biphenol using the procedure described above. Dark orange needles resulted; $\lambda_{max} = 3985$ Å; $\epsilon_{max} = 53{,}200$ (benzene).

Acknowledgment. All spectra were taken with a Cary recording spectrophotometer (Model 11 or 14) at a concentration of approximately $10^{-4}M$. Electronic spin resonance absorption measurements (ESR) were performed with equipment built by Dr. Power B. Sogo of the Radiation Laboratory. Analyses were performed by Dr. Charles Koch of the Microanalytical Laboratory of the Department of Chemistry.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF DELAWARE]

Steric Considerations in Base Catalyzed Condensation; The Darzens Reaction[1]

HAROLD KWART AND LEWIS G. KIRK

Received July 20, 1956

The Darzens condensation of benzaldehyde and choloroacetone has been carried out in good yield. The exclusive glycidic ketone product of this reaction has been shown by a synthetic procedure to have the *trans* arrangement of substituents on the oxide ring. The significance of this observation for the mechanism of the Darzens reaction in particular and aldol condensations in general is discussed. Circumstances are considered under which it is possible to obtain the *cis* isomer.

Ballester[2] has very recently reviewed the evidence that strongly points to a mechanism involving an alpha halogenohydrin anion as intermediate in the Darzens condensation[3] and indicates that the course of oxirane ring formation from this intermediate requires Walden inversion at the halogen bearing carbon atom. Further, the rate determining step in the over-all reaction has been deduced[4] to be the slow formation of this intermediate. The self-condensation[5] and cross-condensation[6] of phenacyl halides have afforded both *cis* and *trans* (substituted) benzalacetophenone oxides depending on the conditions of reaction. The respective structures of these isomers have been assigned on the basis of spectral characteristics and stereospecific chemical reactions.

The mechanism discussed by Ballester[2,7] has not considered the possibility of two diastereomerically related (*cis* and *trans*) intermediate anions; nor has the possibility been suggested that the occurrence of the two isomers in a given Darzens reaction may correspond to the possible formation of two discrete intermediates. In the present investigation we have shown that with simple Darzens reagents the condensation produces only one of the two possible oxiranes. We have determined the configuration of this product and attempted to generalize the significance of its exclusive formation.

RESULTS AND DISCUSSION

The Darzens condensation of benzaldehyde and monochloroacetone, using sodium methoxide in absolute methanol solution as the base, gave only one epoxyketone product. The composition of the product did not vary with the time and temperature of reaction though the yield of undistillable residue was increased beyond a certain optimum adjustment of these variables. The sharp melting, crystalline product was shown to possess the *trans* relationship of the substituents on the oxide ring by synthesis through an established procedure.

Benzalacetone, prepared by cross-aldol of acetone and benzaldehyde, was identified to have the *trans* configuration, (characteristic of the products of base catalyzed condensation reactions),[8] by its facile conversion through sodium hypochlorite oxidation to the known *trans* cinnamic acid. Additional proof of its configuration was afforded by the presence of a strong band in the region 10.2–10.6 microns.[9] Reduction with lithium aluminum hydride

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[1] Part of this work is obtained from the Thesis of Lewis G. Kirk, presented in partial fulfillment of the degree of Master of Science at the University of Delaware.

[2] M. Ballester, *Chem. Rev.*, **55**, 283 (1955).

[3] M. S. Newman and B. J. Magerlein, *Org. Reactions*, **5**, 413 (1949).

[4] M. Ballester, *Anales real soc. españ. fís. y quím.* (*Madrid*), **50B**, 759 (1954).

[5] (a) H. H. Wasserman and J. B. Brous, *J. Org. Chem.*, **19**, 515 (1954). (b) C. L. Stevens and V. J. Traynelis, *J. Org. Chem.*, **19**, 533 (1954). (c) C. L. Stevens, R. J. Church and V. J. Traynelis, *J. Org. Chem.*, **19**, 522 (1954). (d) H. H. Wasserman, N. E. Aubrey, H. E. Zimmerman, *J. Am. Chem. Soc.*, **75**, 96 (1953).

[6] N. H. Cromwell and R. A. Setterquist, *J. Am. Chem. Soc.*, **76**, 5752 (1954).

[7] M. Ballester and P. D. Bartlett, *J. Am. Chem. Soc.*, **75**, 2042 (1953).

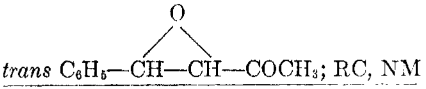
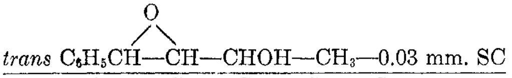
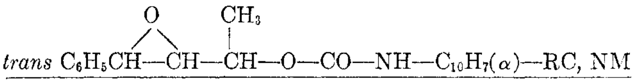
[8] (a) S. E. Boxer and R. P. Linstead, *J. Chem. Soc.*, 740 (1931). (b) R. P. Linstead, E. G. Noble and E. J. Boorman, *J. Chem. Soc.*, 557 (1933).

[9] This absorption has been ascribed to out-of-plane deformation of the two hydrogens attached to the *trans* double bond, a corresponding mode being absent in the *cis*. See particularly R. S. Rasmussen, R. R. Brattain and P. S. Zucco, *J. Chem. Phys.*, **15**, 135 (1947); N. Sheppard and G. B. B. M. Sutherland, *Proc. Roy. Soc.*, **A196**, 195 (1949). The correlation has previously proven valid for a large variety of substituted olefins and has been accepted

TABLE I

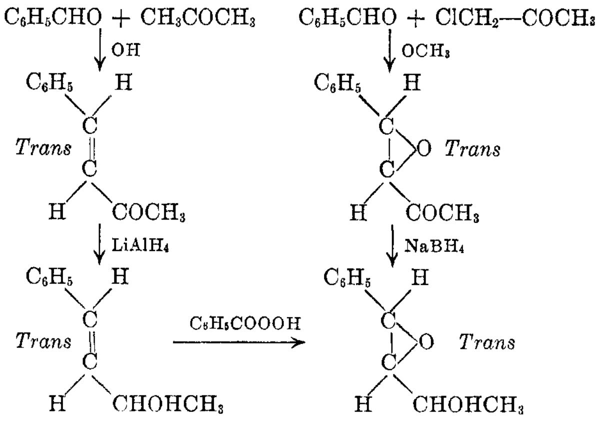
INFRARED SPECTRAL DATA

λ_{max} in microns; S—sharp; B—broad; SC—Sample cell thickness; NM—Nujol Mull; RC—Reference cell-50% Transmission

Strong	Intermediate	Weak
	trans $C_6H_5-CH=CH-COCH_3$; RC, NM	
3.5 B, 6.0 S 6.3 B, 6 9 B 7.3 S, 7.4 S 10.2 B, 13.4 B 14.5 B	8.0 S, 8.5 B	6.7 S, 7.1 B 7.5 S, 7.7 S 8.4 S, 9.3 S 11.0 S
	 *trans* $C_6H_5-\overbrace{CH-CH}^{O}-COCH_3$; RC, NM	
3.4 B, 5.9 S 6.8 S, 7.4 S 8.0 B, 11.3 S 12.0 B, 12.6 S 13.3 B, 14.4 B	7.1 S, 9.2 S, 12.2 B	5.1 B, 5.35, 6.7 S 8.4 S, 8.6 S, 8.9 B
	trans $C_6H_5CH=CH-CHOH-CH_3$—0.025 mm. SC	
3.0 B, 3.4 S, 6.7 S 6.9 S, 7.3 S, 8.8 B 9.3 S, 9.5 B, 10.3 B 10.6 B, 14.5 B	3.3 S, 3.45 S, 3.5 S 6.2 S, 7.1 B, 7.5 S 7.7 B, 9.7 B, 11.4 S 11.7 B, 12.1 S	5.1 S, 5.3 S, 5.5 S 5.7 B, 6.0 S, 6.3 S 8.3 B, 8.5 S, 11.0 B
	 *trans* $C_6H_5\overbrace{CH-CH}^{O}-CHOH-CH_3$—0.03 mm. SC	
2.9 B, 3.35 S 6.9 S, 8.7 B 9.0 B, 9.3 B, 9.7 B 11.3 B, 13.3 B 14.3 B	3.4 S, 3.45 S, 5.9 S, 6.7 S, 7.0 S 7.3 S, 7.45 S, 7.8 S, 8.3 S, 10.0 B, 10.55 S 11.8 B	5.1 B, 5.3 B, 5.5 B 6.25 S, 6.3 B 10.9 B, 12.7 B
	 *trans* $C_6H_5\overbrace{CH-CH}^{O}-\overset{CH_3}{\overset{\mid}{CH}}-O-CO-NH-C_{10}H_7(\alpha)$—RC, NM	
3.3 S, 3.45 S, 3.5 S 6.1 S, 6.25 S, 6.45 B 6.7 S, 6.9 S, 13.2 B 14.3 B	3.1 S, 7.3 B, 7.45 S, 8.0 S 8.3 B, 9.7 B, 11.0 S	5.1 S, 5.3 B 5.55 B, 5.8 B 8.6 B, 10.4 B 11.9 B

did not disturb the configuration about the double bond as has also been established in analogous cases.[10] This product, again, was confirmed as the *trans* alcohol by virtue of the strong infrared absorption near 10.3 and 10.6 microns. Epoxidation with perbenzoic acid gave a glycidic alcohol to which was assigned the *trans* configuration on the (well founded)[11] assumption of a *cis*-addition mechanism of the epoxidation reaction. This substance was characterized by its infrared spectrum (see table) and *alpha* naphthylurethan derivative.

The identical substance (confirmed by infrared spectrum and *alpha* naphthylurethan derivative) was obtained upon reduction with sodium borohydride of the Darzens condensation product, as outlined in the flow diagram.



SIGNIFICANCE OF RESULTS

Ignoring rotational isomers, the two possible intermediates, I and II, may be visualized as being formed from two alternative collision orientations of the respective (planar) carbonyl and enolate anion

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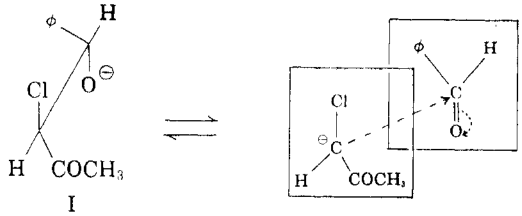
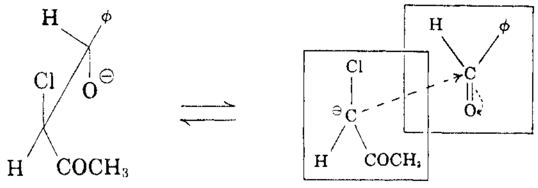
to be of diagnostic importance. See P. C. Rao and B. F. Daubert, *J. Am. Chem. Soc.*, **70**, 1102 (1948); O. S. Shreve, M. R. Heather, H. B. Knight and D. Swern, *Anal. Chem.*, **22**, 1261 (1950); L. Crombie and S. H. Harper, *J. Chem. Soc.*, 1707, 1714 (1950); *J. Chem. Soc.*, 869 (1952); R. N. Jones, *J. Am. Chem. Soc.*, **72**, 5322 (1950).

(10) L. F. Hatch and S. S. Nesbitt, *J. Am. Chem. Soc.*, **72**, 727 (1950).

(11) For a fuller discussion of the basis for this statement see D. Swern, *Chem. Rev.*, **45**, 1 (1949).



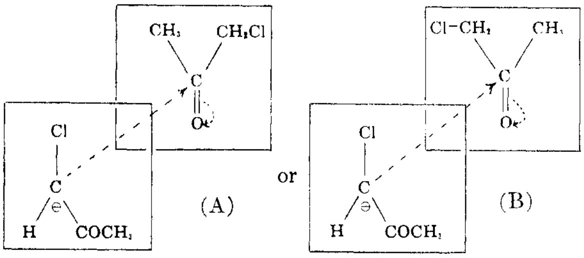
I



II

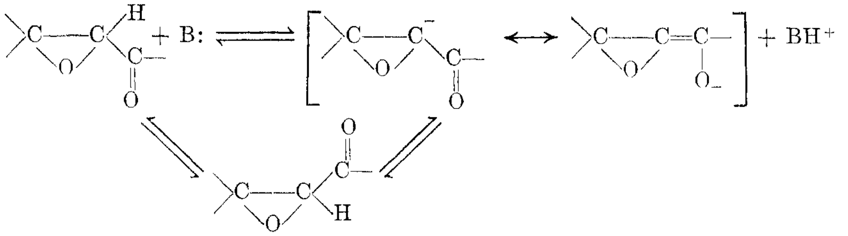
reagents. These possibilities are represented above in the *trans* coplanar arrangement required for effecting the Walden inversion[12] leading to epoxide. If, as Ballester has claimed,[2] the Darzens intermediate commonly is formed in the rate determining step, the exclusive formation of the *trans* product may be attributed to steric inhibition in the formation of II. One might suppose the formation of the product-forming intermediate I to occur only as a result of a very restricted orientation of colliding planes. Here, the transition state for bond formation between the reactive centers of these planes must strongly resemble the intermediate.[13] The steric strains between the adjacent tetrahedra developing at the bond-forming carbon atoms in the transition state tend to be minimized in the staggered conformation (in which the smallest group on the one carbon is accommodated between the two largest groups on the other.) The fact that no significant self-condensation of chloroacetone is observed (under these reaction conditions) suggests that the possible transition states for such reaction formed by collision orientations such as (A) or (B) engender relatively unfavorable steric factors, similar to those that prevent formation of intermediate II.

These deductions about the Darzens reaction are also applicable to the aldol. Enolization, normally the rate determining stop,[14] will be seen to be non-rate determining where factors pertaining to



the (steric) environment of the interacting (planes of) components A and B are involved. The aldol condensation of acetone, where the enolic equilibrium is set up much more rapidly than the condensation equilibrium[15] is a most obvious case in point. Where the enolization is the rate controlling step in the Darzens[4] the formation of the *trans* product must obtain since here such steric factors are minimized.

Finally, one can anticipate the formation of both *alpha* and *beta* glycidates in the Darzens only under very special circumstances, namely where *cis* and *trans* can exist in equilibrium through base catalyzed enolization involving the alpha hydrogen, as in



The argument we have advanced above that a *cis* intermediate anion II is formed with the greater difficulty dismisses the possibility that a *trans-cis* interconversion of epoxyketones is established through reversion of the Darzens product to the halohydrin. We were able, in fact, to test this possibility by means of several experiments with the *cis* and *trans* pair of oxides of *o*-nitrobenzalacetophenone.[6,16]

Each of the isomers was treated with a large excess of chloride ion in alcohol solution for a longer period of time than the original Darzens preparation required. In each case almost pure starting material was recovered on addition of water to the reaction mixture and no isomerization was detectable.[17] Clearly, a *cis* halohydrin anion like II is not the intermediate in the formation of *cis* product in

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(12) For a discussion of this conformational requirement for reaction see, for example, D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953) and other references cited therein.

(13) For a complete discussion on this point see G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

(14) R. P. Bell, *J. Chem. Soc.*, 1637 (1937).

(15) W. D. Walters and K. F. Bonhoeffer, *Z. Physik. Chem.*, **B182**, 265 (1938).

(16) S. Bodforss, *Ber.*, **51**, 192 (1918).

(17) This failure to revert to halohydrin anion occurs despite the fact that chloride ion appears to have a specific effect in opening of oxide ring, (L. P. Hammett, Physical Organic Chemistry, McGraw-Hill and Co., p. 302 et. seq.), and despite the expectation that the benzoyl and o-nitrophenyl substituents on the oxide would increase the rate of displacement.

the (direct) Darzens reaction.[18] Rather, the only possible way in which *cis* can be obtained in the Darzens is through formation of the *trans* product followed by base catalyzed isomerization. The existence of a very large effect (in both the rates and equilibrium of ring-forming reactions) opposing the formation of *cis* substituents on small rings constitutes a further basis for assigning greater thermodynamic stability to a *trans* versus a *cis* oxide.[19] It is very possible, therefore, that when a significant yield of *cis* is obtained it is the result of the peculiar circumstances where the interlocking *enolization equilibria* outlined above are displaced in the direction of separating a *cis* product where it precipitates from solution as the least soluble component of the system, and that these circumstances are not an essential but rather a secondary aspect of the mechanism of the Darzens condensation. This conclusion is only tentative, however, and is receiving further investigation in this laboratory.

EXPERIMENTAL

Preparation of benzalacetone oxide. The best yields were obtained using conditions similar to those suggested in the general method for Darzens condensation by Newman and Magerlein.[3] In an atmosphere of dry nitrogen 86.2 g. (1.6 moles) of sodium methoxide dissolved in 300 ml. of absolute methanol was dropped into a stirred solution containing 102 ml. (1 mole) of benzaldehyde, 128 ml. (1.6 moles) of monochloroacetone and 100 ml. of absolute methanol at a rate such that the temperature did not rise above zero. Agitation was continued for six hours at 0° after which the temperature was raised to 25° for an additional three hours of stirring. The reaction mixture was then poured onto chipped ice-hydrochloric acid and sufficient additional hydrochloric acid added to turn litmus. After two extractions of the aqueous layer with ether the combined extracts were neutralized with saturated sodium bicarbonate solution, followed by washing with saturated sodium chloride before drying over magnesium sulfate. The ether was removed and the residual yellow oil distilled (with a dry nitrogen stream) under high vacuum. The pure epoxyketone fraction was obtained ($b_{0.4}$ 69.0–69.5°) in 74% yield. The liquid (n_D^{20} 1.5347) crystallized on standing. After two recrystallizations from pet. ether the product melted sharply at 56°. The infrared spectrum is summarized in the accompanying table. Other properties were identical with those reported by Temnikova and Martynov[20] who employed much shorter reaction times and excess benzaldehyde and obtained product in 50% yield. No differences, other than in yield, in the nature of the product were observed over a wide range of conditions (temperature, molar ratios, base catalyst) investigated.

Reduction of benzalacetone oxide. To a stirred solution of 200 ml. of absolute methanol and 40 g. (0.25 moles) of epoxyketone (above) was slowly added 150 ml. of absolute methanol containing 9.45 g. of sodium borohydride (Metal Hydrides Corp., Beverly, Mass.). After stirring for half an hour (beyond complete addition), small amounts of ice and hydrochloric acid were dropped into the reaction flask at intervals until hydrogen evolution ceased. The solution, made acid to litmus with additional hydrochloric acid, was saturated with sodium sulfate and extracted with four 100-ml. portions of ether. The combined extracts were washed with sodium bicarbonate solution, saturated salt solution and dried over magnesium sulfate. Removal of the solvent and distillation of the residual oil under high vacuum gave the epoxyalcohol ($b_{0.18}$ = 77–79°) in 87% yield. This product was characterized by its infrared spectrum and that of its *alpha* naphthyl urethan derivative (m. = 240–241° dec.). See accompanying table for infrared data.

Preparation of benzalacetone. A procedure similar to that used in Organic Synthesis[21] was used. The doubly distilled product had the following properties; $b_{16.5}$ 137°, m.p. 42°. See accompanying table for infrared data.

Reduction of benzalacetone. To a stirred solution of 150 ml. of anhydrous ether and 40 g. (0.27 mole) of benzaldehyde was slowly added 200 ml. of an ether solution containing 6 g. of lithium aluminum hydride (Metal Hydrides Corp., Beverly, Mass.). One hr. after the addition was completed the excess lithium aluminum hydride was decomposed with dilute hydrochloric acid. The combined ether extracts of the aqueous layer were neutralized with sodium bicarbonate solution, washed with saturated sodium chloride and dried over magnesium sulfate. Evaporation of the ether and distillation of the residual oil under vacuum gave the unsaturated (see infrared data) alcohol in 90% yield; b_{12} 126°. All properties compared favorably with literature values reported[22] for 4-phenyl-3-butene-2-ol prepared by another method.

Epoxidation of trans 4-phenyl-3-butene-2-ol. To a solution of 23 g. (0.15 mole) of the unsaturated alcohol (above) in anhydrous ether was added in fifteen minutes at room temperature 22 g. (0.16 mole) of perbenzoic acid[23] in 300 ml. of ether. After twenty-four hours a negative test obtained with sodium iodide indicated the reaction was complete. After neutralization with dilute sodium hydroxide the combined ether extracts were washed with water and dried over magnesium sulfate. Removal of solvent and distillation of the residual oil afforded a 60% yield of product, $b_{0.16}$ 76–77°. The properties of this product compared very well both in infrared spectrum and mixed melting point of the *alpha* naphthylurethan derivative with these corresponding properties of the sodium borohydride reduction product of the Darzens reaction described above. (See accompanying table of infrared data.)

Trans-o-nitrobenzalacetophenone oxide. This preparation was carried out according to the directions given by Cromwell and Setterquist[6]; m.p. 112–112.5° (literature[6] m.p. 111–113°) after recrystallizations from absolute ethanol.

Cis-o-nitrobenzalacetophenone oxide. The directions given in reference 6 were again used. After two recrystallizations from absolute ethanol the product melted sharply at 175° (literature[6] 174–175°).

Attempted isomerization of Darzens product with chloride ion. (a). A 2.0 g. sample of *trans* epoxyketone was dissolved in 75 ml. of absolute ethanol containing 1.9 grams of lithium

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(18) J. A. Berson [*J. Am. Chem. Soc.*, **74**, 5177 (1952)] has interpreted the formation of both alpha and beta isomers in the Darzens as a situation in which the kinetically favored product (*trans*) is thermodynamically unstable with respect to a more slowly formed *cis* isomer. (See also reference 6, p. 5752). We have attempted to demonstrate here that this conclusion is neither required nor warranted by the evidence. Indeed, the contrary may be correct in accord with similar observations discussed by D. Y. Curtin in reference (19).

(19) D. Y. Curtin, Thirteenth National Organic Symposium Abstracts, p. 40–49, June 15–18 (1953), Ann Arbor, Michigan.

(20) T. I. Temnikova and V. F. Martynov, *J. Gen. Chem.* (*U.S.S.R.*), **15**, 499 (1945); *C. A.*, **40**, 4694 (1946).

(21) N. L. Drake and P. Allen, Jr., *Org. Synthesis*, **Coll.** Vol. I, 77 (1941).

(22) (a) A. Klages, *Ber.*, **35**, 2649 (1902). (b) J. Sand and F. Singer, *Ber.*, **35**, 3186 (1902).

(23) A. I. Vogel, *A Textbook of Practical Organic Chemistry*, Longmans, Green and Co., New York, 1948, p. 767.

chloride (AR). This corresponded to about a 6 to 1 molar ratio of chloride to epoxide. The solution was permitted to remain at 30° for three hours before drowning in water. The precipitate was identical with starting material on comparison of m.p. and infrared spectrum. (b) The *cis* epoxyketone was far less soluble and the reaction had to be carried out at the boiling point of ethanol. However, after three hours of refluxing, the product recovered was very pure *cis* starting material, as shown by m.p. and infrared spectrum.

NEWARK, DEL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE NEWARK COLLEGE OF ARTS AND SCIENCES OF RUTGERS UNIVERSITY]

Peroxide Induced Reduction of 9,10-Anthraquinone by Sodium Borohydride in Diglyme[1]

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Received July 25, 1956

9,10-anthraquinone is not reduced at room temperature by sodium borohydride in pure diglyme (dimethyl ether of diethylene glycol). In the presence of peroxides, 9,10-anthraquinone is reduced to 9,10-anthradiol in diglyme. A possible mechanism for the peroxide promoted reduction may be the cleavage of the solvent to aldehydes by a peroxide-induced reaction followed by the conversion of the aldehydes so produced to alkoxyborohydrides which are the effective reducing agent.

It has been reported that quinones may be quantitatively reduced to the hydroquinone by aqueous solutions of sodium borohydride at room temperature.[2] It has been found in this laboratory that although such quinones as 1,4-naphthoquinone and 9,10-phenanthrenequinone are readily reduced, 9,10-anthraquinone is not reduced under these conditions.

When 9,10-anthraquinone was treated under an argon atmosphere at room temperature with sodium borohydride in freshly purified diglyme (dimethyl ether of diethylene glycol), no visible evidence of a reaction was observed after 5 hr. Upon acidification of the reaction mixture, the volume of hydrogen evolved was equivalent to the amount of sodium borohydride initially present.

However, when 9,10-anthraquinone was treated with sodium borohydride in diglyme which had been exposed to air for as short a time as one day, a rapid reaction took place. The red color of the 9,10-anthradiol salt appeared within 3 min. A gasometric analysis at the end of 5 hr. showed a loss of borohydride equivalent to 100% reduction of the anthraquinone.

The positive reaction in the aged solvent suggested that peroxides, which form readily in the polyethers, might be involved in the reaction. To determine whether this positive reaction is due to the formation of peroxides in the diglyme, small amounts of various peroxides were added to the solution of anthraquinone and sodium borohydride in freshly purified diglyme under anaerobic conditions. In the case of benzoyl peroxide, lauroyl peroxide and *tert*-butyl hydroperoxide, the anthraquinone was reduced after an induction period of approximately 5 min. In a series of experiments with benzoyl peroxide it was shown that as little as 0.005 mole of the peroxide was sufficient to promote the reduction of a mole of anthraquinone. In a control experiment without added peroxide no reduction took place even after 5 hr. at room temperature.

To determine the role of the benzoyl peroxide in promoting the reduction, combinations of two of the reagents were mixed and allowed to stand for 10 min. before the addition of the other two. In only one case was the induction period for the reaction reduced from the normal value of 5 min. for the quantities used. This was when the benzoyl peroxide and the diglyme were allowed to age together before the addition of the anthraquinone and sodium borohydride. That the reduction was promoted by a product of the reaction between peroxide and the solvent was further proven by experiments with di-*t*-butyl peroxide. This peroxide did not cause a positive reaction under the conditions which were successful with the three mentioned previously. However, when the diglyme was first heated with di-*t*-butyl peroxide, and then cooled to room temperature, the reaction took place upon the addition of the sodium borohydride and anthraquinone.

There remained the possibility that the effect of the peroxide on the diglyme involved the formation of aldehydes by a free radical cleavage of the polyether. Thomas has reported that the peroxide-catalyzed thermal decomposition of a polyether yields aldehydes among other products.[3] While freshly prepared diglyme gave a negative Schiff test, it was found that the addition of a small

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[1] This work was conducted under a research grant provided by Metal Hydrides, Inc., of Beverly, Mass.

[2] B. Lindberg and J. Paju, *Svensk Kem. Tidskr.*, 65, 9-10 (1953).

[3] J. R. Thomas, *J. Am. Chem. Soc.*, 77, 6107-9 (1955).