TABLE II

DMSO-d_6, +drops	δ H_{B_2} 12	δ H_{B_2} 13	δ H_{OH} 12	δ H_{OH} 13
0	5.85	5.85	3.53	3.53
1	5.84	5.87	4.51	4.61
2	5.83	5.90	5.49	5.58
3	5.82	5.90	6.28	6.28
4	5.82	5.90	6.75	6.68
Pure DMSO-d_6	5.98	5.87	7.8 (s, broad)	

Anal. Calcd for $C_{16}H_{12}Br_2O_2$: C, 48.48; H, 8.03. Found: C, 48.51; H, 3.19.

Dehydrations of **12**, and also **14** and **15**, to the corresponding furans were practically quantitative in warm glacial acetic acid (15 min).

2,3,4,5-Tetraphenyl-2,5-hydrofuranol (15). Borohydride reduction of *cis*-dibenzoylstilbene[3,6] (2.8 g in 200 ml of absolute methanol with 2 g of $NaBH_4$ warmed with stirring for 20 min), followed by ice–water quench, and crystallization from hexane gave 2.5 g of **15** (90%), mp 160–161°.

Anal. Calcd for $C_{28}H_{22}O_2$: C, 86.12; H, 5.69. Found: C, 86.01; H, 5.67.

Preparation of 2,5-di-(4-bromophenyl)-3,4-diphenyl-2,5-hydrofuranol (14) was done by $NaBH_4$ reduction of the *cis* unsaturated diketone[4b] (91%, recrystallized from hexane, mp 158–160°): ir (KBr) 3425 cm^{-1} (associated OH), none between 1650 and 1700 cm^{-1} (C=O).

Registry No.—**1**, 25244-40-0; **2**, 25244-41-1; **5**, 25244-42-2; **7**, 25244-43-3; **12**, 25244-44-4; **14**, 1888-40-0; **15**, 25244-46-6.

Acknowledgment.—The preparations of some intermediates and the synthesis of **12** were carried out by L. Hayes.

Aldol Condensations of Leucoquinizarin

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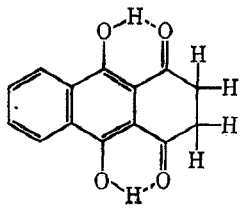
Hydrochloric acid was found to be an effective catalyst for condensation of leucoquinizarin with aromatic mono- and dialdehydes but ineffective with aliphatic aldehydes; monoaldehydes gave 2-alkylquinizarins; *o*-dialdehydes gave polycyclic compounds. Piperidinium acetate was found to be effective for both aliphatic and aromatic aldehydes. 2-Alkylleucoquinizarins likewise gave 2,3-dialkylquinizarins. They are presented in relationship to previously reported alkaline dithionite condensations. A mechanism is proposed in which the dehydration step is suggested to be rate determining.

Leucoquinizarin has been shown by proton magnetic resonance studies to exist, in solution, entirely as the diketo tautomer, 2,3-dihydro-9,10-dihydroxy-1,4-anthracenedione **1**.[1] This diphenolic diketone is known to undergo aldol condensations with aldehydes.



1

Earlier workers[2,3] investigated the condensation of leucoquinizarin with aldehydes in alkaline dithionite solution under nitrogen at 90–95° and then allowed the products to interact with air. Under these conditions formaldehyde gave 2,3-dimethylquinizarin; however, other aliphatic aldehydes up to C_8 and aromatic aldehydes gave condensation products involving only one molecule of aldehyde per molecule of leucoquinizarin. Aldehydes above C_8 failed to give condensation products.

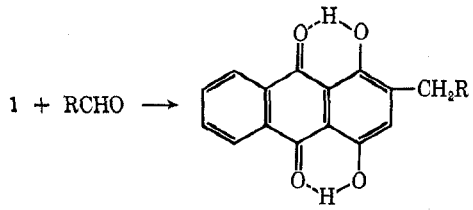
Marschalk, *et al.*,[2] were able to reduce 2-ethylquinizarin with dithionite and then to react the reduced product with formaldehyde; 2-ethyl-3-methylquinizarin was obtained. As will be shown later the failure of most aldehydes (except formaldehyde) to give 2,3-disubstituted products in the alkaline dithionite procedure cannot be attributed to steric hindrance of the monocondensation product, *i.e.*, 2-alkylquiniazrin.

Alkaline Dithionite Condensations.—In the present investigation, we repeated the condensation of leucoquinizarin with a large excess of butyraldehyde in alkaline dithionite and then followed the fate of the aldehyde.

Vapor phase chromatography revealed the absence of butyraldehyde at the end of the reaction; the only product isolated had one molecule of aldehyde per mole of quinizarin as observed by the previous investigators. We conclude that the alkaline dithionite procedure is not a general method for introducing two molecules of aldehyde in quinizarin owing to the competing self-condensation of aldehydes having α hydrogens. The observation that aldehydes above C_8 fail to react at all may simply reflect lack of solubility of these aldehydes in the reaction medium.

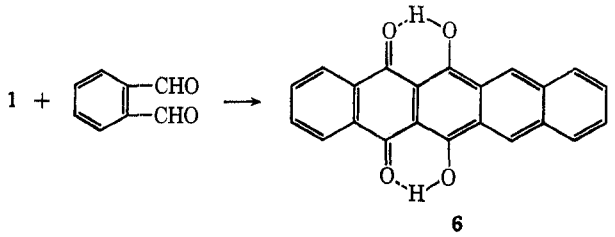
Aqueous Hydrochloric Acid Catalyzed Condensations.—We have studied the reactions of leucoquinizarin with a variety of aldehydes in 2-propanol using concentrated hydrochloric acid as catalyst with the following results. Aliphatic aldehydes[4] C_4 through C_{12} failed to give condensation products. This failure cannot be attributed to the destruction of the aldehyde prior to its condensation with leucoquinizarin, since, at least in the case of butyraldehyde, considerable excess of the aldehyde remained after a 20-hr reaction period. Aromatic monoaldehydes including those with electron-releasing and -withdrawing substituents gave condensation products **2**, **3**, **4**, **5**, involving one molecule of aldehyde per molecule of leucoquinizarin.

(1) S. M. Bloom and R. H. Hulton, *Tetrahedron Lett.*, No. 28, 1993 (1963).
(2) Ch. Marschalk, F. Koenig, and N. Ouroussoff, *Bull. Soc. Chim., Fr.*, 1545 (1936).
(3) A. T. Peters, Jr., and A. T. Peters, *J. Chem. Soc.*, 1125 (1960).
(4) In the present investigation we were concerned only with aldehydes C_4 through C_{12}.

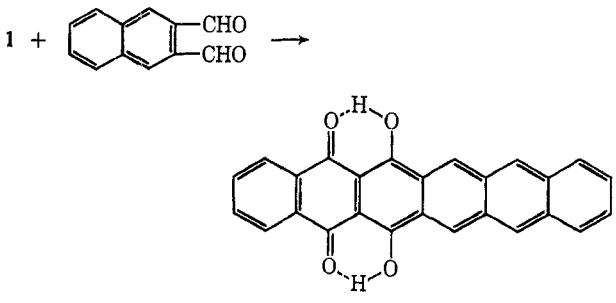


2, R = C_6H_5
3, R = p-C_6H_4Cl
4, R = p-$C_6H_4OCH_3$
5, R = p-$C_6H_4NMe_2$

Aromatic o-dialdehydes, *i.e.*, o-phthaldehyde and naphthalene-2,3-dialdehyde, gave the corresponding pentacence **6** and hexacene **7** derivatives resulting from a two-stage condensation involving one molecule of dialdehyde and one molecule of leucoquinizarin.



6



7

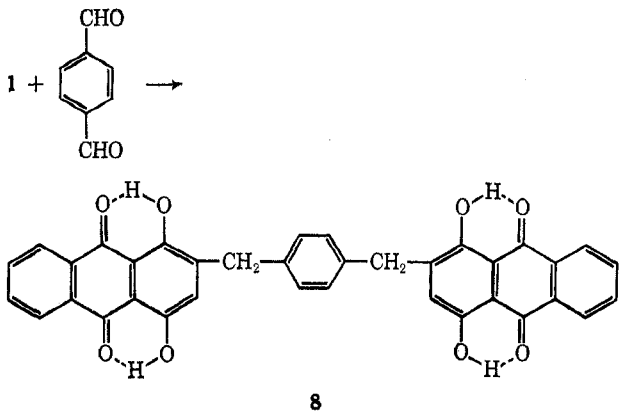
The ease with which o-dialdehydes condense indicates the high degree of reactivity of both the 2 and 3 positions of leucoquinizarin, thus providing a convenient route to polycyclic aromatics.

The pentacene derivative **6** has been described by Weizmann[5] who prepared it by the fusion of naphthalene-2,3-dialdehyde with 1,4-dihydroxynaphthalene in presence of boric acid. We repeated Weizmann's preparation and verified the identity of **6** made by the two methods by mixture melting points and ir and mass spectra. Ir and mass spectral data for the hexacene derivative **7** were also consistent with the assigned structure.

Terephthaldehyde gave a product resulting from the condensation of one molecule of aldehyde with two molecules of leucoquinizarin **8**.

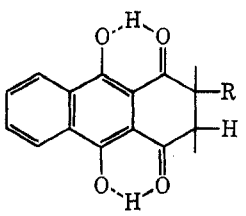
Piperidinium Acetate Catalyzed Condensations.—Piperidinium acetate in 2-propanol was found to be an excellent catalyst for aliphatic aldehydes in the C_4–C_{12} range. Under these conditions 2-n-butyl-, 2-n-decyl-, and 2-n-dodecylquinizarin **9**, **10**, and **11** were readily prepared. Likewise, one molecule of an aromatic aldehyde and dialdehydes condensed with one molecule of leucoquinizarin to give compounds **2**, **6**, and **7**.

(5) C. H. Weizmann, L. Haskelberg, and (in part) T. Berlin, *J. Chem. Soc.*, 398 (1939).



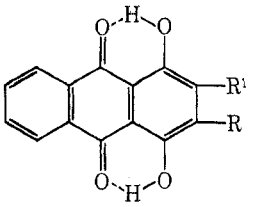
8

A useful extension of the scope of the piperidinium acetate catalyzed condensation consists in reducing the 2-substituted quinizarins to the corresponding leuco form with alkaline dithionite and then condensing these with a second molecule of an aliphatic or aromatic aldehyde. These leuco forms, **12** and **13**, are formulated as diphenolic diketo tautomers on the basis of their ir and nmr spectra. Both **12** and **13** underwent facile



12, R = C_4H_9n
13, R = $CH_2C_6H_5$

condensation with aliphatic and aromatic aldehydes to give 2,3-disubstituted quinizarins **14**, **15**, and **16**.



14, R = C_4H_9n; R^1 = C_4H_9n
15, R = C_4H_9n; R^1 = $CH_2C_6H_5$
16, R = $CH_2C_6H_5$; R^1 = $CH_2C_6H_5$

Benzaldehyde reacted much faster than butyraldehyde; it gave 73 and 67% yields, respectively, of the 2,3-disubstituted products **15** and **16** in a 4-hr reaction period, whereas butyraldehyde required 20 hr to produce a 42% yield when condensed with **12**, and gave a mixture of 2-benzylquinizarin **2** and **15** when condensed with **13**. This is seen as evidence that the failure of most aldehydes to give 2,3-disubstituted products in the alkaline dithionite procedure is due to the reactivity of the aldehyde rather than to steric hindrance.

Mechanism of the Acid-Catalyzed Aldol Condensation of Leucoquinizarin.—Noyce and Pyror[6] have studied the kinetics of the condensation of benzaldehyde with acetophenone in strong acid. They found the rate to be proportional to the concentration of benzaldehyde, the concentration of acetophenone, and to Hammett's

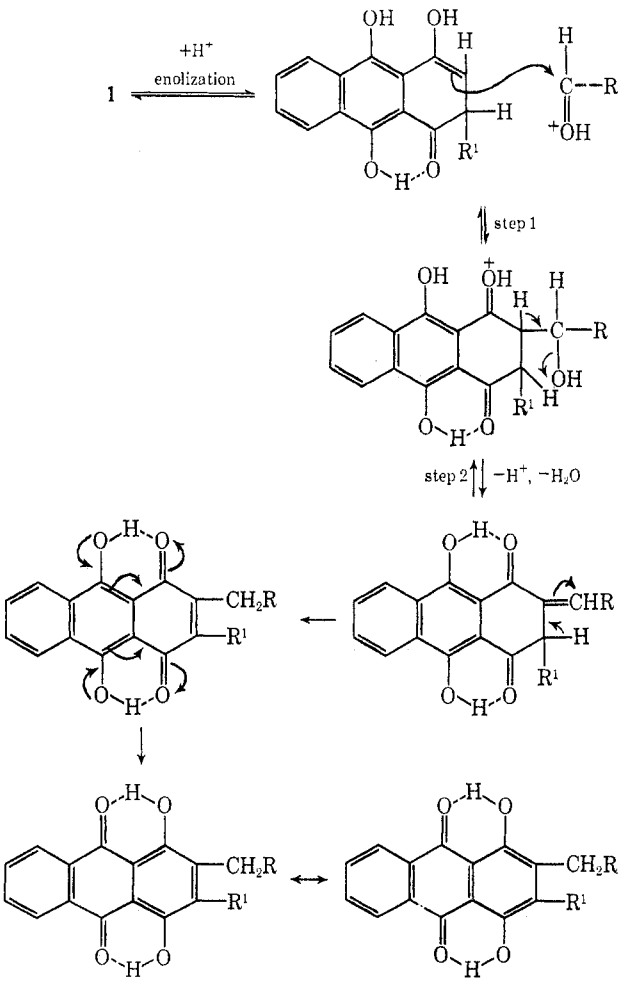
(6) S. D. Noyce and W. A. Pyror, *J. Amer. Chem. Soc.*, **77**, 1397 (1955).

acidity function, h_0. They suggested that the rate-determining step could be either (1) the condensation between the enol of acetophenone and a protonated benzaldehyde or (2) the dehydration of the β-hydroxy ketone intermediate.

Our results can be interpreted by suitable modification of this mechanistic scheme. The following facts must be accommodated: (1) aliphatic aldehydes failed to condense with leucoquinizarin when aqueous hydrochloric acid was the catalyst but did so when piperidinium acetate was used (in both cases 2-propanol was the solvent); (2) aromatic aldehydes condensed readily in the presence of either catalyst; (3) aromatic *o*-dialdehyde involved both aldehydes in the condensation, but only one molecule of monoaldehyde entered in the condensation.

A mechanism for the condensation of leucoquinizarin with monoaldehydes is suggested in Scheme I. Since aliphatic aldehydes, in general, are more reactive than

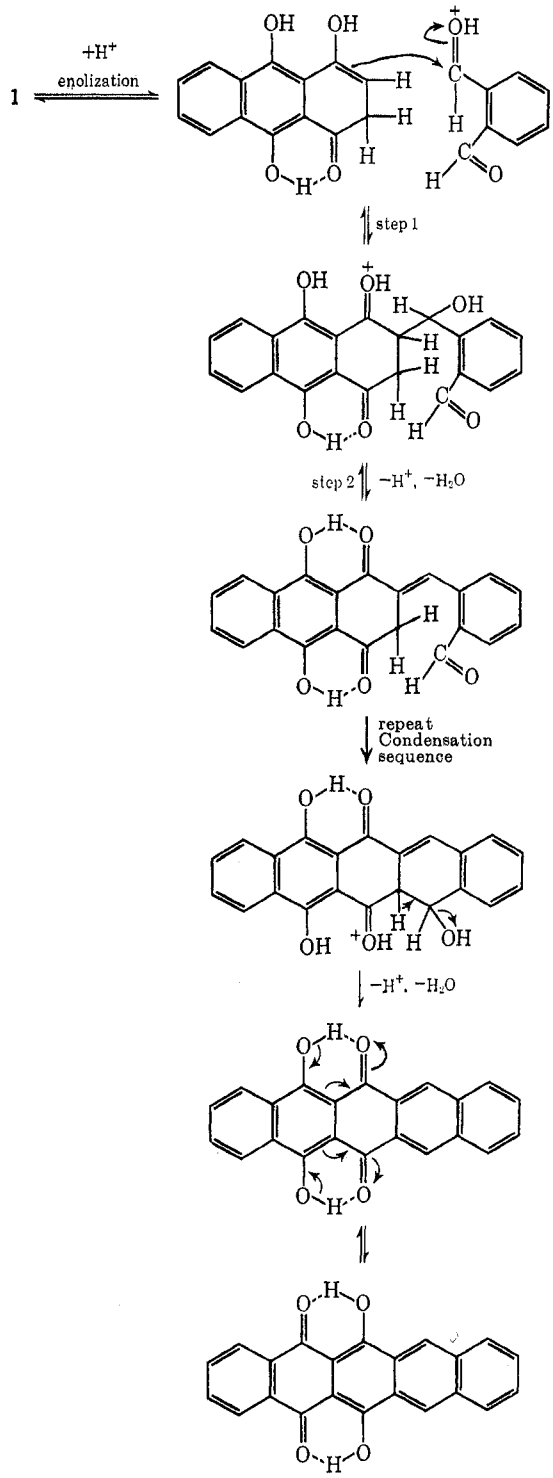
SCHEME I



R = alkyl or aryl
R′ = H, alkyl, or arylmethylene

aromatic aldehydes in aldol condensations, our observations suggest that the dehydration (step 2) may be rate determining in the case of leucoquinizarin. Aromatic aldehydes result in β-aryl, α,β-unsaturated ketones which are more stable and hence provide greater driving force for the dehydration than the corresponding

SCHEME II



β-alkyl unsaturated ketones. Note that the oxidation level of leucoquinizarin is raised to that of quinizarin in this mechanism.

The superior catalytic activity of piperidinium acetate as compared with hydrochloric acid in the condensation of aliphatic aldehydes may be explained in terms of Brønsted's extended theory of acid and basic catalysis.[7] The piperidinium ion (acid) promotes the dehydration step 2 augmented by the acetate ion (base) acting as the proton acceptor.[8]

(7) J. N. Brønsted, *Chem. Rev.*, **5**, 231 (1928).

TABLE I
PHYSICAL DATA

Compd	Aldehyde, mol	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
2	Benzaldehyde, 0.05	181–182[a]	$C_{21}H_{14}O_4$	76.36	4.24	76.03	4.13
3	*p*-Chlorobenzaldehyde, 0.02	181–182[b]	$C_{21}H_{13}O_4Cl$	69.23	3.57	69.40	3.47
4	*p*-Methoxybenzaldehyde, 0.05	144–145[b]	$C_{22}H_{16}O_5$	73.33	4.49	73.44	4.38
5	*p*-Dimethylaminobenzaldehyde, 0.01	208–209[b]	$C_{23}H_{19}NO_4$	73.99	5.09	73.88	4.88
6	*o*-Phthalaldehyde, 0.01	396–398[c]	$C_{22}H_{12}O_4$	77.64	3.53	77.56	3.44
7	Naphthalene-2,3-dialdehyde, 0.01	434–436[b]	$C_{26}H_{14}O_4$	80.00	3.59	79.93	3.48
8	Terephthaldehyde, 0.005	>400[d]	$C_{36}H_{22}O_8$	74.24	3.78	73.93	4.00

[a] Reference 2a. [b] Crystallized from Methyl Cellosolve. [c] Reference 5b. [d] Crystallized from *o*-dichlorobenzene.

TABLE II
PHYSICAL DATA

Compd	Aldehyde	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
9	Butyraldehyde	123–124[a]	$C_{18}H_{16}O_4$	72.97	5.40	72.90	5.32
10	*n*-Decylaldehyde	86–87[b]	$C_{24}H_{28}O_4$	75.79	7.37	75.57	7.41
11	*n*-Dodecylaldehyde	91–92[c]	$C_{26}H_{32}O_4$	76.47	7.84	76.56	7.74

[a] Reference 2a. [b] Crystallized from ethanol. [c] Crystallized from 1-butanol.

TABLE III
PHYSICAL DATA

Compd	Reactants: Leucoquinizarin	Reactants: Aldehyde	% yield: 4 hr	% yield: 20 hr	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
14[a]	2-*n*-Butyl	*n*-Butyraldehyde	0	42	136–137	$C_{22}H_{24}O_4$	75.00	6.82	75.05	6.77
15[b,c]	2-*n*-Butyl	Benzaldehyde	73		136–137	$C_{25}H_{22}O_4$	77.72	5.70	77.58	5.56
15[b,c]	2-Benzyl	*n*-Butyraldehyde	0	*d*	136–137					
16[a]	2-Benzyl	Benzaldehyde	67		198–199	$C_{28}H_{20}O_4$	80.00	4.65	80.17	5.01

[a] Crystallize from methylcyclohexane. [b] Crystallized from 2-propanol. [c] Mixture melting point of products made by these two routes showed no depression. [d] Mixture of 2-*n*-butyl- and 2-*n*-butyl-3-benzylquinizarin (identified by comparing tlc with tlc of authentic samples on silica gel plate, eluent ethyl acetate–chloroform).

This picture is consistent with the ready formation of the pentacene and hexacene from *o*-dialdehydes as shown in Scheme II. Note that the intermediate in the condensation would be sufficiently stabilized by the α,β-unsaturated ketone system (chalcone structure) to permit aromatization. Eventually a series of tautomerizations can lead to the stable form of the substituted quinizarin.

Experimental Section

Melting points were taken on a Mel-Temp electrically heated melting point unit and are uncorrected. Infrared spectra were measured on a Perkin-Elmer Model 21 spectrophotometer; visible spectra were measured on a No. 2 Hardy General Electric spectrophotometer in ODCB; nmr spectra were obtained on a Varian A-60 spectrophotometer.

Hydrochloric Acid Catalyzed Condensation.—A mixture of 0.01 mol of leucoquinizarin,[9] the aldehyde (quality given in Table I), and 2 ml of concentrated hydrochloric acid in 50 ml of 2-porpanol was refluxed 4 hr. The reaction mixture was cooled to room temperature; the precipitate was removed by filtration, washed with methanol, and dried at 80°. The product was purified by recrystallization. Compounds prepared by this procedure are listed in Table I.

In one experiment where butyraldehyde was used, the reaction was refluxed for 20 hr. The only product isolated was leucoquinizarin, mp 155–156°. The filtrate was treated with dinitrophenylhydrazine; the product isolated had mp 123–124°; mixture melting point with the dinitrophenylhydrazone of butyraldehyde was not depressed.

(8) A. C. Cope, *J. Amer. Chem. Soc.*, **59**, 2327 (1937), reported piperidinium acetate to be more effective as catalyst for the condensation of ketones with cyanoacetic esters. He attributed the effectiveness of the salt to its ability to act as both acid and basic catalyst, according to Brønsted's definition.

(9) Commercial leucoquinizarin recrystallized from Methyl Cellosolve was used in this study.

Piperidinium Acetate Catalyzed Condensations. A. With Leucoquinizarin.—A mixture of 0.01 mol of leucoquinizarin, 0.03 mol of the aldehyde, and 0.5 g of piperidinium acetate in 50 ml of 2-propanol was refluxed 4 hr, cooled, filtered, washed with methanol, and dried at 80°. It was then purified by recrystallization. The compounds thus prepared, with physical data, are listed in Table II.

B. With 2-Substituted Leucoquinizarin.—The above procedure was followed. In each case reaction times of 4 and 20 hr were used. The physical data are given in Table III.

2-Butylleucoquinizarin (12).—To 280 cc of 6% sodium hydroxide solution in a flask continuously swept with nitrogen was added 8.0 g of 2-butylquinizarin, and the mixture was stirred at 45–50° until solution was complete. To this blue solution was added 20 g of sodium dithionite, and after the blue color was discharged stirring was continued 2 hr at 45–50°. Then 100 ml of 20% sulfuric acid solution was added dropwise making the reaction mixture acid to congo red indicator paper. Nitrogen was blown through to expel the excess sulfur dioxide. The precipitate was separated by filtration and washed acid free. The wet cake was crystallized twice from ethanol to give 7.4 g (93%) of purified material, mp 99–100°.

Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.48; H, 5.70. Found: C, 72.16; H, 5.55.

2-Benzylleucoquinizarin (13).—This compound was prepared by the above procedure in 92% yield, mp 153–155°.

Anal. Calcd for $C_{21}H_{16}O_4$: C, 57.90; H, 4.82. Found: C, 58.11; H, 5.00.

Alkaline Dithionite Condensation with Butyraldehyde.—To 500 cc of 1.4% sodium hydroxide solution was added 5 g (0.02 mol) of quinizarin (mp 194–195°); the mixture stirred under N_2 at 30° until it dissolved; 10 g of sodium dithionite was added and; stirring was continued 0.5 hr until the blue color was discharged. Then 7.5 g (0.1 mol) of butyraldehyde was added and the reaction mixture was heated 1.25 hr at 95°. It was cooled to room temperature and aerated until the product was oxidized. After acidification to congo red indicator paper with dilute sulfuric acid the reaction mixture was filtered. The precipitate (2-butylquinizarin **2**) was washed with water and crystallized from Methyl Cellosolve to yield 4.0 g (67%), mp 123–124°.

The volume of filtrate was 550 cc. Analysis of the filtrate on a F & M Model 500 gas chromatograph using a Porapak Q column showed that only a trace of butyraldehyde was present.

Registry No.—**1**, 17648-03-2; **2**, 2106-03-5; **3**, 21016-05-7; **4**, 23861-68-9; **5**, 25158-10-5; **6**, 25109-60-8; **7**, 25158-11-6; **8**, 25109-61-9; **9**, 23861-69-0; **10**, 23861-74-7; **11**, 23861-70-3; **12**, 25109-64-2; **13**, 25109-65-3; **14**, 25109-66-4; **15**, 25109-67-5; **16**, 25109-68-6.

Acknowledgments.—Appreciation is expressed to Professor F. Ramirez for timely suggestions and assistance in the preparation of this manuscript, Mr. J. Kobliska for microanalysis, Dr. J. Gove for nmr interpretations, Dr. T. Mead for mass spectra data, and Mr. J. Morath for vapor phase chromatographic analysis.

Molecular Rearrangements. X.[1] The Boron Trifluoride Etherate Catalyzed Rearrangements of *trans*-2,3-Diphenyl-2,3-epoxypropionitrile and Its *p*- and *p'*-Methyl Derivatives

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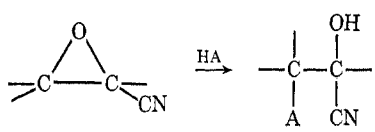
Received February 17, 1970

The syntheses of *trans*-2,3-diphenyl- (**1a**), *trans*-2-phenyl-3-(*p*-tolyl)- (**1b**), and *trans*-3-phenyl-2-(*p*-tolyl)-2,3-epoxypropionitrile (**1c**) are presented. Boron trifluoride etherate catalyzed rearrangement of **1a** and **1c** leads exclusively to the product of phenyl migration, α-cyanodiphenylacetaldehyde (**6**) and α-cyanophenyl-*p*-tolylacetaldehyde (**5**), respectively, while **1b** yields 47% **5** and 53% phenyl-*p*-tolylpyruvonitrile (**7a**), the products of *p*-tolyl and phenyl migration, respectively. Treatment of **7a** with base yields the stable enol form, **7b**. The catalyzed rearrangements of **1a–1c** are discussed in terms of a stepwise, ionic mechanism. Thermally, **1b** and **1c** produce *trans* → *cis* isomerization only.

There have been several reported studies of the rearrangements of α-cyano epoxides.[3] Cyano group migration has been observed in the formation of α-cyano ketones in a few cases where the intermediate α-cyano epoxide has been produced by treatment of an α-halocyanohydrin with base. Acid (protonic or Lewis) promoted rearrangements of α-cyano epoxides generally lead to α-substituted cyanohydrins as the products. In our general study of the chemistry of α-electronegatively substituted epoxides we have investigated the thermal and boron trifluoride etherate



catalyzed rearrangements of *trans*-2,3-diphenyl-2,3-epoxypropionitrile (**1a**), *trans*-2-phenyl-3-(*p*-tolyl)-2,3-epoxypropionitrle (**1b**), and *trans*-3-phenyl-2-(*p*-tolyl)-2,3-epoxypropionitrile (**1c**). These substrates were chosen because of our previous success in demonstrating exclusive chlorine migration from the intermediate α-chloro epoxides in the epoxidation of *trans*-α-chlorostilbenes.[4]

Synthesis of 2,3-Diaryl-2,3-epoxypropionitriles.—The synthetic approach to **1a–c** involved the preparation of the *trans*-α,β-diarylacrylonitriles (**2**) followed by base catalyzed peroxidation. The *trans*-α,β-diarylacrylonitriles (**2a–c**) were readily prepared by the condensation of the appropriate arylacetonitrile and arylcarboxaldehyde in the presence of sodium ethoxide.[5] The *trans* configuration was assigned to these products on the basis of the observed ultraviolet spectra compared with those of *cis*- and *trans*-α,β-diphenylacrylonitrile (**2a**) previously reported[6] (Table I).

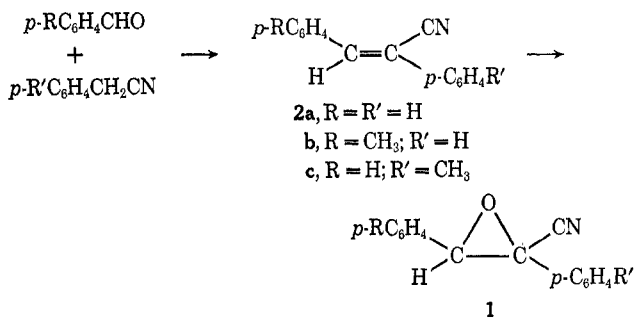


TABLE I
OBSERVED ULTRAVIOLET SPECTRA OF *cis*- AND *trans*-α,β-DIARYLACRYLONITRILES

	cis, λ_{max} (log ε)	*trans*, λ_{max} (log ε)
2a	224 (4.36), 295 (4.22)[6]	227 (4.27), 312 (4.41)[6]
2b		232 (4.13), 317 (4.40)
2c		229 (4.21), 317 (4.39)

Of the two literature methods for synthesizing **1a**, (1) treatment of desyl chloride with sodium cyanide in ethanol[7] and (2) basic peroxidation of **2a** with *t*-butyl hydroperoxide in the presence of benzyltrimethylammonium hydroxide,[8] the latter method was chosen since only *trans* isomer **1a** was obtained and in good yield. Applying this procedure to **2a–c** gave **1a–c** in

(1) For paper IX in this series, see R. N. McDonald and R. N. Steppel, *J. Org. Chem.*, **35**, 1250 (1970).

(2) Taken from the M. S. Thesis of D. G. Hill, 1969. A portion of these results were communicated in *Chem. Commun.*, 671 (1969).

(3) For a review of this and related rearrangements of α-substituted epoxides, see R. N. McDonald in "Mechanisms of Molecular Migrations," Vol 3, B. S. Thyagarajan, Ed., Interscience, New York, N. Y., in press.

(4) R. N. McDonald and P. A. Schwab, *J. Amer. Chem. Soc.*, **85**, 4004 (1963).

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