held at reflux for 3 days and then evaporated to dryness under reduced pressure. The residue was washed with water and recrystallized from hot ethanol to yield 979 mg. (64%) of XII: m.p. 156–158°; infrared (KBr) bands 2.92 (w), 3.00 (w), 3.08 (w), 5.92 (s), 6.31 (s), 6.53 (m) μ; λ_{max} mμ (log ϵ), 217 (4.37), 249 (4.22), 325 (4.18); λ_{min}, mμ (log ϵ), 240 (4.18), 283 (3.62).

Anal. Calcd. for $C_{13}H_{13}Cl_2NO_3$: C, 51.7; H, 4.3; Cl, 23.5; N, 4.6. Found[b]: C, 51.6; H, 4.3; Cl, 23.6; N, 4.5.

Reaction of XII with Less than 1 Equiv. of Sodium Ethoxide.—To a refluxing solution of 3.10 g. (10.3 mmoles) of XII in 50 ml. of absolute ethanol was added 100 ml. of a 0.102 *M* solution of sodium ethoxide in ethanol during 34 min. The reaction mixture was held at reflux an additional 30 min., cooled to room temperature, and filtered. The precipitate was washed with several portions of distilled water and dried to yield 1.47 g. (54%) of XIII: m.p. 310–312°; infrared (KBr) bands 2.95 (m), 6.09 (s), 6.30 (s), 6.43 (s) μ; λ_{max} mμ (log ϵ), 212 (4.22), 238 (4.22), 298 (4.02), 308 (4.14), 338 (3.99); λ_{min}, mμ (log ϵ), 225 (4.03), 275 (3.38), 320 (3.89).

Anal. Calcd. for $C_{13}H_{12}ClNO_3$: C, 58.8; H, 4.6; Cl, 13.4; N, 5.3. Found[a]: C, 58.8; H, 4.5; Cl, 13.4; N, 5.3.

The ethanolic filtrate from the above was evaporated to dryness under reduced pressure and the residue was recrystallized from 95% ethanol to yield 1.26 g. (40%) of XIV: m.p. 107–109°; infrared (KBr) bands 3.07 (broad), 6.00 (s), 6.27 (s), 6.42 (s) μ; λ_{max}, mμ (log ϵ), 211 (4.23), 240 (4.22), 263 (sh) (3.98), 295 (sh) (4.17), 302 (4.23), 306 (4.23), 330 (sh) (3.91); λ_{min}, mμ (log ϵ), 224 (4.11), 274 (3.75), 304 (4.20).

Anal. Calcd. for $C_{15}H_{13}ClNO_4$: C, 57.8; H, 5.8; Cl, 11.4; N, 4.5. Found[a]: C, 57.9; H, 5.8; Cl, 11.3; N, 4.5.

Reaction of XII with Sodium Hydride.—A refluxing solution of 1.51 g. (5.00 mmoles) of XII in 50 ml. of 1,2-dimethoxyethane was treated with 255 mg. of a 53% dispersion of sodium hydride (5.67 mmoles) in mineral oil. The resulting mixture was held at reflux under nitrogen. After 25 min., a 10-ml. aliquot was removed and quenched with 50 ml. of water to yield 227 mg. (85%) of XIII. The remainder of the solution was quenched with 100 ml. of water after 4.5 hr. to yield 996 mg. (94%) of XIII.

3,6-Dichloro-4-(2-mercaptoethylamino)coumarin (XV).—A solution of 4.80 g. (42.0 mmoles) of 2-mercaptoethylamine hydrochloride in 50 ml. of methanol was added to a methanol solution (50 ml.) containing 40.5 mmoles of sodium methoxide. This solution of free 2-mercaptoethylamine was then added to a refluxing solution of 5.02 g. (20.1 mmoles) of 3,4,6-trichlorocoumarin in 100 ml. of methanol. The resulting mixture was held at reflux for 1 hr., cooled to room temperature, and filtered. The precipitate was washed with several portions of water, triturated with benzene, washed with acetone, and dried thoroughly to yield 5.54 g. (95%) of XV: m.p. 262–264° dec.; infrared (KBr) bands 2.99 (m), 5.99 (s), 6.26 (s), 6.54 (s) μ. No solvent could be found for recrystallization. The ultraviolet absorptions for a saturated solution were λ_{max} 210, 223, 240, 250, and 300–342 mμ; λ_{min} *ca.* 275 mμ.

Anal. Calcd. for $C_{11}H_5Cl_2NO_2S$: C, 45.5; H, 3.1; Cl, 24.4; N, 4.8; S, 11.1. Found[a]: C, 45.2; H, 2.8; Cl, 24.3; N, 4.6; S, 11.0.

Reaction of XV with Sodium Hydride.—A solution of 1.48 g. (5.10 mmoles) of XV in 50 ml. of N,N-dimethylformamide was held at a bath temperature of 145° and treated with 299 mg. of a 53% dispersion of sodium hydride (6.63 mmoles) in mineral oil. The reaction mixture was maintained under an atmosphere of nitrogen at 145° for 2 hr. and was then poured into 400 ml. of water. The mixture was filtered and the precipitate was dried and recrystallized from hot acetone to yield 375 mg. (29%) of 9-chloro-2,3-dihydro[1]benzopyrano[3,4-*b*][1,4]thiazin-5(1H)-one (XVI): m.p. 300–302° dec.; infrared (KBr) bands 3.02 (m), 6.02 (s), 6.24 (m), 6.49 (s) μ; λ_{max}, mμ (log ϵ), (222 (4.24), 243 (4.01), 264 (3.85), 320 (3.44), 365 (3.89); λ_{min}, mμ (log ϵ), 290 (3.24).

Anal. Calcd. for $C_{11}H_6ClNO_2S$: C, 52.1; H, 3.2; Cl, 14.0; N, 5.5; S, 12.6. Found[a]: C, 52.0; H, 3.4; Cl, 14.3; N, 5.8; S, 12.9.

Reaction of XV with Less than 1 Equiv. of Sodium Ethoxide.—To a solution of 2.91 g. (10.0 mmoles) of XV in 100 ml. of N,N-dimethylformamide held at a bath temperature of 95–100° was added 100 ml. of a solution containing 9.97 mmoles of sodium ethoxide during 60 min. The reaction mixture was allowed to stir at elevated temperature for an additional 30 min., cooled, and filtered. The precipitate was washed with water and dried to yield 59 mg. (2%) of starting material. The filtrate was poured into 200 ml. of water and allowed to stand overnight. The mixture was filtered, and the precipitate was triturated with 2-butanone. The residue was dried to yield 347 mg. (14%) of XV. The butanone solution, upon concentration, yielded 1.11 g. (37%) of 6-chloro-3-ethoxy-4-(2-mercaptoethylamino)coumarin (XVII): m.p. 170–172°; infrared (KBr) bands 3.03 (w), 6.08 (s), 6.26 (s), 6.42 (s) μ; λ_{max} (saturated solution) 210, 235, 260 (sh), 290 (sh), 305, 314, 347 mμ; λ_{min} 223, 280, 321 mμ.

Anal. Calcd. for $C_{13}H_{14}ClNO_3S$: C, 52.1; H, 4.7; Cl, 11.8; N, 4.7. Found[a]: C, 52.2; H, 4.7; Cl, 11.9; N, 4.7.

The Rearrangement of 3,4-Disubstituted Coumarins to Coumarilic Acid Derivatives in Basic Media[1]

MELVIN S. NEWMAN AND CECILE K. DALTON

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received August 4, 1965

The reaction of 3-chlorocoumarin (I) with sodium methoxide to produce methyl coumarilate (II) has been shown to proceed only if methanol is present. A mechanism for this reaction is proposed. Several 4-substituted 3,6-dichlorocoumarins have been converted into alkyl 3-substituted 5-chlorocoumarilates. In earlier work, these dichlorocoumarins had supposedly been converted into other coumarin derivatives. The correct structures for the compounds in question are shown. All are derivatives of coumarilic acid.

Because of the unexpected reactivity of the 3-chloro substituent in certain 4-substituted aminocoumarins,[2] a study of the reactivity of the 3-chlorine in coumarins bearing different substituents in the 4-position was started. During this study certain errors in previously reported work[3,4] were discovered and are herein corrected. In addition, the general picture of the reaction of 4-substituted 3-chlorocoumarins with alkoxide ions is clarified.

On treatment of 3-chlorocoumarin (I)[5] with sodium methoxide in methanol a good yield of methyl coumarilate (II)[6] was obtained. Although analogous reactions of 3-chloro- and 3-bromocoumarin with alcoholic potassium hydroxide are known,[7] to our knowledge no attempt has been made to explain the results. At first

(1) This work was supported by U. S. Public Health Service Grant GM-07450-03 and in part by a special research grant from The Ohio State University.

(2) M. S. Newman and C. K. Dalton, *J. Org. Chem.*, **30**, 4122 (1965).

(3) M. S. Newman and S. Schiff, *J. Am. Chem. Soc.*, **81**, 2266 (1959).

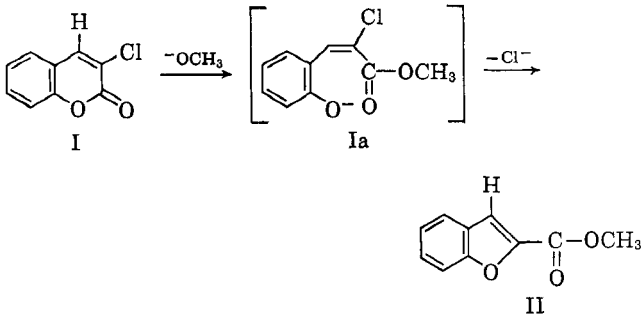
(4) M. S. Newman and C. Y. Peery, *J. Org. Chem.*, **28**, 116 (1963).

(5) We thank the Dow Chemical Co., Midland, Mich., for a generous gift of this compound.

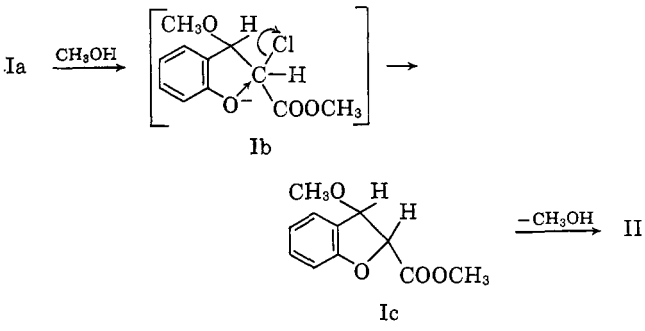
(6) Compare W. H. Perkin, *J. Chem. Soc.*, **24**, 37 (1871).

(7) R. C. Fuson, J. W. Kneisley, and E. W. Kaiser, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 209.

glance, one would postulate that the methoxide ion attacks the carbonyl group of I to yield a phenoxide ion (Ia), which cyclizes to II with loss of a chloride ion. The mechanism of the loss of chloride is the interesting feature of this reaction. As in the previously described



reactions,[2] the net result is the facile displacement of a vinylic halide with no apparent driving force. Two mechanisms may account for this phenomenon: (a) direct cyclization of Ia; or (b) a Michael addition of methanol to the double bond of Ia (or its conjugate acid) to give an intermediate, Ib, having an sp^3 carbon bearing chlorine which could then undergo an intramolecular displacement easily to yield Ic followed by loss of methanol to yield II. In support of mechanism b may be cited the fact that, when I was treated with



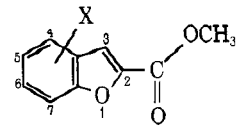
dry sodium methoxide in N-methylpyrrolidone, no II was obtained and 65% of I was recovered.

The above rearrangement of a coumarin to a coumarilate stimulated re-examination of the structures of several compounds reported previously.[3,4] Infrared spectroscopy proved to be of no value as a diagnostic tool since no bands could be found which were peculiar to the coumarins as opposed to the coumarilates. Proton resonance also proved of little value since there are no protons located in strategic positions in the compounds studied. The most valuable correlations were drawn on the basis of ultraviolet spectra. The spectra of a large number of compounds reported in the literature and investigated here indicated that compounds possessing the coumarilate structure very rarely absorb at wave lengths above 300 mμ, while coumarins almost invariably have one or more absorption bands above 300 mμ. Representative spectra are listed in Table I and II.

With this background we re-examined the reaction of 3,4,6-trichlorocoumarin (III)[3] with ethylene glycol in the presence of slightly less than 1 equiv. of sodium ethylene glycoxide. Under these conditions three compounds were obtained: 3,6-dichloro-4-(2-hydroxyethoxy)coumarin (IV), 2-hydroxyethyl 5-chloro-3-(2-hydroxyethoxy coumarilate (V), and the lactone of 5-

TABLE I

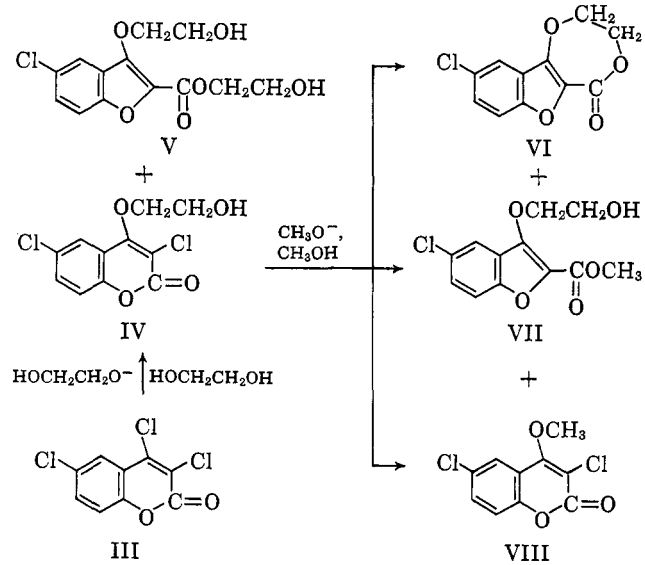
ULTRAVIOLET SPECTRA OF METHYL COUMARILATES



X	λ_{max} (log ε)	
H[a]	218 (3.94)	273 (4.28)
3-Cl[a]	222 (4.04)	277 (4.29)
5-Cl[a]	... ...	269 (4.27)
3-CH_3[b]	220 (4.01)	276 (4.29)
5-CH_3[b]	... ...	274 (4.30)
3-OCH_3[c]	227 (4.04)	287.5 (4.28)
5-NO_2[d]	256 (4.54)	295 (3.70)
3-OH[e]	227 (4.11)	289 (4.31)

[a] R. Andrisano and F. Duro, *Gazz. chim. ital.*, **85**, 381 (1955). [b] R. Andrisano and G. Pappalardo, *ibid.*, **83**, 108 (1953). [c] R. Andrisano, F. Duro, and G. Pappalardo, *Boll. Sci. Fac. chim. Ind. Bologna*, **14**, 96 (1956). [d] R. Adrisano, F. Duro, and G. Pappalardo, *Gazz. chim. ital.*, **86**, 1257 (1956). [e] This work.

chloro-3-(2-hydroxyethoxy)coumarilic acid (VI). In addition, about 35–40% of III was recovered. In previous work,[4] in which excess alkoxide was used, VI was obtained in 81% yield, although the incorrect structure, X, was assigned to the product.

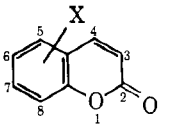


We assume that IV is the first reaction product and that V and VI are produced from IV by attack of alkoxide ion by mechanisms similar to b above. When IV was treated with less than 1 equiv. of sodium methoxide in methanol, VI was formed in 61% yield, methyl 5-chloro-3-(2-hydroxyethoxy)coumarilate in 13% yield, and, significantly, 3,6-dichloro-4-methoxycoumarin (VIII) in 18% yield. The production of VIII provides evidence that Michael addition of alcohols to the coumarins involved occurs as previously postulated.[2] In a similar experiment, treatment of 3,6-dichloro-4-phenoxycoumarin with ethanolic sodium sodium ethoxide afforded a good yield of 3,6-dichloro-4-ethoxycoumarin.

In addition to the spectral evidence for the coumarilate structure of VI and VII, the ready alkaline hydrolysis under mild conditions at room temperature (see Experimental Section) to yield 5-chloro-3-(2-hydroxyethoxy)coumarilic acid (IX) bespeaks the lac-

TABLE II

ULTRAVIOLET SPECTRA OF COUMARIN DERIVATIVES



X	λ_{max}, mμ (log ε)				
H[a]		275 (4.02)	284 (3.96)	310 (3.73)	
3-CH_3[a]		276 (4.04)	284 (4.01)	310 (3.83)	
4-CH_3[a]		272 (4.02)	280 (3.95)	310 (3.77)	
6-CH_3[a]	215 (4.32)	277 (4.05)	287 (3.97)	322 (3.70)	
3-Cl[a]		230 (3.53)	286 (4.05)	315 (3.90)	
4-Cl[a]		274 (4.02)	285 (3.95)	316 (3.72)	
6-Cl[a]	222 (4.38)	272 (4.02)	279 (3.94)	321 (3.65)	
3-OH[a]	229–230 (3.74)		300 (4.03)	310–311 (4.06)	340 (3.45)
3-OCH_3[a]	226 (3.78)		290 (4.06)	304 (4.04)	
4-OCH_3[a]	258 (3.90)	265 (4.05)	276 (4.02)	303 (3.80)	310 (3.67)
6-NO_2[a]		265 (4.38)	315 (3.84)	325 (3.78)	340 (3.75)
6-NH_2[a]		242 (4.35)	282 (4.03)		370 (3.43)
3,4-Cl_2[b]		225 (4.20)	282 (3.99)	291 (3.91)	335 (3.72)
3,4,6-Cl_3[b]		223 (4.32)	282 (4.08)	293 (3.98)	330 (3.78)
3,6-Cl_2-4-OCH_3[b]		223 (4.37)	280 (4.08)	291 (4.04)	320 (3.91)
3,6-Cl_2-4-$N(CH_3)_2$[b]		225 (4.28)	255–275 (3.86)		334 (3.88)

[a] A. Mangini and R. Passerini, *Gazz. chim. ital.*, **87**, 243 (1957). [b] This work.

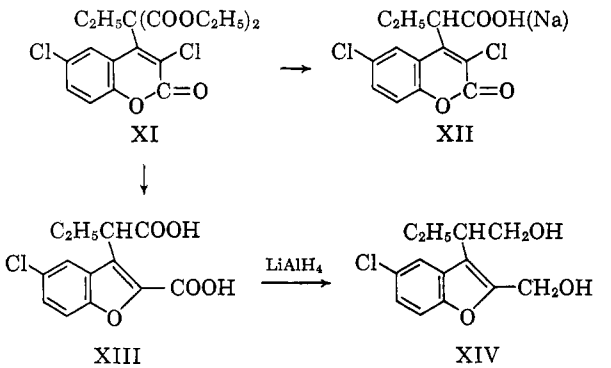
tonic and ester groupings, respectively, since methyl coumarilate (II) and methyl 3-methoxy coumarilate also hydrolyze readily under similar conditions. On attempted alkaline hydrolysis with aqueous sodium hydroxide for 7 days, IV was recovered in 70% yield. Thus coumarin derivatives are much more resistant to alkaline hydrolysis than coumarilic esters.

As compound VI had previously been reported[4] to be 9-chloro-2,3-dihydro-5H-*p*-dioxino[2,3-*c*][1]-benzopyran-5-one (X), an error has been corrected. An attempt to prepare X by treatment of IV in 1,2-dimethoxyethane (glyme) with sodium hydride proved unsuccessful. This failure provides evidence that displacement of the 3-chlorine atom in a coumarin in the absence of an alcohol, even by an intramolecular path, is difficult. A path involving the addition of alcohol to provide an sp^3 carbon prior to displacement of chloride ion[2] thus derives further support (mechanism b above).

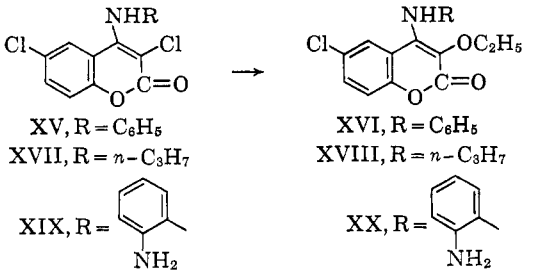
We have further shown that other compounds reported[3,4] as coumarins are in reality derivatives of coumarilic acid. These errors are corrected and the correct structures are shown in Table III.

A compound postulated to be 3,4-dimethoxycoumarin by Arndt[8] has the same melting point as methyl 3-methoxycoumarilate and was probably that. Also, the compound reported[8] to be 3-hydroxy-4-methoxycoumarin was probably 3-methoxycoumarilic acid.

In an attempt to obtain a coumarin with a ring fused in the 3,4-positions by a method involving a ring closure in which a substituent in the 4-position contained a function which could intramolecularly displace a chlorine in the 3-position, we prepared 3,6-dichloro-4-(1,1-dicarboethoxypropyl)coumarin (XI), by condensation of diethyl ethylmalonate with III. We hoped to be able to hydrolyze XI, to decarboxylate the resulting malonic acid to 3,6-dichloro-4-(1-carboxypropyl)coumarin (XII), to form the sodium salt of XII, and to displace intramolecularly the 3-chloro group of XII. However, on alkaline hydrolysis XI was converted into 5-chloro-3-(1-carboxypropyl)coumarilic acid (XIII), which was cyclized to the corresponding anhydride by heating with acetyl chloride. XIII was reduced to the corresponding diprimary alcohol XIV.



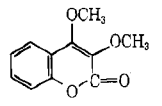
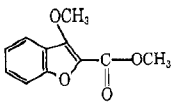
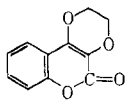
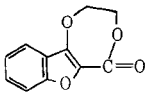
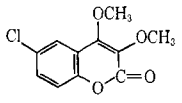
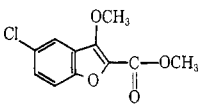
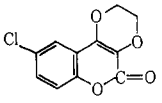
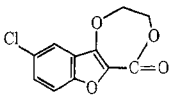
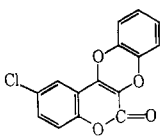
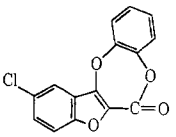
Thus, it appears that only when nitrogen occupies the 4-position of coumarin can a 3-chlorine be displaced by a nucleophile without loss of the coumarin ring system.[2] Other nitrogen-substituted coumarins which exhibited similar behavior on treatment with less than 1 equiv. of sodium ethoxide are as follows: 3,6-dichloro-4-anilinocoumarin (XV) yielded XVI, XVII yielded XVIII, and XIX yielded XX.



In a nonalcoholic medium, however, cyclization with retention of the coumarin ring system may be accomplished, as illustrated by the conversion of XXI to

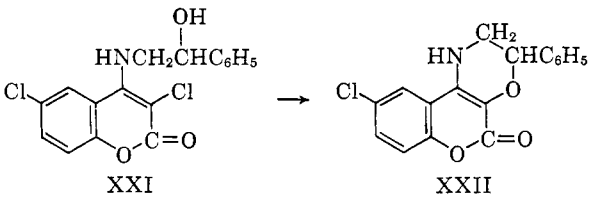
(8) F. Arndt, *Ber.*, **84**, 319 (1951). No spectral data were reported.

TABLE III
STRUCTURE CORRECTIONS

Previously reported incorrect structures[a]	Correct structures	λ_{max}, mμ (log ε)				
		217 (4.01)	227 (4.05)	288 (4.27)		
			227 (4.14)	290 (4.35)		
		208 (4.34)	225 (sh) (4.23)	280 (sh) (4.23)	288 (4.25)	
 X		211 (4.18)	230 (4.15)	291 (4.30)	302 (sh) (4.12)	
		210 (4.41)	216 (sh) (4.40)	252 (3.98)	265 (4.03)	292 (4.09)

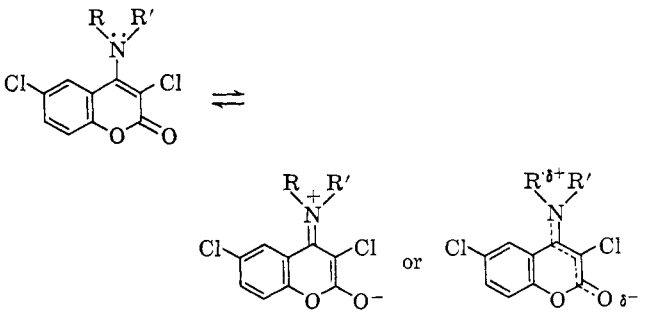
[a] References 3 and 4.

XXII in excellent yield by treatment with sodium hydride in 1,2-dimethoxyethane.



XXI XXII

Thus, the question that still remains is why nitrogen in the 4-position tends to protect the coumarin system against ring contraction to the coumarilate system in the presence of nucleophiles. The only answer which suggests itself is the possibility that 4-aminocoumarins exist in tautomeric equilibrium or as a resonance hybrid which greatly reduces the electrophilic character of the carbonyl carbon, thus discouraging attack at this site which must be the prelude to the coumarin-to-coumarilate ring contraction. The unusual nature of the carbonyl group in 4-aminocoumarins (vinylogous amides[9]) is supported by the high wave length absorption (5.9–6.1 μ) attributed to the carbonyl in a previous publication[4] as well as the unusually low field (γ 6.83, $CDCl_3$ solution) of the N-methyl group in 3,6-dichloro-4-(2-hydroxyethylmethylamino)coumarin[2] compared with a γ value of about 7.0 for N-methylamides and 7.8 for N-methylamines.[10]



(9) See footnote 19 of ref. 3.

Experimental Section[11]

Reaction of 3-Chlorocoumarin with Sodium Methoxide.—To a refluxing solution of 1.79 g. (9.90 mmoles) of 3-chlorocoumarin in 50 ml. of methanol was added a solution of 10.1 mmoles of sodium methoxide in methanol during 37 min. After being held at reflux an additional 80 min., the cooled mixture was evaporated to dryness under reduced pressure. The residue was worked up in the usual way to yield an oil which crystallized on cooling with Dry Ice to give a 91% crude yield of an off-white solid, m.p. 36–46°.

Recrystallization from ethanol yielded 1.01 g. (58%) of methyl coumarilate,[12] m.p. 51–53°. The ultraviolet spectrum is identical with that reported (see Table I).

Reaction of 3-Chlorocoumarin with Sodium Methoxide in N-Methylpyrrolidone.—To a solution of 586 mg. (3.24 mmoles) of 3-chlorocoumarin in 5 ml. of N-methylpyrrolidone maintained at a bath temperature of 75–80° was added a solution of 185 mg. (3.43 mmoles) of dry sodium methoxide in 30 ml. of N-methylpyrrolidone during 5 min. The resulting orange solution was allowed to stir at elevated temperature for an additional 80 min., cooled, and poured into 100 ml. of water. Filtration afforded 312 mg. of starting material; acidification of the weakly basic filtrate yielded an additional 64 mg. of I. Total recovery was 378 mg. (65%).

(10) Tables prepared by G. V. D. Tiers, Minnesota Mining and Manufacturing Co.

(11) All melting point determinations were made on a Fisher-Johns block and are uncorrected. Microanalyses marked b are by Bernhardt, Mülheim, Germany, and s by Schwarzkopf Laboratories, Woodside, N. Y. All infrared spectra were taken in chloroform solution unless otherwise indicated and were run on a Perkin-Elmer Model 137 Infracord spectrophotometer. All ultraviolet spectra were taken in 95% ethanol solution and were run on a Perkin-Elmer Model 202 spectrophotometer. N.m.r. spectra were run on a Varian Associates Model A-60 spectrometer. All reaction solvents were dried over molecular sieves. Where usual work-up is indicated it consisted of extracting the residue with an organic solvent, washing the organic extract with water until neutral, drying over anhydrous magnesium sulfate, filtering, and evaporating to dryness.

(12) C. F. Koelsch and C. R. Stephens, Jr., *J. Am. Chem. Soc.*, **72**, 2209 (1950).

Reaction of 3,4,6-Trichlorocoumarin (III) with Sodium Ethylene Glycoxide.—A solution prepared by treating 594 mg. (25.8 mg.-atoms) of sodium with 100 ml. of ethylene glycol was added over a period of 35 min. to a solution of 6.47 g. (25.9 mmoles) of III[3] in 150 ml. of ethylene glycol maintained at a bath temperature of 110°. The reaction mixture was kept under nitrogen and stirred at 110° for an additional 75 min. Cooling and filtration yielded 1.25 g. (19%) of III. Chromatography over silica gel of the materials isolated from the filtrate on dilution with water afforded an additional 1.33 g. (20%) of III (elution with 1:9 chloroform–benzene), 0.42 g. (7%) of VI, 2.61 g. (37%) of VI, and 1.33 g. (17%) of V. When a similar experiment was carried out on the same scale but at a temperature of 152–158°, the same products were obtained but in slightly different amounts.

3,6-Dichloro-4-(2-hydroxyethoxy)coumarin (IV).—A pure sample of IV [m.p. 141–142°; infrared band at 5.80 μ (s); λ_{max}, mμ (log ϵ), 218 (m) (4.28), 225 (4.31), 281 (4.06), 293 (4.01), 323 (3.83); λ_{min}, mμ (log ϵ), 252 (3.52), 306 (3.72)] was obtained by crystallization from chloroform.

Anal. Calcd. for $C_{11}H_8Cl_2O_4$: C, 48.0; H, 2.9; Cl, 25.8. Found[b]: C, 48.0; H, 3.0; Cl, 26.0.

2-Hydroxyethyl 5-Chloro-3-(2-hydroxyethoxy)coumarilate (V).—A pure sample of V [m.p. 123–124°; infrared band at 5.87 μ (s); λ_{max}, mμ (log ϵ), 215 (4.28), 230 (4.18), 288 (4.28); λ_{min}, mμ (log ϵ), 255 (3.69)] was obtained by crystallization from ethanol.

Anal. Calcd. for $C_{13}H_{13}ClO_6$: C, 51.9; H, 4.4; Cl, 11.8. Found[a]: C, 52.0; H, 4.3; Cl, 12.1.

The di-*p*-nitrobenzoate of V, m.p. 157–160°, was obtained by crystallization from methanol–chloroform.

Anal. Calcd. for $C_{27}H_{19}ClN_2O_{12}$: Cl, 5.9; N, 4.7. Found[b]: Cl, 6.1; N, 4.9.

Lactone of 5-Chloro-3-(2-hydroxyethoxy)coumarilic Acid (VI).—This compound was previously reported as 9-chloro-2,3-dihydro-5H-*p*-dioxino[2,3-*c*][1]benzopyran-5-one.[4] The analytical sample of VI [m.p. 205–207°, was compared with the earlier sample[4] by mixture melting point and infrared spectra. The ultraviolet data for VI are given in Table III.

Reaction of IV with Sodium Methoxide.—A solution of 4.70 mmoles of sodium methoxide in 50 ml. of methanol was added during 50 min. to a refluxing solution of 1.35 g. (4.91 mmoles) of IV in 30 ml. of methanol. The resulting solution was held at reflux for 30 min., and then evaporated to dryness under reduced pressure. The residue was washed with water. By crystallization from hot ethanol and chromatography over 24 g. of silica gel using dichloromethane as eluent, a total of 715 mg. (61%) of VI was obtained. This was preceded off the column by 150 mg. (13%) of 3,6-dichloro-4-methoxycoumarin (VIII), identical with that prepared by another route (see below). A solution of 1% methanol in dichloromethane was then used to elute 220 mg. (17%) of methyl 5-chloro-3-(2-hydroxyethoxy)coumarilate (VII): m.p. 97–98°; infrared band at 5.86 μ (s); λ_{max}, mμ (log ϵ), 213 (4.15), 230 sh (4.05), 287 (4.18); λ_{min}, mμ (log ϵ), 254 (3.56).

Anal. Calcd. for $C_{12}H_{11}ClO_5$: C, 53.2; H, 4.1; Cl, 13.1. Found[a]: C, 53.3; H, 4.3; Cl, 13.0.

3,6-Dichloro-4-methoxycoumarin (VIII).—A solution of 10.0 mmoles of sodium methoxide in 25 ml. of methanol was added to a refluxing solution of 2.49 g. (10.0 mmoles) of III in 350 ml. of methanol. The resulting solution was held at reflux for 24 hr. and then evaporated to dryness. The residue was washed with water and dried to yield 2.13 g. (87%) of 3,6-dichloro-4-methoxycoumarin (VIII): m.p. 163–164°; infrared band at 5.80 μ (s); λ_{max}, mμ (log ϵ), 215 (4.39), 223 (4.37), 280 (4.08), 291 (4.04), 320 (3.91); λ_{min}, mμ (log ϵ), 250 (3.56), 303 (3.79).

Anal. Calcd. for $C_{10}H_6Cl_2O_3$: C, 49.0; H, 2.5; Cl, 28.9. Found[b]: C, 49.0; H, 2.8; Cl, 28.8.

Reaction of 3,6-Dichloro-4-(2-hydroxyethoxy)coumarin (IV) with Sodium Hydride.—A solution of 286 mg. (1.04 mmoles) of IV in 10 ml. of 1,2-dimethoxyethane was treated with 8.50 mg. (3.54 mmoles) of sodium hydride (in a mineral oil dispersion). When the gas evolution had ceased, the reaction mixture was heated to reflux under nitrogen for 1.5 hr., then poured into 100 ml. of water. The product was shown not to contain any VI by thin layer chromatography.

5-Chloro-3-(2-hydroxyethoxy)coumarilic Acid (IX).—A suspension of 130 mg. (0.544 mmole) of VI in 5.0 ml. of a 0.1006 *N* sodium hydroxide solution containing 0.05 ml. of ethanol was stirred at room temperature for 24 hr. The reaction mixture was filtered, and the residue was washed with water and dried to yield 8.6 mg. (6.6%) of VI. Acidification of the filtrate yielded 119 mg. (92%) of 5-chloro-3(-2-hydroxyethoxy)coumarilic acid (IX): m.p. 195–200°; infrared band (KBr) at 5.93 μ (s); λ_{max}, mμ (log ϵ), 215 (4.20), 230 (sh) (4.14), 285 (4.20); λ_{min}, mμ (log ϵ), 253 (3.64).

Anal. Calcd. for $C_{11}H_9ClO_5$: C, 51.5; H, 3.5; Cl, 13.8. Found[b]: C, 51.2; H, 3.7; Cl, 13.6.

By similar hydrolyses, V was converted into IX in 85% yield, methyl coumarilate (II) into coumarilic acid, m.p. 196–198°, in quantitative yield, and methyl 3-methoxycoumarilate into 3-methoxycoumarilic acid,[13] m.p. 181° (subl.), in 83% yield.

However, when a suspension of 139 mg. (0.506 mmole) of IV in 5.0 ml. of a 0.1 *N* aqueous sodium hydroxide was allowed to stir at room temperature for 7 days, no acidic material was obtained and 70% of IV was recovered.

3,6-Dichloro-4-phenoxycoumarin.—A solution of 930 mg. (9.88 mmoles) of phenol in 10 ml. of *t*-butyl alcohol was added to a solution containing 9.95 mmoles of potassium *t*-butoxide in 20 ml. of *t*-butyl alcohol under nitrogen. To this solution was added 2.50 g. of III and 15 ml. of *t*-butyl alcohol. The resulting mixture was held at reflux for 3.5 hr. The cooled mixture was filtered and the resulting precipitate was washed with water and dried to yield 2.26 g. (74%) of 3,6-dichloro-4-phenoxycoumarin: m.p. 125–127°; infrared band at 5.75 μ (s); λ_{max}, mμ (log ϵ), 213 (4.44), 220 (4.46), 280 (4.09), 289 (4.01), 328 (3.84); λ_{min}, mμ (log ϵ), 250 (3.41), 308 (3.75).

Anal. Calcd. for $C_{15}H_8Cl_2O_3$: C, 58.7; H, 2.6; Cl, 23.1. Found[b]: C, 58.5; H, 2.7; Cl, 23.2.

A solution of 5.04 mmoles of sodium ethoxide in ethanol was added during 1 hr. to a refluxing solution of 1.55 g. (5.04 mmoles of 3,6-dichloro-4-phenoxycoumarin in 25 ml. of ethanol. After an additional 30 min. at reflux the mixture was evaporated to dryness. The residue was washed with water and recrystallized from 95% ethanol to yield 660 mg. (51%) of 3,6-dichloro-4-ethoxycoumarin: m.p. 95–96°; infrared band at 5.76 μ (s); λ_{max}, mμ (log ϵ), 220 (sh) (4.54), 267 (sh) (4.05), 278 (4.17), 284 (sh) (4.12), 290 (4.12), 322 (3.96); λ_{min}, mμ (log ϵ), 247 (3.55), 285 (4.10), 302 (3.79).

Anal. Calcd. for $C_{11}H_8Cl_2O_3$: C, 51.0; H, 3.1; Cl, 27.4. Found[a]: C, 51.3; H, 3.5; Cl, 27.3.

More of this compound was present in the mother liquors, but no attempt to maximize the yield was made.

3,6-Dichloro-4-(1,1-dicarbethoxypropyl)coumarin (XI).—A solution of 3.76 g. (20.0 mmoles) of diethyl ethylmalonate in 50 ml. of N,N-dimethylformamide was added slowly to 929 mg. of a 53.4% dispersion of sodium hydride in (20.6 mmoles) in mineral oil under nitrogen. To the clear, pale yellow solution was added a solution of 4.99 g. (20.0 mmoles) of III in 50 ml. of N,N-dimethylformamide. The reaction mixture was allowed to stir at room temperature for 1 hr., at 110° for 1.5 hr., and was then poured into 600 ml. of water. The precipitate was washed and dried to yield 6.11 g. (76%) of XI: m.p. 128–130°; infrared band at 5.83 μ (s); λ_{max}, mμ (log ϵ), 223, (4.21), 286 (3.91), 333 (3.68); λ_{min}, mμ (log ϵ), 253 (3.41), 314 (3.60).

Anal. Calcd. for $C_{18}H_{18}Cl_2O_6$: C, 53.9; H, 4.5; Cl, 17.7. Found[14]: C, 54.3; H, 4.5; Cl, 17.6.

5-Chloro-3-(1-carboxypropyl)coumarilic Acid (XII).—A suspension of 2.0 g. (5.0 mmoles) of XI in a solution of 9.8 g. (170 mmoles) of potassium hydroxide in 20 ml. of water was heated to reflux for 1 hr. (homogeneous solution within 15 min.), cooled in an ice bath, acidified slowly, and extracted with one 200-ml. portion and two 100-ml. portions of ether. After the usual work-up, the resulting oil was decarboxylated by heating on a steam bath until the oil solidified. The solid was recrystallized from ether to yield 0.45 g. (32%) of XII: m.p. 226–226.5°; infrared band at 5.93 μ (s); λ_{max}, mμ (log ϵ), 217 (4.24), 265 (sh) (4.05), 274 (4.11), 282 (sh) (4.05), 303 (sh) (3.64); λ_{min}, mμ (log ϵ), 242 (3.51).

Anal. Calcd. for $C_{13}H_{11}ClO_5$: C, 55.2; H, 3.9; Cl, 12.5. Found[14]: C, 55.1; H, 3.9; Cl, 12.8.

Anhydride of XII.—A mixture of 1.41 g. of XII and 50 ml. of acetyl chloride was held at reflux for 20 hr. and evaporated to dryness under reduced pressure. Ether was added to the residue and the mixture was filtered to yield 0.76 g. (58%) of the anhydride: m.p. 191–193°; infrared bands at 5.55 (s), 5.65 μ (s); λ_{max}, mμ (log ϵ), 217 (4.36), 270 (4.19), 277 (4.27), 288 (sh) (4.13), 303 (sh) (3.75), 312 (sh) (3.60); λ_{min}, mμ (log ϵ), 245 (3.47).

---

(13) K. von Auwers, *Ann.*, **393**, 338 (1912).

(14) Microanalysis was by Micro-Analysis, Inc., Wilmington, Del.

(15) Microanalysis were by Galbraith Laboratories, Knoxville, Tenn.

Anal. Calcd. for $C_{13}H_{19}ClO_4$: C, 59.0; H, 3.4; Cl, 13.4. Found[15]: C, 58.9; H, 3.5; Cl, 13.3.

Reduction of XIII with Lithium Aluminum Hydride.—To a slurry of 175 mg. (4.62 mmoles) of lithium aluminum hydride in 20 ml. of ether was added 281 mg. (0.993 mmoles) of XIII in several portions. The mixture was heated to reflux when hydrogen evolution ceased. After 18 hr. at reflux, the cooled mixture was treated with saturated ammonium chloride solution and acidified with 20% sulfuric acid. After the usual work-up, the resulting colorless oil could not be crystallized, but was undoubtedly mainly the diol XIV, as indicated by n.m.r. analysis. The oil was converted to the di-*p*-nitrobenzoate which was a solid, m.p. 128–129°, in high yield.

Anal. Calcd. for $C_{27}H_{21}ClN_2O_9$: C, 58.7; H, 3.8; Cl, 6.4; N, 5.1. Found[b]: C, 58.7; H, 3.9; Cl, 6.6; N, 5.2.

3,6-Dichloro-4-(2-phenyl-2-hydroxyethylamino)coumarin (XXI).—A refluxing solution of 2.50 g. (10.0 mmoles) of III in 100 ml. of ethanol was treated with a solution of 2.77 g. (20.2 mmoles) of 2-hydroxyphenethylamine in 10 ml. of ethanol at reflux for 2.5 hr. After cooling, the resulting precipitate was washed with several portions of distilled water and dried to yield 2.99 g. (86%) of XV: m.p. 193–195°; infrared bands (KBr) at 2.87 (m), 2.99 (m), 6.01 μ (s); λ_{max}, mμ (log ϵ), 220 (4.57), 250 (sh) (4.09), 312 (4.09), 325 (4.09), 337 (sh) (4.00); λ_{min}, mμ (log ϵ), 276 (3.34), 320 (4.07).

Anal. Calcd. for $C_{17}H_{13}Cl_2NO_3$: C, 58.3; H, 3.7; Cl, 20.3; N, 4.0. Found[a]: C, 58.4; H, 3.9; Cl, 20.2; N, 4.0.

2-Phenyl-9-chloro-2,3-dihydro[1]benzopyrano[3,4–6][1,4]oxazin-5(1H)-one (XXII).—A refluxing solution of 2.72 g. (7.77 mmoles) of XXI in 85 ml. of 1,2-dimethoxyethane was treated with 389 mg. of a 53% dispersion of sodium hydride (8.58 mmoles) in mineral oil. The reaction mixture was maintained under a nitrogen atmosphere and held at reflux for 3 hr. The cooled reaction mixture was filtered and the precipitate was washed with several portions of water and dried to yield 2.24 g. (92%) of XXII, m.p. 305–310° dec. Recrystallization from acetone yielded the analytical sample: m.p. 310–312° dec.; infrared bands (KBr) at 2.99 (m), 3.04 (w), 6.02 μ (s); λ_{max}, mμ (log ϵ), 210 (4.38), 230 (4.19), 251 (4.05), 290 (sh) (3.66), 298 (3.87), 302 (3.90), 309 (4.02), 341 (3.91); λ_{min}, mμ (log ϵ), 277 (3.28), 319 (3.75).

Anal. Calcd. for $C_{17}H_{12}ClNO_3$: C, 65.1; H, 3.9; Cl, 11.3; N, 4.5. Found[b]: C, 65.0; H, 4.2; Cl, 11.4; N, 4.4.

3,6-Dichloro-4-anilinocoumarin (XV).—A mixture of 2.55 g. (10.2 mmoles) of III, 1.96 g. (21.0 mmoles) of aniline, and 20 ml. of N,N-dimethylformamide was heated on a steam bath for 30 min. The cooled reaction mixture was poured into 500 ml. of water and filtered. The precipitate was dried and recrystallized from benzene to yield 2.43 g. (78%) of XV: m.p. 222–224°; infrared bands at 2.92 (w), 5.83 μ (s); λ_{max}, mμ (log ϵ), 220 (4.27), 228 (4.30), 254 (4.14), 278 (3.89), 333 (4.08); λ_{min} mμ (log ϵ), 244 (4.11), 295 (3.79).

Anal. Calcd. for $C_{15}H_9Cl_2NO_2$: C, 58.9; H, 3.0; Cl, 23.2; N, 4.6. Found[b]: C, 59.1; H, 2.9; Cl, 23.3; N, 4.5.

3-Ethoxy-4-anilino-6-chlorocoumarin (XVI).—To a refluxing solution of 650 mg. (2.12 mmoles) of 3,6-dichloro-4-anilinocoumarin in 10 ml. of ethanol was added 20 ml. of 0.1 *N* sodium ethoxide in ethanol during 10 min. The resulting mixture was held at reflux for an additional 60 min., diluted with water, and cooled. There was obtained 544 mg. (85%) of XVI, m.p. 115–117°. Crystallization from 95% ethanol afforded the analytical sample: m.p. 116–117°; infrared bands at 3.03 (w), 5.97 μ (s); λ_{max}, mμ (log ϵ), 208 (4.42), 220 (sh) (4.34), 260 (4.36), 304 (3.97), 313 (4.04), 350 (4.05); λ_{min}, mμ (log ϵ), 232 (4.03), 287 (3.78), 321 (3.80).

Anal. Calcd. for $C_{17}H_{14}ClNO_3$: C, 64.7; H, 4.5; Cl, 11.2; N, 4.4. Found[a]: C, 64.7; H, 4.7; Cl, 11.3; N, 4.4.

6-Chloro-3-ethoxy-4-(1-propylamino)coumarin (XVIII).—A refluxing solution of 543 mg. (1.99 mmoles) of 3,6-dichloro-4-(*n*-propylamino)coumarin[4] in 10 ml. of ethanol was treated with 20 ml. of a 0.1 *N* sodium ethoxide solution during 13 min. The reaction mixture was held at reflux for 30 min., cooled to room temperature, and filtered. The filtrate was evaporated to dryness, and the residue was washed with water and dried to yield 536 mg. (96%) of colorless XVIII: m.p. 70–71°; infrared bands at 3.00 (w), 6.00 μ (s); λ_{max}, mμ (log ϵ), 208 (4.41), 234 (4.19), 262 (4.02), 303 (3.88), 311 (3.95), 347 (3.98); λ_{min}, mμ (log ϵ), 223 (4.09), 255 (3.99), 281 (3.45), 320 (3.78).

Anal. Calcd. for $C_{14}H_{16}ClNO_3$: C, 59.7; H, 5.7; Cl, 12.6; N, 5.0. Found[a]: C, 59.7; H, 5.7; Cl, 12.6; N, 5.2.

3-Ethoxy-4-(*o*-aminoanilino)-6-chlorocoumarin (XX).—A refluxing solution of 653 mg. (2.03 mmoles) of 3,6-dichloro-4-(*o*-aminoanilino)coumarin (XIX)[4] in 10 ml. of ethanol was treated with 20 ml. of a 0.1 *N* sodium ethoxide in ethanol during 21 min. The reaction mixture was held at reflux for an additional 30 min. and cooled to room temperature. The precipitate was collected, washed with several portions of ethanol and with water, and dried to yield 408 mg. of XX as yellow needles, m.p. 146–148°. An additional 188 mg. of XX (total yield 89%) was obtained from the filtrate. Recrystallization from ethanol afforded the analytical sample: m.p. 146–148°; infrared bands at 3.00 (w), 5.98 μ (s); λ_{max}, mμ (log ϵ), 210 (4.19), 240 (4.03), 255 (3.98), 299 (4.12), 303 (4.12), 310 (4.11), 345 (4.04); λ_{min}, mμ (log ϵ), 277 (3.91), 301 (4.11), 306 (4.09), 321 (3.91).

Anal. Calcd. for $C_{17}H_{15}ClN_2O_3$: C, 61.7; H, 4.6; Cl, 10.7; N, 8.5. Found[a]: C, 61.9; H, 4.8; Cl, 10.8; N, 8.5.

Reactions of Alkyl Allyl and Alkyl Propenyl Ethers with *n*-Butyllithium

C. D. BROADDUS

The Procter & Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45239

Received July 13, 1965

The reaction of alkyl allyl ethers with *n*-butyllithium in hydrocarbon solvent has been found to be quite temperature dependent. At −33° isomerization to the more stable alkyl *cis*-propenyl isomer occurs. At 70° a cleavage reaction produces an *n*-alkyl alcohol and heptene-1, and, at intermediate temperatures, mixtures of products are obtained. The alkyl *cis*-propenyl ethers were shown to be stable to the reaction conditions.

Reactions of ethers with alkyllithium reagents have received considerable study and various mechanistic pathways have been described for these rather complex reaction systems. Among these are displacement,[1] metalation adjacent to the oxygen atom,[2] ring metalation *ortho* to an ether substituent,[3] α elimination,[4] Wittig rearrangement,[5] and β elimination reactions.[6] In the special case of ethers which are capable of producing a resonance-stabilized anionic intermediate, benzyl compounds have been the most thoroughly studied, with Wittig rearrangement being the most commonly reported reaction. The corresponding reactions of allyl and vinyl ethers are relatively unexplored although

(1) K. Ziegler and H.-G. Gellert, *Ann.*, **567**, 185 (1950).

(2) See H. Hoberg, *ibid.*, **656**, 1 (1962), for leading references.

(3) H. Gilman and J. W. Morton, Jr., *Org. Reactions*, **8**, 258 (1954).

(4) U. Schöllkopf and M. Eisert, *Angew. Chem.*, **72**, 349 (1960); *Ann.*, **664**, 76 (1963).

(5) P. T. Lansbury and V. A. Pattison, *J. Org. Chem.*, **27**, 1933 (1962), and references therein.

(6) R. L. Letsinger and E. Bobko, *J. Am. Chem. Soc.*, **75**, 2649 (1953); R. L. Letsinger and D. F. Pollart, *ibid.*, **78**, 6079 (1956).