

Table IV. Reaction of DNCB in Different Systems^a

system	product	$k_{\psi}/[\text{OH}^-]$, $\text{M}^{-1} \text{s}^{-1}$	k_{rel}
H ₂ O	2,4-dinitrophenoxide	1.4×10^{-4}	1
CTABr (micelles)	2,4-dinitrophenoxide	1.2×10^{-2} ^{b,c}	82
1 (micelles)	ether	2.0 ^{b,d}	14000
CTABr- <i>t</i> -AmOH (microemulsions)	2,4-dinitrophenoxide	1.6×10^{-3} ^e	11
CTABr-1-BuOH (microemulsions)	ether (major)	1.5×10^{-2} ^e	105
1- <i>t</i> -AmOH (microemulsions)	ether	3.5×10^{-2}	246

^a In 0.01 M NaOH, 25.0 °C. ^b Maximum k_{ψ} . ^c In 0.01 M CTABr. ^d In 0.005 M 1. ^e Reference 2.

Table V. Reaction of DNFB in Different Systems^a

system	product	$k_{\psi}/[\text{OH}^-]$, $\text{M}^{-1} \text{s}^{-1}$	k_{rel}
H ₂ O	2,4-dinitrophenol	0.12	1
CTABr micelles	2,4-dinitrophenol	6.72 ^{b,c}	56
1 (micelles)	ether	720 ^{b,d}	6000
CTABr- <i>t</i> -AmOH (microemulsions)	2,4-dinitrophenol	0.7 ^e	6
CTABr-1-BuOH (microemulsions)	ether (major)	8 ^e	66
1- <i>t</i> -AmOH (microemulsions)	ether	35	292

^a In 0.01 M NaOH, 25.0 °C. ^b Maximum k_{ψ} . ^c In 0.03 M CTABr. ^d In 0.005 M 1. ^e Reference 2.

Rate enhancements are smaller in microemulsions than in aqueous micelles, as shown by values of $k_{\psi}/[\text{OH}^-]$ for reactions of DNCB and DNFB (Tables IV and V). These comparisons are however qualitative, because the micellar

reactions are typically less than first order with respect to OH⁻, and values of $k_{\psi}/[\text{OH}^-]$ go through maxima with increasing surfactant.¹³⁻¹⁵ In addition, the halonitrobenzenes are not fully micellar bound in dilute surfactant,¹⁶ but they should bind at the micelle-water interface, close to OH⁻,¹⁷ whereas they may spend some time in the apolar interior of an o/w microemulsion droplet. Qualitatively, the greater reactivity in systems in which alkoxide, rather than hydroxide, ion is the nucleophile is consistent with reactivities in the absence of surfactant.^{3b,8} An additional point is that rate enhancements in functional and non-functional micelles and microemulsions are consistently larger for aromatic nucleophilic substitution than for dephosphorylation, regardless of substrate hydrophobicity.^{2b,18}

Acknowledgment. Support of this work by the National Science Foundation (Chemical Dynamics Program) is gratefully acknowledged.

Registry No. 1, 20317-32-2; 1a, 54385-45-4; 2, 61095-52-1; OH⁻, 14280-30-9; DNCB, 97-00-7; DNFB, 70-34-8; DNCN, 2401-85-6; CTABr, 57-09-0; 1-butanol, 71-36-3.

(13) Romsted, L. S. In ref 1a, p 509.

(14) Cordes, E. H. *Pure Appl. Chem.* 1978, 50, 617.

(15) Bunton, C. A. *Catal. Rev. Sci.-Eng.* 1979, 20, 1.

(16) Bunton, C. A.; Robinson, L. *J. Am. Chem. Soc.* 1968, 90, 5972; *J. Org. Chem.* 1969, 34, 773.

(17) Mukerjee, P. In ref 1b, p 153. Menger, F. M. *Acc. Chem. Res.* 1979, 12, 111.

(18) Bunton, C. A.; Gan, L.-H.; Moffatt, J. R.; Romsted, L. S.; Savelli, G. *J. Phys. Chem.* 1981, 85, 4118.

Remarkably Selective Chlorination of Phthalic Anhydride and Its Monochlorinated Derivatives

John W. Verbicky, Jr.,* and Louella Williams

General Electric Research and Development Center, Schenectady, New York 12301

Received December 7, 1982

The vapor-phase chlorination of phthalic anhydride 1 and its monochlorinated derivatives 2 and 3 in the temperature range from 390 to 600 °C with elemental chlorine has been investigated and found to be highly selective. Thus, chlorination of 1 in the temperature range from 390 to 450 °C was found to give high yields of monochlorinated products accompanied by only small amounts of dichlorination with a high degree of regioselectivity favoring the formation of 4-chlorophthalic anhydride. Chlorination of a 3-chlorophthalic anhydride 3 by this method has provided the first direct synthesis of 3,5-dichlorophthalic anhydride 7 from phthalic anhydride via chlorination.

Electrophilic substitution reactions of phthalic anhydride 1 have received considerable attention over the years, and the lack of regioselectivity exhibited by these reactions is well-known. The nitration of phthalic anhydride under typical electrophilic substitution conditions gives rise to a nearly equal mixture of 3-nitro- and 4-nitrophthalic anhydrides.¹ Recently Zweig and Epstein have reported² that the Lewis acid catalyzed chlorination of phthalic anhydride in the molten state yields a mixture of monochlorinated isomers exhibiting regioselectivity similar to that observed in the nitration of phthalic anhydride and that polychlorination is a significant competing reaction.

These workers also reported the detailed product isomer distribution of dichlorinated products obtained in the chlorination of phthalic anhydride and have rationalized their results in terms of the ortho- and para-directing effect of a chlorine substituent consistent with electrophilic substitution reactions. It has also been reported that the thermal and photochemical vapor-phase halogenation of monosubstituted benzene derivatives gives rise to rather unusual substitution patterns which differ markedly from those obtained in conventional electrophilic halogenations;^{3,4} we were curious to see if the processes that lead

(1) Private communication with N. C. Cook, 1974.

(2) Zweig, A.; Epstein, M. *J. Org. Chem.* 1978, 43, 3690.

(3) deMay, C. A.; Kooyman, E. C. *Recl. Trav. Chim. Pays-Bas* 1971, 90, 1337.

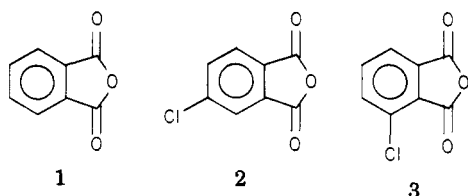
(4) Kooyman, E. C. *J. Pure Appl. Chem.* 1963, 7, 193.

Table I. Vapor-Phase Chlorination of Phthalic Anhydride

entry	temp, ^a °C	flow rate ^b	% Cl ₂ ^c	2/3 ratio ^d	% yield of products		% conversion ^e
					2 + 3	6 + 7	
1	390	4	75	10.7	98.4	1.6	29.5
2	400	4	75	10.5	97.4	2.6	39.0
3	400	4	50	9.2	98.2	1.8	27.5
4	420	3	100	10.6	96.7	3.3	61.0
5	420	2	100	10.5	88.5	11.5	78.0
6	420	1	100	10.5	86.6	13.4	89.0

^a Temperature at the center of the tube furnace. ^b Total flow of gases (Cl₂ + N₂) through the hot tube reactor in standard cubic feet/h. ^c The percent Cl₂ in the chlorine-nitrogen gas mixture swept through the reactor. ^d Composition of monochlorinated products. ^e Overall percent conversion based on recovered starting material.

to the unusual substitution patterns obtained in these halogenations might well be used advantageously to improve the isomer distribution obtained in the halogenation of phthalic anhydride. Since Zweig and Epstein had reported that their attempt to accomplish a photochemical chlorination of phthalic anhydride failed even at 235 °C, it appeared that somewhat harsher conditions would be required in order to effect this type of reaction. Furthermore, although there are data available regarding isomer product distributions obtained in such substitution reactions of monosubstituted benzene derivatives,^{5,6} there are no detailed product distribution data available for such substitutions on aromatic substrates which are more highly substituted and, in particular, not for phthalic anhydride. These factors have prompted us to investigate the thermal vapor-phase chlorination of phthalic anhydride (1) and its



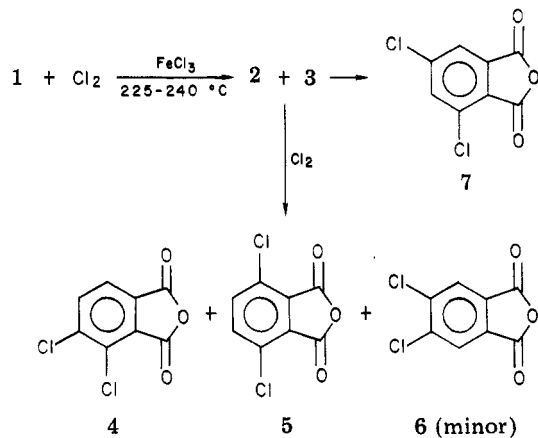
monochlorinated derivatives 2 and 3 in the temperature range from 390 to 600 °C, and the results of this investigation are reported herein.

Results and Discussion

Chlorination of phthalic anhydride (1) under conditions of Lewis acid catalysis in the molten state is reported to lead to nearly equivalent amounts of the two possible monochlorinated isomers (2 and 3), and when the chlorination is carried out to the extent of 75% conversion, the chlorinated products consist of greater than 20% of a mixture of dichlorinated isomers. Specifically, the dichlorinated products consist primarily of an equal mixture of 3,4-dichlorophthalic anhydride (4) and 3,6-dichlorophthalic anhydride (5) along with a small amount of the 4,5-dichlorinated isomer 6. The 3,5-dichlorophthalic anhydride isomer 7 was not observed under these conditions (Scheme I).

In contrast, we have found that the thermal vapor-phase chlorination of 1 proceeds with a high degree of regioselectivity, yielding the monochlorinated adducts 2 and 3 in a molar ratio of 5–11:1. Monochlorination at overall conversions of 60% is accompanied by relatively small amounts of dichlorinated products (~4%); at even higher conversions of starting material (nearly 90%) the amount of dichlorination is still relatively small (<15%). The results obtained in several typical runs showing the effect

Scheme I. Products of the Lewis Acid Catalyzed Chlorination of Phthalic Anhydride

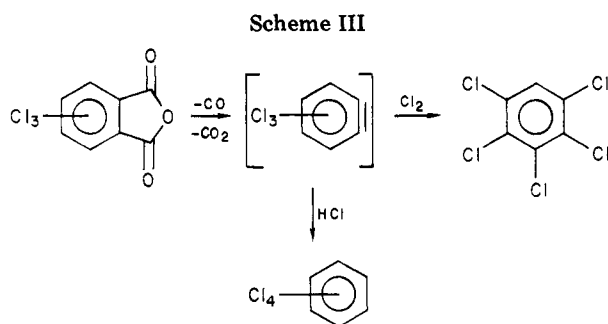
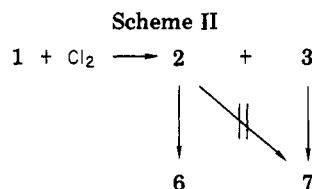


of temperature, flow rate, and chlorine concentration in the gas phase are summarized in Table I. The molar ratio of chlorine to phthalic anhydride in the vapor phase in all cases reported was greater than 20:1. The thermal reaction sets in at approximately 360 °C and proceeds at a reasonable rate at temperatures of 390 °C and above, at residence times in the reactor between 8 and 32 s. Thus, 4-chlorophthalic anhydride (2) can be produced in high overall yield with a remarkable degree of regioselectivity under these conditions.

Aside from the high degree of selectivity observed in the formation of monochlorinated products, it was most interesting to note that under the conditions shown in Table I, the isomers 6 and 7 were the only major dichlorinated products observed in these reactions and that they are formed in nearly equal amounts. This contrasts sharply with the results reported in the Lewis acid catalyzed reaction in which the isomer 6 was reported as a minor component of the dichlorinated products and the formation of isomer 7 was not observed at all. The actual molar ratio of 6 to 7 observed in the vapor-phase chlorinations reported here was consistently 1.0:1.2 in all cases, and this result suggested that 7 was formed somewhat more rapidly than 6. This observation was not surprising since if the polychlorination of 1 proceeds in a stepwise fashion, the formation of 7 could in principle arise from the subsequent chlorination of both 2 and 3 while isomer 6 could only be formed from the subsequent chlorination of 2. In order to test this hypothesis we examined the vapor-phase chlorination of 2 and 3 under identical conditions and found much to our surprise that the chlorination of 2 in the vapor phase led exclusively to the formation of isomer 6 while the chlorination of 3 led exclusively to the formation of isomer 7. The conversion of 3 to 7 represents the first direct method for the preparation of 7 from 3-chlorophthalic anhydride. The only previous synthesis of this compound was based on the oxidation of the corre-

(5) Louw, R.; Dorrepaal, W. *J. Chem. Soc., Perkin Trans. 2* 1973, 650.

(6) Louw, R.; Dorrepaal, W. *Recl. Trav. Chim. Pas-Bas* 1971, 90, 700.



sponding chloroxylene which is itself derived as a byproduct from the reaction of 5,5-dimethyl-1,2-cyclohexanedione with PCl_5 .⁷ Thus, the remarkable selectivity of the monochlorination of 1 is reflected in the chlorination of its monochlorinated isomers 2 and 3. On the basis of these results we must conclude that the course of the reaction leading to the formation of 6 and 7 in the vapor-phase chlorination of 1 proceeds as shown in Scheme II. It should be further noted that neither 2 nor 3 underwent any thermal or acid-catalyzed rearrangements under the reaction conditions studied, and hence the regioselectivity observed in this reaction does not arise from an equilibration or rearrangement of the initially formed products. We have also observed similar selectivity in the chlorination of the phthalonitrile and in the bromination of phthalic anhydride under these conditions.

In those cases where the chlorination of 1 has been carried out to higher conversions (i.e., >70%), we have observed traces (<0.2%) of pentachlorobenzene and tetrachlorobenzene. These products as well as more highly chlorinated products are observed when the reaction is conducted at temperatures above 450 °C, and their occurrence increases rapidly in the temperature range from 450 to 600 °C. The tetrachlorobenzene and pentachlorobenzene products are thought to have arisen from the thermal decomposition of small amounts of trichlorinated phthalic anhydrides via loss of CO_2 and CO and subsequent addition of HCl or chlorine (Scheme III) in a fashion analogous to that reported by Fields and Meyerson⁸ on the thermal decomposition of phthalic anhydride itself.

The differences in the product distribution data obtained here for the thermal vapor-phase chlorination of 1-3 and those reported for the Lewis acid catalyzed chlorination of these substrates would seem to suggest that these reactions are occurring by fundamentally different processes. The exact nature of the mechanism of these reactions is currently being investigated in our laboratory.

Conclusion

The thermal vapor-phase chlorination of phthalic anhydride gives rise to high yields of the monochlorinated isomers 2 and 3 in a ratio of 5-11:1 with only minor amounts of dichlorination even at high overall conversions. The high degree of regioselectivity exhibited by this process provides the first direct method for the preparation

of 3,5-dichlorophthalic anhydride via the chlorination of 3-chlorophthalic anhydride. The general method described here may provide an attractive alternative to conventional electrophilic substitution reactions for the selective substitution of a number of aromatic substrates.

Experimental Section

Melting points were taken with a Mel-Temp apparatus and the uncorrected. ^1H NMR spectra were recorded on a Varian A-60 spectrometer, and chemical shifts are reported in parts per million downfield from an internal tetramethylsilane standard. Liquid chromatographic analyses were performed on a Waters Associates gradient liquid chromatograph equipped with a UV detector and operating in the isocratic mode with an isooctane/tetrahydrofuran (97:3 v/v) solvent mixture and a Waters Associates Bondapak $\mu\text{-CN}$ column. Commercial samples of all reagents were used as purchased without further purification.

General Procedure for Vapor-Phase Chlorinations. The apparatus used in all experiments was the same and is described below. Chlorine and nitrogen gas sources were connected to separate flow meters, and the flow meter effluent gases were channeled into a single gas line which was connected to a gas-inlet tube affixed to a 100-mL three-necked flask containing the molten substrate to be chlorinated at 140 °C. The gas mixture was swept over the surface of the molten substrate and the through a Pyrex elbow joint heated to 150 °C which was connected to the quartz tube reaction chamber maintained in the temperature range desired in a split tube furnace. The quartz tube reaction chamber was 47.5 cm long and had an inside diameter of 1.25 cm. The reaction chamber was filled along 40 cm of its heated length with hollow quartz cylinders approximately 0.3 cm in diameter and 0.6 cm long. The exit end of the reaction chamber was connected by means of a Pyrex elbow to a trapping flask cooled to 0 °C in an ice-water bath and equipped with a water-cooled reflux condenser to further cool effluent gases. The products were condensed from the vapor phase upon exiting the reaction chamber and were collected as white crystalline solids. The products were analyzed by liquid chromatography. LC response factors were determined for authentic samples relative to a benzophenone internal standard. The product analyses were further confirmed by gas chromatography-mass spectroscopy.

4-Chlorophthalic Anhydride. A 20.0-g (0.1 mol) sample of 4-chlorophthalic acid was heated at reflux for 3 h with 50 mL of anhydrous acetic anhydride. The solid anhydride precipitated from the reaction mixture on cooling and was filtered. The crude product was dissolved in methylene chloride, extracted with cold sodium bicarbonate, and dried over MgSO_4 , and the solvent was removed to yield 18.0 g (98%) of 4-chlorophthalic anhydride (2) as a white solid, mp 96 °C (lit.² mp 94-96 °C).

3-Chlorophthalic Anhydride. A sample of 30.0 g (0.15 mol) of 3-nitrophthalic anhydride was heated to 240 °C, and chlorine gas was passed through the molten solid for 2 h at a rate of approximately 10-15 mL/min. The reaction mixture was cooled, and the crude product was sublimed at 150 °C to yield 16.5 g (60.6%) of 3-chlorophthalic anhydride (3) as white needles, mp 125 °C (lit.² mp 126 °C).

4,5-Dichlorophthalic Anhydride. Treatment of a commercial sample of 4,5-dichlorophthalic acid according to the procedure described for the preparation of 2 yielded 4,5-dichlorophthalic anhydride (6) as white crystals, mp 184 °C (lit.² mp 185-185 °C).

3,5-Dichlorophthalic Anhydride. A solution of 100.0 g (0.71 mol) of 5,5-dimethyl-1,3-cyclohexanedione in 200 mL of dry chloroform was treated with 297 g (1.22 mol) of phosphorous pentachloride according to the procedure described by Crosseley.⁷ The crude product obtained by this method was distilled and gave in a late-boiling fraction 1.36 g (1.1%) of 3,5-dichloro-*o*-xylenes as a pale yellow oil: b.p. 140 °C (42 mmHg); ^1H NMR (CDCl_3) δ 7.33 (d, J = 2 Hz, 1 H), 7.13 (d, J = 2 Hz, 1 H), 2.16 (m, 6 H); ^{13}C NMR (CDCl_3) δ 139.7, 135.0, 133.0, 131.1, 128.2, 126.5, 20.76, 15.80. Oxidation of the 3,5-dichloro-*o*-xylenes to 3,5-dichlorophthalic acid with dilute nitric acid in a sealed tube followed by dehydration with acetyl chloride afforded the anhydride 7 as a white solid: mp 87-88 °C (lit.⁷ mp 89 °C); ^{13}C NMR ($\text{Me}_2\text{SO}-d_6$) δ 160.3, 141.6, 136.2, 134.9, 132.0, 126.8, 124.2; ^1H NMR ($\text{Me}_2\text{SO}-d_6$) δ 8.10 (m). The spectral properties, melting point, and LC re-

(7) Crosseley, L. J. *Chem. Soc.* 1982, 82, 826.

(8) Fields, E. K.; Meyerson, S. *Chem. Commun.* 1965, 474.

tention time of this material were identical in every way with those of a sample isolated by gas-liquid chromatography of the product obtained from the vapor-phase chlorination of 3.

Acknowledgment. We express our gratitude to Dr. A. R. Gilbert, Dr. D. M. White, and Dr. H. M. Relles for their many helpful discussions and to H. Grade, R. May, and

P. Donahue for their spectroscopic analysis.

Registry No. 1, 85-44-9; 2, 118-45-6; 3, 117-21-5; 6, 942-06-3; 7, 51971-64-3; 4-chlorophthalic acid, 89-20-3; 3-nitrophthalic anhydride, 641-70-3; 4,5-dichlorophthalic acid, 56962-08-4; 5,5-dimethyl-1,3-cyclohexanedione, 126-81-8; 3,5-dichloro-*o*-xylene, 70172-92-8; 3,5-dichlorophthalic acid, 25641-98-9.

Ring-Chain Tautomerism in Anions Derived from Substituted (Arylideneamino)toluenes and (Arylideneamino)oxindoles

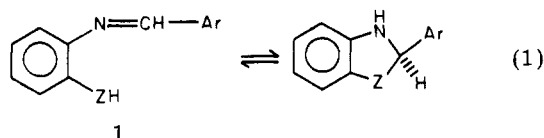
Frederick J. Goetz, Jerry A. Hirsch,* and Robert L. Augustine

Department of Chemistry, Seton Hall University, South Orange, New Jersey 07079

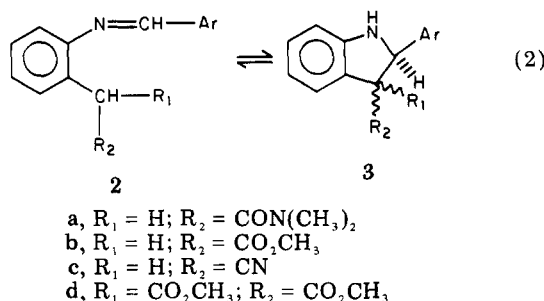
Received December 17, 1982

Intramolecular nucleophilic attack by carbon and nitrogen anions on imine and enone double bonds, respectively, has been investigated as a synthetic route to fused five-membered azacycles. In both (arylideneamino)toluenes and (arylideneamino)oxindoles, cyclization occurs only when a relatively localized anion attacks an electron-deficient double bond.

A recent report¹ of ring-chain tautomerism promoted by acids prompts us to report studies of ring-chain tautomerism catalyzed by bases. The tautomerism of 1-substituted 2-arylideneaminobenzenes (1, eq 1) have been ex-



tensively investigated.² In these systems the mobile hydrogen is attached to an electronegative atom in both the ring and chain tautomers. It was the intent of our study to evaluate the positions of these tautomeric equilibria in the 2-substituted 2-(arylideneamino)toluenes (2), where the tautomerism is generated by removal of an acidic benzylic hydrogen (eq 2).



The required substituted 2-aminotoluenes were prepared by variations of literature methods and were rapidly treated with the desired aromatic aldehyde under acid catalysis to produce the desired chain tautomers 2a-d. All compounds exhibited proton magnetic resonance, infrared, and ultraviolet spectra consistent with the chain tautomeric structures. The aldehydes utilized were 4-nitrobenzaldehyde, 2,4-dinitrobenzaldehyde, 2,4,6-trinitrobenzaldehyde, and 3,4,5-trimethoxybenzaldehyde. The nitroaldehydes were chosen because (a) the electron-

withdrawing groups facilitate nucleophilic attack on the azomethine bond,³ (b) the electron-withdrawing groups cause a downfield shift in the aromatic protons of the arylidene unit relative to those in the toluene aromatic groups and in any ring tautomer, and (c) the nitro-arylideneanilines possess ultraviolet absorption maxima⁴ at longer wavelengths than other arylideneanilines or in any ring tautomer. The 3,4,5-trimethoxybenzylidene system was chosen for ease of handling as a non-electron-withdrawing entity. The chemical shifts of the benzylic protons in 2a-d also varied as expected with the electronegativity of the benzylic carbon substituents.

When each α -substituted 2-(arylideneamino)toluene (2a-d) was treated with a catalytic amount of potassium *tert*-butoxide in dimethyl sulfoxide (Me₂SO), no spectral changes were observed except with the malonates 2d. Even upon being heated at temperatures up to 120 °C, systems 2a-c did not produce the ring tautomer 3 on quenching with cold dilute acetic acid. The malonates 2d were completely converted to ring tautomer 3d as determined from spectral evidence and from isolation of 3d as a crystalline solid. Tautomerization occurred readily with the *tert*-butoxide/Me₂SO system at room temperature or with the weaker base 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) in tetrahydrofuran with both electron-withdrawing and mild electron-donating arylidene groups. Since the benzylic hydrogen would be more acidic in the malonate than in the less substituted analogues, a stoichiometric amount of base was added to each substrate to confirm carbanion formation in each system.

The observation of base-catalyzed tautomerism in the malonate 2d and not in the other systems (2a-c) may have several explanations. The major factor probably is that the malonate carbanion for steric reasons assumes a geometry where the negative charge is not significantly delocalized into the benzene ring, while the other benzylic carbanions are effectively delocalized into the benzene-azomethine system. The malonate carbanion would then

(3) McDonagh, A. F.; Smith, H. E. *J. Org. Chem.* 1968, 33, 1, 8.

(4) The extinction coefficients in the 2,4,6-trinitro compounds were distinctly lower, presumably from steric distortion from coplanarity of the benzylideneamino chromophore. The 2,4-dinitro series were sensitive to visible light.

(1) Lambert, J. B.; Majchrzak, M. W. *J. Am. Chem. Soc.* 1980, 102, 3588.

(2) For a literature survey, see: Goetz, F. J. Dissertation, Seton Hall University, 1974.