

Anal. Calcd. for (monohydrate) $C_9H_{10}O_3N_2 \cdot H_2O$: C, 48.01; H, 6.05; N, 14.02. Found: C, 48.14; H, 6.15; N, 14.12. Calcd. for (anhydrous) $C_8H_{10}O_3N_2$: C, 52.75; H, 5.53. Found: C, 52.43; H, 5.54.

Synthetic *dl*-Leucenol.—A suspension of 0.9 g. of 3-methoxy-4-pyridone^{2d} and 0.95 g. of α -acetamidoacrylic acid in 5 ml. of dioxane was heated at 95–100° for five hours. The dioxane was removed in a stream of air during the last hour of heating. A solution of the brown reaction mixture in 20 ml. of aqueous hydriodic acid (sp. gr. 1.50) was heated under reflux for six hours. The water and excess acid were removed under reduced pressure, and the residue was allowed to stand overnight in a vacuum desiccator over solid potassium hydroxide. The dry residue was dissolved in 20 ml. of water, and the solution was filtered to remove a small amount of insoluble brownish material. The filtrate was made just acid to brom cresol green (*pH* range, 3.8–5.4) by addition of dilute potassium hydroxide solution. Most of the water was distilled off under reduced pressure, and the residue was dried in a vacuum desiccator. The dry residue was washed with 200 ml. of hot methanol in 20-ml. portions to remove the potassium iodide and by-products. The insoluble material weighed 425 mg. and was reddish-brown in color. One recrystallization carried out by evaporating a water solution of the product at room temperature gave pinkish needles, m. p. 225–227° (cor.) with decomposition, and having the infrared absorption spectrum of *dl*-leucenol hemihydrate (Fig. 1). The yield was 380 mg. (25.5%). Two more recrystallizations carried out in the same way gave a white product; it darkens at 215–226° and melts at 227–228° (cor.) with decomposition. The melting point

of a mixture of this product with racemized natural leucenol hemihydrate showed no depression.

Anal. Calcd. for (hemihydrate) $C_8H_{10}O_4N_2 \cdot \frac{1}{2}H_2O$: C, 46.46; H, 5.33; N, 13.55. Found: C, 46.21; H, 5.60; N, 13.56.

A portion of the hemihydrate was dissolved in water and the solution boiled down until crystals separated. The hot solution was filtered to give anhydrous *dl*-leucenol, m. p. 235–236° (cor.) with decomposition. The melting point of a mixture of this product with anhydrous racemized natural leucenol showed no depression.

Anal. Calcd. for (anhydrous) $C_8H_{10}O_4N_2$: C, 48.48; H, 5.05; N, 14.14. Found: C, 48.47; H, 5.16; N, 14.24.

Condensation of 3-hydroxy-4-pyridone^{2b} with α -acetamidoacrylic acid proceeded much less smoothly than the reaction described above. Only a 4% yield of *dl*-leucenol was obtained.

Summary

1. Natural leucenol, which is levorotatory, is racemized when heated in aqueous solution for forty-eight hours.

2. The *dl*-leucenol has been synthesized by condensation of 3-methoxy-4-pyridone with α -acetamidoacrylic acid, and hydrolysis of the primary condensation product.

3. *dl*-Leucenol can be isolated in an anhydrous or a hydrated form.

URBANA, ILLINOIS

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[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Ethylene Imine Ketones. IV.¹ Isomerism and Absorption Spectra²

BY NORMAN H. CROMWELL AND HERMAN HOEKSEMA³

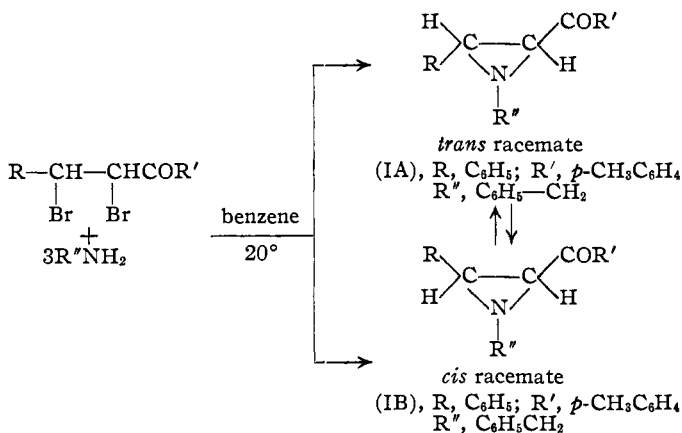
In previous investigations¹ of the reaction of primary amines with α,β -dibromoketones, ethylene imine ketones were obtained in yields of about

yields may have been due to the formation of pairs of geometrical isomers, of which only the less soluble was isolated in each instance studied. It is also possible, of course, that products of other types, such as piperazines and α -imino ketones, are formed along with one or more forms of the ethylene imine ketones.

The reaction of benzylamine with α,β -dibromobenzyl-*p*-methylacetophenone¹ has now been found to give the isomeric products (IA) (29%) and (IB) (37%), when carried out in dry benzene solution at temperatures between 20 and 30°. No evidence for the formation of a piperazine was observed in these studies.

The low melting isomer (IB) was the more labile of the two. This compound partially decomposed and rearranged to the higher melting isomer (IA) when

saturated petroleum ether solutions of it were exposed to sunlight at room temperature. An inspection of scale models for such ethylene imine ketone structures indicated that the racemate (IB) would be a more highly strained arrangement than (IA). Thus (IB) might be expected to undergo rearrangement, possibly through an enol form, to the less strained structure (IA). Acid and base catalyzed rearrange-



25%. The fact that diphenylethylenimine exists in *cis* and *trans* forms⁴ suggests that these low

(1) For the previous paper in this series see Cromwell, *This Journal*, **69**, 258 (1947).

(2) Presented before a session of the Division of Organic Chemistry, 113th Meeting of the American Chemical Society, Chicago, Illinois, April 20, 1948.

(3) Abstracted from the Ph.D. thesis (June, 1948); du Pont Fellow, 1946–1947.

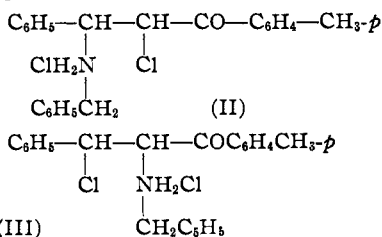
(4) Weissberger and Bach, *Ber.*, **64**, 1095 (1931).

ments of ethylene imine ketones are under investigation at present in this laboratory.

Hot aqueous hydrogen chloride reacted with the isomers, (IA) and (IB), to give mixed chloro-amino ketone hydrochlorides. Analysis and iodine release studies⁵ of these two products indicated them to be mixtures of the two probable ring cleavage products, α -chloro- β -benzylaminobenzyl-*p*-methylacetophenone hydrochloride (II) and β -chloro- α -benzylaminobenzyl-*p*-methylacetophenone hydrochloride (III).

Excess dry hydrogen chloride reacted with (IA) to give good yields of the hydrochloride (III). The *cis* racemate (IB) gave a mixed hydrochloride product (IV) with this same reagent. Iodine release studies indicated this latter substance (IV) to be made up of approximately 46% (II) and 54% (III).

The reaction with two equivalents of hydrogen chloride is characteristic of an ethylene imine. If either (IA) or (IB) had possessed the structure of a β -amino- α,β -unsaturated ketone, or an α -amino- α,β -unsaturated ketone, or an α -imino ketone, hot aqueous hydrogen chloride should have formed a 1,3-diketone or a 1,2-diketone, respectively.⁶ The following paper in this series⁷ reports a more detailed study of the cleavage of ethylene imine ketone rings by hydrogen chloride.



Ultraviolet absorption spectra studies (see Table I and Fig. 1) of (IA), (IB) and 1-benzyl-2-phenyl-3-benzoyl ethylenimine⁸ revealed a strong fundamental absorption band in the region of 2400–2600 Å. A low intensity absorption near 3300 Å. was again observed.⁹

These ethylene imine ketones show absorption spectra very similar to those of the parent saturated ketones (see Fig. 2). The only important grouping, other than the benzene rings, affecting ultraviolet light absorption by (IA), (IB) and 1-benzyl-2-phenyl-3-benzoyl ethylenimine is the two-chromophore, arylcarbonyl structure. The related β -amino- α,β -unsaturated ketones have a strong fundamental absorption band near 3450 Å.^{9,10} α -Amino- α,β -unsaturated ketones absorb strongly at 2800–2900 Å. and at 2500 Å., and mildly and generally from 3600 to 4000 Å.^{9,10}

The maximum absorption band of the isomer

(5) Cromwell and Wankel, *THIS JOURNAL*, **70**, 1320 (1948).

(6) For a review of the properties of such amino ketones, see Cromwell, *Chem. Rev.*, **33**, 83-137 (1946).

(7) Cromwell and Wankel, *THIS JOURNAL*, **71**, 711 (1949).

(8) Cromwell, Babson and Harris, *ibid.*, **65**, 312 (1943).

(9) Cromwell and Johnson, *ibid.*, **65**, 318, 2481 (1943).

(10) Watson, M.S. Thesis, University of Nebraska, 1948.

(IB) was 30–80 Å. nearer the red, with a 2000–3000 greater extinction coefficient value, as compared with (IA). The more strained structure (IB) would be expected to absorb light of longer wave lengths.

The changes in the absorption spectra after sunlight irradiation of solutions of (IA) and (IB) are shown in Tables III and IV and in Fig. 3. Hexane solutions of (IA) or (IB) were stable when stored in the dark for several days. Solutions of (IA) were unaffected by sunlight irradiation. It was found that hexane solutions of (IB) underwent considerable change upon exposure to sunlight. A general broadening (90 Å.) of the maximum absorption band was observed for this latter substance. A freshly prepared 50-50 mixture of (IA) and (IB) showed a similar absorption curve. This is further evidence of the ability of (IB) to rearrange to (IA) under the influence of sunlight.

Acknowledgment.—The senior author appreciates a grant from the Research Council of the University of Nebraska which aided in the completion of this investigation.

Experimental

1-Benzyl-2-phenyl-3-*p*-toluylethylenimines (IA) and (IB).—To a suspension of 60.0 g. (0.15 mole) of α,β -dibromobenzyl-*p*-methylacetophenone¹¹ in 150 ml. of benzene was added 50.0 g. (0.45 mole) of benzylamine. The mixture was kept cool (15°) and stirred one hour, stored in the dark at room temperature for twenty-four hours, then filtered to remove 55 g. of benzylamine hydrobromide (94%). The volume of the residual reaction solution was reduced about two-thirds by vacuum distillation and 100 ml. of petroleum ether added to give 15.5 g. (29% yield) of a colorless crystalline product, m. p. 113–114°. One recrystallization of this product (IA) from absolute alcohol, raised the m. p. to 120–121°, while further recrystallization often lowered it to 116–118°.¹

Upon exposure to light these colorless crystals rapidly developed a deep pink color. When returned to a dark environment for several days, the crystals again became colorless. This same color change was observed with (IA) under a nitrogen atmosphere in a sealed quartz tube.

The benzene-petroleum ether filtrate from (IA) was evaporated and the residue mixed with 200 ml. of petroleum ether and cooled for two days in the ice chest. Filtration gave 25.0 g. (49% yield) of a colorless, fluffy solid, m. p. 70–85°. Recrystallization of this product from low-boiling petroleum ether gave 19 g. (37% yield) of a colorless, fluffy product, m. p. 70–74°. Upon exposure to light this product, (IB), slowly acquired a yellow tint. Extensive manipulation of (IB) in various solvents converted some of it to (IA). Exposure of saturated petroleum ether solutions of (IB) to direct sunlight caused the precipitation of small amounts of (IA).

Anal. Calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}$: mol. wt., 327; C, 84.37; H, 6.47; N, 4.28. Found for (IA): mol. wt., 318; C, 84.73; H, 6.64; N, 4.20. Found for (IB): mol. wt., 337; C, 84.51; H, 6.24.

Reaction of 1-Benzyl-2-phenyl-3-*p*-toluylethylenimines (IA) and (IB) with Hydrogen Chloride

1. With Aqueous Hydrogen Chloride.—Mixtures of 16 ml. of 6 *N* hydrochloric acid with 2.0-g. samples of (IA) and (IB) were refluxed for two hours and then allowed to stand at room temperature for a day. The solid precipitates were filtered from the solutions and recrystallized once from boiling methanol.

(11) Weygand, *Ber.*, **35**, 1068 (1902).

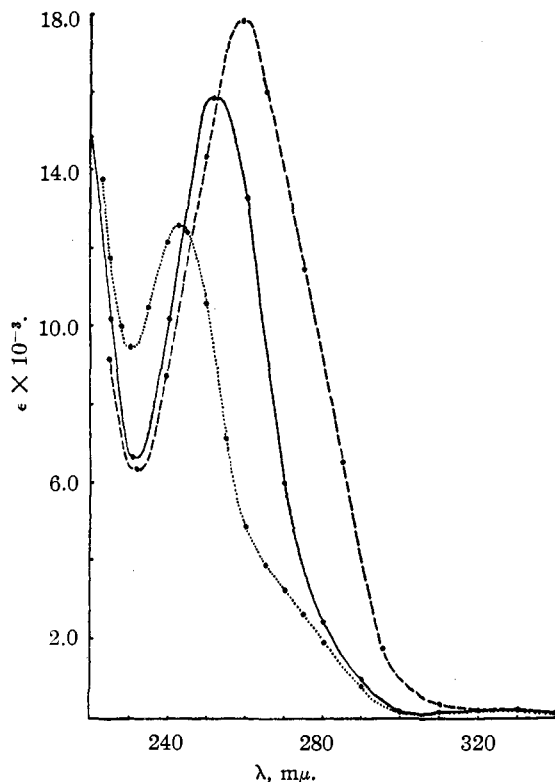


Fig. 1.—1-Benzyl-2-phenyl-3-benzoylethylenimine,; (IA), —; (IB), ----.

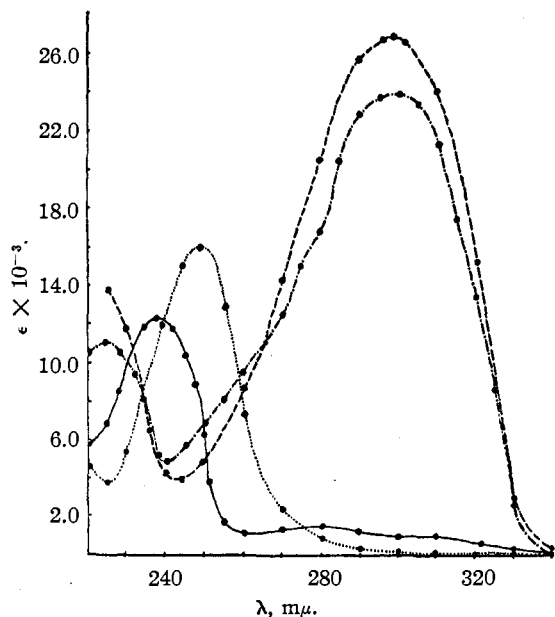


Fig. 2.—Benzal-*p*-methylacetophenone, ----; benzalacetophenone, —; benzyl-*p*-methylacetophenone,; benzylacetophenone, —.

(IA) gave 1.5 g., m. p. 161–162.5°; iodine release was 33% in fifteen minutes at 66°.

(IB) gave 1.94 g., m. p. 161–162°; iodine release was 20% in fifteen minutes at 66°.

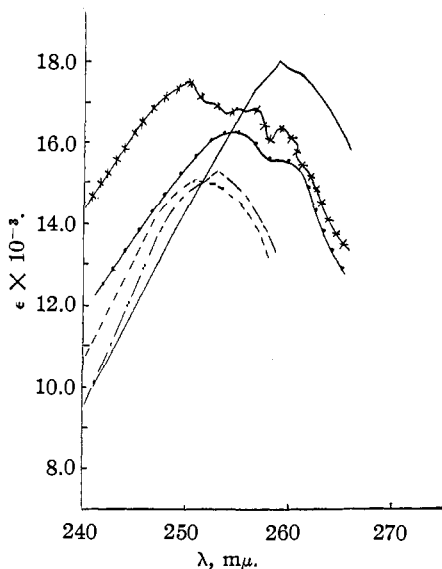


Fig. 3.—Absorption spectra in hexane of (IA): fresh solution, —; after two days in dark + two days in light, ----; of (IB), fresh solution, —; after two days in dark + two days in light —×—×—; 50% (IA) + 50% (IB), fresh solution, —●—●—.

Anal. Calcd. for $C_{23}H_{23}NOCl_2$: Cl, 17.72. Found: for product from (IA), Cl, 17.80; for product from (IB), Cl, 17.91.

Mixtures of these two products showed m. p. 160–162°. 2. With Excess Dry Hydrogen Chloride.—Samples (2.0 g.) of (IA) and (IB) were dissolved in 10 ml. of acetone and the solutions cooled in an ice-bath. An excess of a saturated, dry, ether solution of hydrogen chloride was added, with stirring, in two minutes. After standing in the ice-chest for one day, the solutions were filtered.

(IA) gave 2.0 g. of a colorless crystalline product (III), m. p. 163–165°; recrystallized from methanol and ether, m. p. 167–170°; iodine release in thirty minutes at 66° was 0.0%.

(IB) gave 1.9 g. of colorless product (IV), m. p. 155–158°; recrystallized from methanol and ether, m. p. 161–165°; iodine release in fifteen minutes was 46.5% at 66°.

Anal. Calcd. for $C_{23}H_{23}NOCl_2$: C, 68.99; H, 5.79; N, 3.50; Cl, 17.72. Found for (III): C, 68.72; H, 5.79; N, 3.69; Cl, 17.48. Found for (IV): C, 68.79; H, 5.76; N, 3.57; Cl, 18.00.

Absorption Spectra Studies of Ethylene Imine Ketones.—These measurements were made with a Beckmann Model DU Photoelectric Quartz Spectrophotometer. At the sensitivity used, the maximum band width was one millimicron with an accuracy of 0.1% for the density measurements. The two solvents used were laboratory grade 95% ethyl alcohol and hexane-from-petroleum, purified by the procedure recommended by Weissberger.¹²

Using purified hexane, the ultraviolet absorption spectra of (IA), (IB), 1-benzyl-2-phenyl-3-benzoylethylenimine, benzal-*p*-methylacetophenone, benzylacetophenone, benzalacetophenone, and benzyl-*p*-methylacetophenone were observed. These studies were made within two hours of the time the solutions were prepared. The results are summarized in Table I, and the complete curves are shown in Fig. 1 and Fig. 2.

In Table II is given the summary of the results obtained when some of these compounds were studied in 95% alcohol solutions.

(12) Weissberger, "Physical Methods of Organic Chemistry," Vol. II, Interscience Publishers Inc., New York, 1946, p. 766; "Organic Solvents," the Clarendon Press, Oxford, 1935, p. 99.

TABLE I

ABSORPTION SPECTRA DATA OF SOME CHALCONE DERIVATIVES (IN HEXANE SOLUTION)

Compound	Molar concn. $\times 10^3$	Maxima		Minima	
		$\lambda_{\text{A.}}$	$\epsilon \times 10^{-3}$	$\lambda_{\text{A.}}$	$\epsilon \times 10^{-3}$
(IA) m. p. 120-121°	12.50	2510	15.90	2310	6.59
		3150	0.19		
(IB) m. p. 71-72°	11.15	2590	17.91	2320	6.46
		3300	0.21		
50% (IA) + 50% (IB)	10.10	2555	16.25
1-Benzyl-2-phenyl-3-benzoyl-ethylenimine	10.81	2430	12.62	2300	9.56
		3250	0.16		
Benzyl- <i>p</i> -methylacetophenone	11.90	2485	16.01	2250	3.93
Benzal- <i>p</i> -methylacetophenone	9.13	2990	26.86	2440	4.00
Benzylacetophenone	23.81	2380	12.40	2600	1.10
		2800	1.50		
Benzalacetophenone	14.50	2260	12.10	2410	4.85
		2990	23.90		

TABLE II

ABSORPTION SPECTRA DATA OF SOME CHALCONE DERIVATIVES (IN 95% ALCOHOL SOLUTION)

Compound	Molar concn. $\times 10^4$	Maxima		Minima	
		$\lambda_{\text{A.}}$	$\epsilon \times 10^{-3}$	$\lambda_{\text{A.}}$	$\epsilon \times 10^{-3}$
(IA) m. p. 120-121°	6.07	2595	17.0	2320	4.71
(IB) m. p. 71-72°	0.477	2620	18.3	2310	5.30
(IB) (crude) m. p. 71-74°	0.621	2620	18.3	2320	5.25
Benzyl- <i>p</i> -methylacetophenone	1.14	2540	15.2	2350	2.61
Benzal- <i>p</i> -methylacetophenone	1.08	3100	27.8	2480	3.39

Effect of Time and Light Exposure on the Absorption Spectra of *cis* and *trans* Ethylene Imine Ketones (IB) and (IA).—A 0.000117 to 0.000100 molar solution in hexane of each of the highly purified samples of (IA) and (IB) was prepared. These solutions were stored in new, volumetric flasks which had been bathed in concentrated sulfuric acid for several days, and then rinsed with distilled

water and dried. These solutions were stored in the dark. The ultraviolet spectra were examined periodically and little or no change observed. After two days the solutions were each divided into two portions, one portion of each being exposed to direct sunlight for about forty-eight hours. The remaining portions were again stored in the dark. No significant changes in the spectra of (IA) were observed with either portion. With (IB) the portion again stored in the dark showed no change, but that exposed to sunlight displayed approximately a 100 Å. shift in the wave length of the maximum absorption band and a general broadening of the band.

TABLE III

EFFECT OF LIGHT ON LOW MELTING 1-BENZYL-2-PHENYL-3-*p*-TOLUYLETHYLENE IMINE (IB)

Storage time	λ_{max} Å.					
	0	24	48	96	2500	2600
Dark storage	0	24	48	96	48	48
Light storage	0	0	0	0	48	48
Total hours	0	24	48	96	96	96
$\epsilon_{\text{max}} \times 10^{-3}$	18.08	17.91	17.92	17.74	17.57	16.30

TABLE IV

EFFECT OF LIGHT ON HIGH MELTING 1-BENZYL-2-PHENYL-3-*p*-TOLUYLETHYLENE IMINE (IA)

Storage time	λ_{max} Å.				
	0	24	48	96	48
Dark storage	0	24	48	96	48
Light storage	0	0	0	0	48
Total hours	0	24	48	96	96
$\epsilon_{\text{max}} \times 10^{-3}$	15.24	15.27	15.27	15.25	15.15

In Table I and Fig. 3 are given the results of a study made with a freshly prepared 50-50 mixture of (IA) and (IB) in hexane solutions. These studies were made within two hours of the time the solution was prepared.

Summary

cis and *trans* racemates of 1-benzyl-2-phenyl-3-*p*-toluylethylenimine have been isolated from the reaction of benzylamine with α,β -dibromobenzyl-*p*-methylacetophenone. The physical properties, absorption spectra and behavior with hydrogen chloride are consistent with the configurations that have been assigned. The interconvertibility of these geometrical isomers has been studied.

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[CONTRIBUTION FROM AVERY LABORATORY OF THE UNIVERSITY OF NEBRASKA]

Ethylene Imine Ketones. V.¹ Reaction with Hydrogen Chloride²

BY NORMAN H. CROMWELL AND RONALD A. WANKEL³

Previous investigations of the reactions of ethylene imine ketones with hydrogen halides have shown that the ethylene imine ring cleaves in the two directions under various conditions.^{1,4}

It was of interest to re-investigate the reaction

(1) For paper IV see, Cromwell and Hoeksema, *THIS JOURNAL*, **71**, 708 (1949).

(2) Presented before a session of the Division of Organic Chemistry, 113th Meeting of the American Chemical Society, Chicago, Illinois, April 20, 1948.

(3) Abstracted from the Ph.D. thesis (1949); du Pont Fellow, 1947-1948.

(4) Cromwell and Caughlan, *THIS JOURNAL*, **67**, 2235 (1945).

of benzylamine with α,β -dibromobenzylacetophenone⁵ in an attempt to account for a larger portion of the starting materials. A further aim of this investigation was a quantitative product study of the reaction of ethylene imine ketones with minimum amounts of hydrogen chloride.

We were unable to isolate a lower-melting, more soluble form of 1-benzyl-2-phenyl-3-benzoyl-ethylenimine. However, when the filtrate from the isolation of the higher-melting, less soluble form of this compound (I) (m. p. 108°)⁵ was treated with

(5) Cromwell, Babson and Harris, *ibid.*, **65**, 312 (1943).