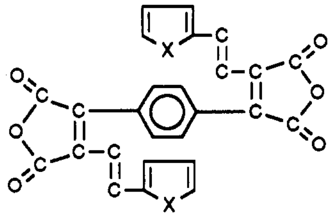
Reaction of benzoyl formate with propionic and higher aliphatic homologues gave lower yields, 20–30%. Aryl alkyl disubstituted maleic anhydrides are listed in Table III.

In contrast to the difficulty of obtaining high yields with pyruvic acid condensations, styrylglyoxylic acid, from benzaldehyde and pyruvic acid, condenses readily with phenylacetic acid and phenylenediacetic acids (para compound is **14**).



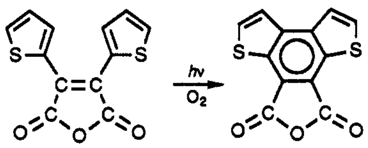
14, 95%

These are highly unsaturated aryl compounds, and especially their furan and thiophene analogues (**15**) are orange to deep red, with metallic sheens, and fluoresce strongly.

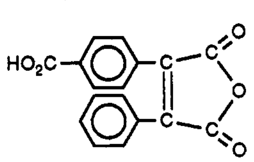


15: X = O, S

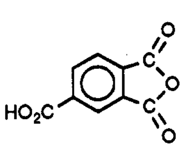
Arylenebis(arylmaleic anhydrides) are listed in Table IV. UV and O_2 bring about ring closure among the heterocyclic derivatives also, e.g., to give **16**:



Carboxyphenylacetic acids condense readily with benzoyl formate; the rate of reaction to give 70–80% yields is in the order ortho > para ≫ meta. The resulting phenyl(carboxyphenyl)maleic anhydrides, e.g. **11**, are analogues of trimellitic anhydride, from air oxidation of pseudocumene. Thermal stabilities of all the polyamide imides are about the same; the new carboxy anhydrides appear to give polyamide imides that are easier to process.

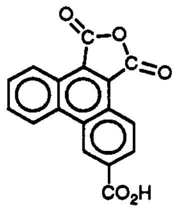


11, Table I



trimellitic anhydride

UV and oxygen convert **11** to the wholly aromatic trimellitic anhydride analogue **17**:



17, mp 375–7 °C

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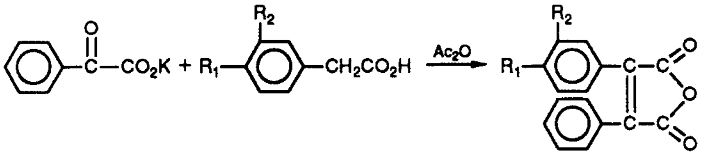
(14) Reid, W.; Reitz, W. *Ibid.* **1956**, *89*, 2570.

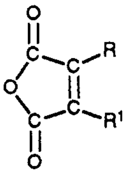
(15) From 4-cyanobenzyl bromide with CN^-, followed by hydrolysis Mellinghoff, W. *Ber.* **1889**, *22*, 3207.

Table II. Substituted Diphenyl Maleic Anhydrides



	R_1	R_2	comment	% yield	mp, °C
1.	NO_2	H	rapid reaction	80	124–6
2.	$NHCOCH_3$	H		72	194–5
3.	NH_2	H	by hydrolysis of 2	88	170 (homopolymerization to a glass)
4.	OAc	H		78	142–4
5.	OH	H	by hydrolysis of 4	90	190–2
6.	CH_3	CH_3	fluorescent green	30	106–8
7.	CH_3	H		83	125–6
8.	Br	H		78	172–8
9.	OCH_3	H		89	136–7
10.	OCH_3	OCH_3		70	114–5
11.	COOH	H		87	247–9

Table III. Aryl Alkyl Disubstituted Maleic Anhydrides



	R	R^1	yield, mol %	mp, °C
1.	CH_3	$4\text{-}(CH_3CONH)C_6H_4$	50	171–172
2.	CH_3	$4\text{-}(CH_3CO_2)C_6H_4$	39	108–109
3.	CH_3	2-naphthyl	48	179–180
4.	CH_3	2-thienyl		138–139
5.	CH_3	$2\text{-}HO_2C(C_6H_4)$	28	213–215, dec
6.	$(CH_3)_2CHCH_2$	C_6H_5	42	oil
7.	$(CH_3)_2CH$	C_6H_5	35	121–122

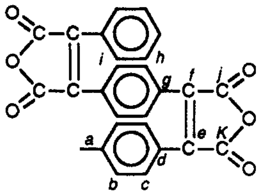
Our novel dianhydrides condensed with aromatic diamines such as 4,4′-diaminodiphenyl ether to give polyimides of high thermal and hydrolytic stability for use as high-performance engineering resins. These results will be described elsewhere.

Experimental Section

The mass spectra were measured on a CEC Model No. 21-110B or V. G. Corp. ZAB-2F instrument at a resolution of 10000 by using 70-eV electrons and direct-probe injection. Chemicals were purchased from Aldrich and used as received, unless noted otherwise.

Preparation of 2-(4-Carboxyphenyl)-3-phenylmaleic Anhydride (11). This synthesis is typical for the other compounds in Table II. A mixture of 20 g (0.11 mol) of 4-carboxyphenylacetic acid,[16] 20.7 g (0.11 mol) of potassium benzoyl formate, and 200 mL of acetic anhydride was stirred and refluxed for 3 h. The cooled mixture was poured into 1.4 L of water; the precipitate was dried and crystallized from acetone to give 28 g (87 mol %) of 11, mp 247–9 °C. ^1H and ^{13}C NMR, infrared, and mass spectra confirmed structure 11.

Preparation of 1,4-Phenylenebis(phenylmaleic anhydride) (2). This synthesis is typical for the other compounds in Table IV. A mixture of 29.13 g (0.15 mol) of *p*-phenylenediacetic acid, 56.5 g (0.3 mol) of potassium benzoyl formate, and 200 mL of acetic anhydride was stirred and refluxed for 1 h. The solid that crystallized from the cold reaction mixture was recrystallized from acetone to give 56 g (88 mol %) of fluorescent yellow crystals, mp 260–262 °C. Anal. Calcd for $C_{26}H_{14}O_6$: C, 73.9; H, 3.3. Found: C, 73.5; H, 3.2. IR (Nujol mull): ν (C=O) 1825 (m), 1760 (s) cm^{-1}. ^{13}C NMR (Me_4Si) δ (a) 130.7, (b) 128.6, (c) 129.3, (d) 127.1, (e) 137.3, (f) 139.1, (g) 129.4, (h) 129.6, (i) 129.6, (j) 164.8, (k) 164.7.



2

UV-visible spectrum in methylene chloride, 1.43 × 10^{-4} M, showed these absorption peaks:

λ_{max}, nm	A	$\epsilon \times 10^{-3}$
383	2.78	15.9
360	1.96	13.7
310	1.56	10.9

2 is slightly soluble in acetone, tetrahydrofuran, and dimethyl sulfoxide: the dimethyl sulfoxide solution is deep green.

Preparation of Dibenz[*a*,*h*]anthracene-5,6,12,13-tetracarboxylic 5,6:12,13-Dianhydride (4). This oxidative photochemical ring closure is typical of all others mentioned in the text. A mixture of 8.44 g (0.02 mol) of 2, 0.02 g (0.08 mmol) of iodine, and 300 mL of acetone was stirred and irradiated for 16 h in an Ace-Hanovia reactor by a 450-W medium-pressure mercury vapor lamp in a water-jacketed immersion well, with air at 50 cm^3/min bubbling through the acetone solution. The yellow-orange powder was washed with acetone and air-dried: 2.17 g (26 mol %); mp 402 °C dec. Anal. Calcd for $C_{26}H_{10}O_6$: C, 74.6; H, 2.4. Found: C, 73.9; H, 2.6. Structure 4 was confirmed by high-resolution mass spectrometry.

Photodimer of 3,4-dihydro-1,2-naphthalic anhydride resulted in 22 mol % yield by GE sunlamp irradiation for 5 days in acetone with benzophenone sensitizer. It melted at 317–320 °C. Anal. Calcd for $C_{12}H_8O_3$: C, 72.0; H, 4.1. Found: C, 72.0; H, 4.0. ^1H and ^{13}C NMR and mass spectrometry data confirmed the structure.

Phenylmaleic Anhydride Dimer. The photodimer of phenylmaleic anhydride, mp 315–20 °C dec, resulted in 2 mol % yield after 3-day irradiation of an acetone solution of phenylmaleic anhydride sensitized with benzophenone. The mass spectrum confirmed 348 as the parent ion mass.

Arylalkylmaleic Anhydrides. The compounds mentioned in Table III from pyruvic acid and homologues were all prepared by a Perkin condensation of the α-keto acid potassium salt with the appropriate phenylacetic acid or arylenediacetic acid as described for 2-(4-carboxyphenyl)-3-phenylmaleic anhydride (11) and 1,4-phenylene-bis(phenylmaleic anhydride) (2). All new compounds had satisfactory elemental and ^1H and ^{13}C NMR

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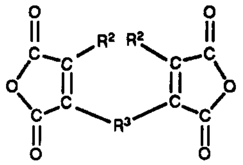
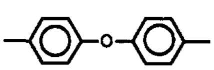
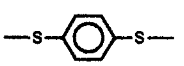
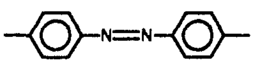
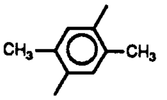
[16] Fields, E. K.; Winzenburg, M. L.; Behrend, S. J. U.S. 4,596,867; U.S. 4,638,072.

Table IV. Arylenebis(arylmaleic anhydrides)



	R^2	R^3	yield, mol %	mp, °C
1.	C_6H_5	1,4-C_6H_4	74	264–266
2.	C_6H_5	1,3-C_6H_4	56	188–190
3.	C_6H_5		76	304–305
4.	C_6H_5		77	198–200
5.	C_6H_5		40	212–214
6.	C_6H_5		79	319–321
7.	4-$C_4H_9C_6H_4$	1,4-C_6H_4	70	295–296
8.	$C_6H_5CH{=}CH^{13}$	1,4-C_6H_4	81	268–269
9.	$C_6H_5CH{=}CH^{13}$	1,3-C_6H_4	71	235–236
10.	 $CH{=}CH^{14}$	1,4-C_6H_4	65	>300, dec
11.	 $CH{=}CH^{15}$	1,4-C_6H_4	77	286–287
12.	C_6H_5		71	289–290

analyses, and in some cases, identification by mass spectrometry.

Preparation of 1,4-Phenylenedithioacetic Acid. A mixture of 170 g of the copper salt of ethyl thioglycollate, 100 g of *p*-dibromobenzene, 425 mL of quinoline, and 130 mL of pyridine was stirred and refluxed for 6 h. The filtered solution was diluted with 2 L of water plus ice and treated with 500 mL of concentrated hydrochloric acid. Ether extraction and evaporation of the ether solution gave 75 g (56.3 mol %) of the diethyl ester as an oil that was hydrolyzed by aqueous potassium hydroxide, followed by acidification to give the acid, mp 215–217 °C. Elemental analysis and mass spectrum confirmed the structure.

Analogues of compounds in Tables II–IV can be found in ref 17.

Crystallographic Data. For crystal studies, a yellow rectangular plate of $C_{26}H_{14}O_6$ having approximate dimensions of 0.45 × 0.28 × 0.08 mm was mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with Mo Kα radiation (λ = 0.71073 Å) on a Nicolet/Syntex $P2_1$ computer controlled diffractometer equipped with a graphite crystal, incident beam monochromator.

Cell constants and an orientation matrix for data collection were obtained from least-squares refinement, using the setting angles of 24 reflections in the range $6 < 2\theta < 20$. The monoclinic cell parameters and calculated volume are: a = 11.094 (10), b = 6.778 (4), c = 13.216 (30) Å; β = 93.85 (12)°; v = 991.6 Å^3, based on a constrained refinement with the base on the crystal system and cell choice. For $Z = 2$ and FW = 422.40 the calculated density is 1.41 g/cm^3. As a check on crystal quality, ω scans of several intense reflections were measured. These scans showed a central major peak with two other minor peaks which were half as intense. The central peak was resolved to quarter-height, half-height 0.41°, while the other peaks merged into a high background presumable from other platelets. From examining several crystal specimens the plates were made up of several thinner plates each having an approximate thickness of 0.02 mm.

Since several attempts to grow larger single crystals were unsuccessful, and the thinner crystals proved too fragile and small for data collection, the above crystal was used in order to get some stereochemical information on the molecule. From the systematic absences of $h0l$, $l = 2n + 1$; $0k0$, $k = 2n + 1$ and from subsequent least-squares refinement, the space group was determined to be $P2_1/c$ (14).

The data were collected at a temperature of 23 (1) °C using the θ–2θ scan technique. The scan rate varied from 0.8 to 8.0 deg/min (in ω). The variable scan rate allows rapid data collection for intense reflections where a fast scan rate is used and assures good counting statistics for weak reflections where a slow scan rate is used. Data were collected to a maximum of 2θ of 45.0°. The scan range (in deg) was determined as follows to correct for the separation of the K_0 doublet.

$$2\theta \text{ scan width} = 1.1 + 2\theta(K\alpha) - (2\theta(K\alpha 1) - 1.1)$$

Stationary background counts were made at the scan extremes such that the ratio of peak counting time to background counting time was 2:1. The counter aperture was adjusted to exclude as much of the secondary diffracting crystals as possible. The horizontal aperture width was set at 2.65 mm. The diameter of the incident beam collimator was 0.75 mm, and the crystal to detector distance was 21 cm.

A total of 1521 reflections were collected, of which 1299 were unique and not systematically absent. As a check on crystal and electronic stability, two representative reflections were measured every 98 reflections. The slope of the least-squares line through a plot of intensity versus time was 13 (3) counts/h, which corresponds to a total gain in intensity of 3.3%. A linear decay correction was applied. The correction factors on I ranged from 0.966 to 1.000 with an average value of 0.984.

Lorentz and polarization corrections were applied to the data. The linear absorption coefficient is 0.9 cm^{-1} for Mo Kα radiation. Intensities of equivalent reflections were averaged. The agreement factors for the averaging of the 63 observed and accepted reflections were 12.1% based on intensity and 6.8 based on F_0.

The structure was solved by direct methods using the program SIMPEL. Using 210 reflections (minimum E of 1.40) and one symbol, one phase set was produced that led to the location of 16 atoms from the resulting E map. Hydrogen atom positions were calculated and added to the structure factor calculations, but their positions and thermal parameters were not refined.

The standard deviation on intensities, $\sigma(F_0^2)$, is defined as follows

$$\sigma^2(F_o^2) = \sigma(I) + (pF_o^2)P^2$$

where $\sigma(I)$ is the standard deviation of the reduced intensity due to counting statistics and the parameter p is a factor introduced to downweight intense reflections. Here p was set to 0.030. Scattering factors were taken from Cromer and Waber.[17] Anamalous dispersion effects were included in F_c;[18] the values for f' and f'' were those of Cromer.[19] Only the 594 reflections having intensities greater than 2.0 times their standard deviation were used in the refinements. The final cycle of refinement included 65 variable parameters and converged (largest parameter shift was 0.32 times is esd) with unweighted and weighted agreement factors of:

$$R_1 = \sum||F_o| - |F_c||/\sum|F_o| = 0.182$$

$$R_2 = \sqrt{(\sum w(|F_o| - |F_c|)^2/\sum wF_o^2)} = 0.190$$

The standard deviation of an observation of unit weight was 3.46. The highest peak in the final difference Fourier had a height of 0.85 e/Å^3. The high residuals are due to the molecules in the other minor crystals as seen in the omega scans. No attempt was made to include them in this model.

All calculations were performed on a PDP-11/34a computer using DSP-PLUS.[9] A complete listing of crystallographic data can be found in the supplementary material.

Acknowledgment. We are happy to acknowledge the contributions to this work of G. R. Chipman and R. W. Dunlap of Amoco Corporation.

Supplementary Material Available: X-ray data for $C_{26}H_{14}O_6$ (7 pages); table of structure factors for $C_{26}H_{14}O_6$ (4 pages). Ordering information is given on any current masthead page.

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(17) Cromer, D. T.; Waber, J. T. *International Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2B.

(18) Ibers, J. A.; Hamilton, W. C. *Acta Crystallogr.* **1964**, *17*, 781.

(19) Cromer, D. T. *International Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.3.1.

Selective Transformation of *O*-2-(Trimethylsilyl)ethyl and *O*-*tert*-Butyl Carbamates into *O*-Benzyl Carbamates Using Benzyl Trichloroacetimidate

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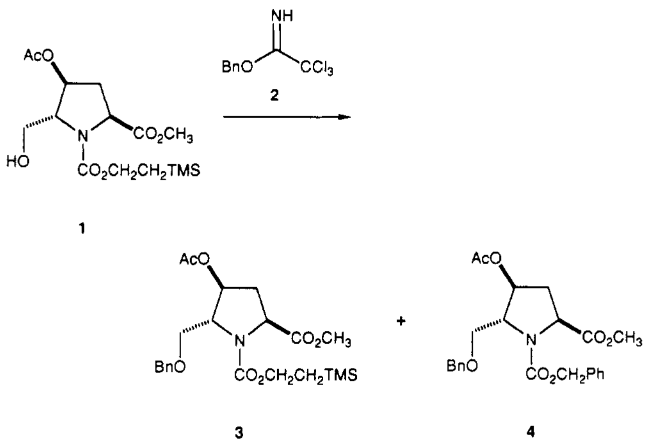
Received January 8, 1990

We recently attempted to benzylate the hydroxyl group of the bulgecinine derivative (1)[1] with benzyl trichloroacetimidate (2) in the presence of a catalytic amount of trifluoromethanesulfonic acid.[2] Upon workup, the expected benzyl ether (3) was isolated (50%) along with the *O*-benzyl carbamate benzyl ether (4) (20%). To our knowledge, the direct conversion of an *O*-alkyl carbamate into an *O*-benzyl carbamate (Cbz) (1 to 4) has not been described. However, a two-step procedure for converting *O*-*tert*-butyl carbamates (BOC) into *O*-benzyl carbamates via the *O*-*tert*-butyldimethylsilyl carbamate has been reported by Ohfune and co-workers.[3] The reactive *O*-*tert*-butyldimethylsilyl carbamate intermediate is also available from *O*-benzyl carbamates by the reductive cleavage of the benzyl group using *tert*-butyldimethylsilane and palladium acetate.[4] We report that the benzylating agent benzyl trichloroacetimidate (2) readily converts *O*-2-(trimethylsilyl)ethyl carbamates (TEOC)[5] and *O*-*tert*-butyl carbamates into the corresponding *O*-benzyl carbamates in moderate yields in a one-step process that proceeds without "racemization". The conversion procedure is compatible with ester, amide, and silyl ether functionalities.



The *cis*-hydroxyproline derivative (5) was used in optimizing the reaction conditions for the TEOC to Cbz transformation. Six equivalents of benzyl trichloroacetamidate and a minimum of 0.3 equiv of trifluoromethanesulfonic acid were required to consume **5** and give the Cbz derivative (**6**) in a 56% yield (Chart I). No pyrrolidine-containing compounds were among the components isolated during the purification of **6** by silica gel chromatography. Presumably, the remaining amount of **5** was converted into polar compounds, such as the free and benzylated amine derivatives, and removed by the aqueous workup or not eluted from silica gel. With these conditions, the conversion of **1** to **4** proceeded with a 48% yield while the conversion of TEOC-Leu-OMe (**7**) gave a 68% yield of the Cbz derivative **8**. The above procedure was also found to convert *O*-*tert*-butyl but not *O*-methyl (**9**) carbamates into *O*-benzyl carbamates. A series of *O*-*tert*-butyl carbamates (**10, 12, 14, 16, 18, 20**) were converted into the corresponding Cbz derivatives in modest yields. Noteworthy results are the stability of the *tert*-butyldimethylsilyl ether (**21**) and the selective conversion of the *O*-*tert*-butyl carbamate in the presence of a *tert*-butyl ester (**19**). No epimerization was detected by ^{1}H NMR spectroscopy for the Cbz derivatives **4, 6,** and **17**. In order to detect any racemization in the Cbz derivatives **11, 13,** and **15**, the Cbz group was removed by hydrogenolysis and the amino esters converted to Mosher amides.[6] In each case only the *R,S* diastereoisomer was detected by ^{1}H NMR spectroscopy.

The course of the reaction is rationalized as a nucleophilic attack of the carbamate carbonyl oxygen at the benzylic position of the protonated benzyl trichloroacetimidate to give a cation (Scheme I). If R^2 is a *tert*-butyl group, the intermediate cation fragments to form the *O*-benzyl carbamate plus the *tert*-butyl cation. Alterna-

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(1) Barrett, A. G. M.; Pilipauskas, D., submitted to *J. Org. Chem.*

(2) Wessel, H.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2247.

(3) Sakaitani, M.; Ohfune, Y. *Tetrahedron Lett.* **1985**, *26*, 5543. Sakaitani, M.; Ohfune, Y. *J. Org. Chem.* **1990**, *55*, 870.

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