hydrazone (no infrared carbonyl absorption) was heated in 30 g. of polyphosphoric acid at 100° for 3 hr. and at 170° for 3 min. Dilution with 150 ml. of water, addition of excess ammonia, and extraction with ether gave 4.0 g. of an oil from which 1.0 g. of the crude indole compound (XIII), m.p. 60–64°, was obtained by crystallization from ether–petroleum ether. A pure sample had m.p. 76–77°.

Anal. Calcd. for $C_{14}H_{10}BrN$: C, 61.86; H, 3.71; N, 5.15. Found: C, 61.85; H, 3.71; N, 5.19.

Alternatively, 3.0 g. of crude phenylhydrazone was heated for 5 min. at 170° with 20 g. of powdered zinc chloride and 40 g. of sand. Addition of 10 ml. of concentrated hydrochloric acid, extraction with ether, concentration, and chromatography on 25 g. of Woelm neutral I alumina in benzene gave 1.5 g. of crude product, m.p. 68–70°.

2-(3′-Bromophenyl)indole (XVII).—A solution of 8.2 g. (0.020 mole) of *m*-bromoacetophenone and 4.5 g. (0.020 mole) of phenylhydrazine in 5 ml. of ethanol deposited 10.4 g. of phenylhydrazone, m.p. 100–101° after recrystallization from ethanol. This compound decomposed to a black tar on standing in air for 3 days. A solution of 10.0 g. of the phenylhydrazone in 100 g. of polyphosphoric acid was heated at 80–90° for 2 hr. and at 135° for 5 min. Dilution with water, filtration, and crystallization from ethanol gave 7.0 g. of XVII, m.p. 152–154°, recrystallized to m.p. 157–158°.

Anal. Calcd. for $C_{14}H_{10}BrN$: C, 61.80; H, 3.71; N, 5.15. Found: C, 61.95; H, 3.83; N, 5.06.

Reaction of 2-(2′-Bromophenyl)indole (XIII) with Sodium Amide.—Within 10 min. a solution of 0.65 g. (2.4 mole) 2-(2′-bromophenyl)indole in 10 ml. of dry ether was added dropwise to a stirred solution of sodium amide, prepared from 0.30 g. (0.012 g.-atom) of sodium in 150 ml. of liquid ammonia. After 20 min., 0.80 g. (0.015 mole) of ammonium chloride was added, the ammonia was evaporated, the residue was dissolved in methylene chloride, and the solution was washed with 5% aqueous hydrochloric acid and evaporated.

Preparative thin layer chromatography of 0.4 g. of residual oil on Merck alumina G with 1:1 benzene–cyclohexane gave 0.150 g. of recovered starting material, 0.10 g. of an aminophenylindole (XIV) (m.p. 165–167°, recrystallized from dichloromethane and cyclohexane), and 120 mg. of dark oils in three fractions. Mass spectrum of the crystalline compound showed *m/e* 208 for the molecular peak.

Anal. Calcd. for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.47. Found: C, 80.62; H, 6.04; N, 13.27.

Reaction of 2-(2′-Bromophenyl)indole (XIII) with Piperidyllithium.—A solution of piperidyllithium, made by adding 2.7 ml. of a 13% solution of *n*-butyllithium in cyclohexane to 0.35 ml. of piperidine in 20 ml. of dry ether, was added to 0.54 g. of 2-(2′-bromophenyl)indole in 30 ml. of ether under nitrogen. After stirring for 18 hr., 1 ml. of water was added, the solvent was removed *in vacuo*, the residue was dissolved in dichloromethane, and the filtered solution was evaporated to 0.80 g. of oil. Successive preparative thin layer chromatography on Merck alumina G with 7:3 and 1:2 benzene–cyclohexane gave 0.25 g. of 2-phenylindole, m.p. and m.m.p. 176–178°, and 0.09 g. of a 2-piperidinophenylindole (XV), m.p. 86–87°; ultraviolet absorption showed $\lambda_{\max}^{\text{methanol}}$ 230 mμ (log ε 4.52), 320 (4.20).

Anal. Calcd. for $C_{19}H_{10}N_2$: C, 82.00; H, 7.30; N, 10.14. Found: C, 82.40; H, 7.50; N, 9.95.

Reaction of 2-(2′-Bromophenyl)indole with *n*-Butyllithium.—To a stirred solution of 0.85 g. (0.0031 mole) of 2-(2-bromophenyl)-indole in 50 ml. of dry tetrahydrofuran was added, under nitrogen, 20 ml. of ether containing 3.6 ml. of 14% butyllithium in cyclohexane. After refluxing for 18 hr., 1 ml. of water was added, the solvent was removed *in vacuo*, the residue was extracted with acetone, and the concentrate (0.75 g.) was subjected to preparative thin layer chromatography on Merck alumina G with 1:1 benzene–cyclohexane to give 0.43 g. of 2-phenylindole, m.p. and m.m.p. 175–178°, and several small oily fractions.

Acknowledgment.—We thank Professor Klaus Biemann, Massachusetts Institute of Technology, and Dr. Francis Johnson, Dow Chemical Company, for mass spectra; and the National Institutes of Health for support under USPHS Grant No. GM-09381.

The Oxidation of Phenylhydrazides to Carboxylic Acids with Manganese Dioxide. II. By-products[1]

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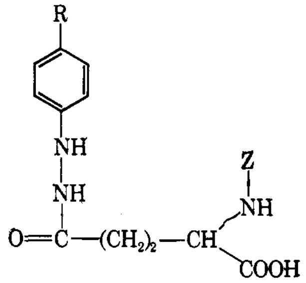
Received July 25, 1963

In a recent publication,[2] the smooth oxidation of phenylhydrazides to carboxylic acids with manganese dioxide was reported. The reaction is carried out in aqueous acetic acid at room temperature and is completed within 30 min. The γ-phenylhydrazide and the γ-(*p*-tolylhydrazide) of N-carbobenzoxy-L-glutamic acid (Ia and Ib, respectively), and dipeptides thereof, were found to undergo this reaction in good yield[3a] leaving protecting carbobenzoxy and ester groups intact and without racemization. These results prompted the suggestion that the phenylhydrazide group might well be used as a protective group in peptide chemistry.[2]



Ia, R = H; Z = $PhCH_2OCO$
b, R = CH_3; Z = $PhCH_2OCO$

In the present paper we report some investigations which have resulted in the discovery of essentially all of the products of the reaction and, consequently, have shed light on the mechanism.[3] All experiments were carried out on Ia under the conditions described in the preceding paper.[2]

Careful measurement of the nitrogen, which is rapidly evolved during the course of the reaction, showed that the nitrogen of the phenylhydrazide group is totally eliminated as elementary nitrogen within 30 min. Thus, obvious limitations are placed on the type of mechanism in operation.[3b]

In order to determine the fate of the aromatic ring of the phenylhydrazide group, we resorted to analysis of reaction mixtures by gas chromatography. The following three aromatic products were detected in the yields indicated: benzene (30%), phenol (27%), and phenyl acetate (41%). It has already been demonstrated that the N-carbobenzoxy group survives intact the conditions of the reaction[2,3a] and, moreover, none of these products could be detected by gas chromatography when N-carbobenzoxyglycine was submitted to the reaction conditions. Therefore, the aromatic products and the nitrogen have their origin in the

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[1] For the preceding paper, see ref. 2.

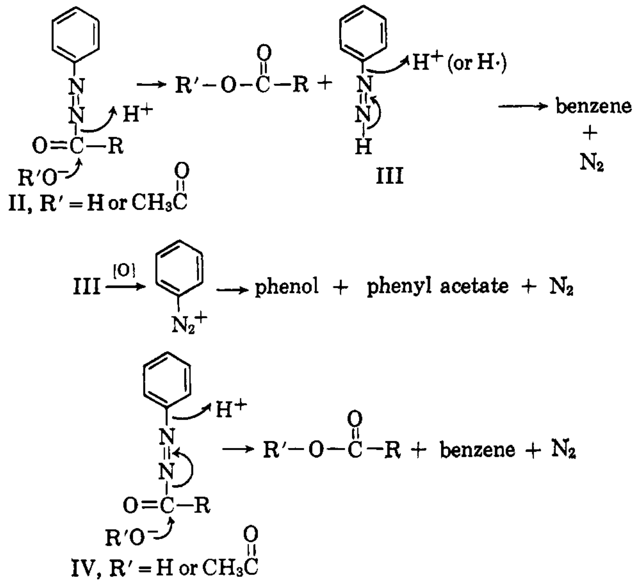
[2] R. B. Kelly, *J. Org. Chem.*, **28**, 453 (1963).

[3] (a) Yields of 80–90% of crystalline acids have been obtained (ref. 2); (b) see ref. 6d.

phenylhydrazide group and not in the N-carbobenzoxy group.

The presence of benzenediazonium ion in the reaction mixture is indicated by the appearance of dyes, due to coupling, when the reaction mixture is added to alkaline solutions of various phenols.[4] However, when benzenediazonium ion was substituted for phenylhydrazide and the reaction carried out as usual, both phenol and phenyl acetate were found in the reaction mixture by gas chromatography, *but no benzene could be detected.* Thus, under the conditions of the reaction, benzenediazonium ion cannot be a precursor of benzene, but it is a likely intermediate in the formation of phenol and phenyl acetate.

The mechanism of the reaction cannot be firmly established from the data presented above. However, the following sequence, that accounts for all the results, is suggested: (a) a preliminary oxidation of the hydrazide to the azo compound II; (b) solvolysis of II to a carboxylic acid or its mixed anhydride[5] (see II) and phenyldiimide[6] (III); (c) oxidation of some of III, by abstraction of a hydride ion, to benzenediazonium ion and decomposition of the ion to nitrogen, phenol, and phenyl acetate by interaction with hydroxyl ion and acetate ion; (d) decomposition of the remainder of III, by net transfer of hydrogen either as a proton or a hydrogen atom,[6b,c] to benzene and nitrogen (see III). Another possibility, which would account for only the carboxylic acid, benzene, and nitrogen, is the direct elimination of nitrogen from the azo compound by interaction with the solvent (see IV).[6d]



II, R' = H or $CH_3\overset{O}{\overset{\|}{C}}$

IV, R' = H or $CH_3\overset{O}{\overset{\|}{C}}$

Experimental

For gas chromatography, an F and M Model 720 apparatus was used fitted with a 72 × 0.25 in. stainless steel column. The column was packed with 10% Carbowax 20M on Gas Chrom Z (80–100 mesh). The helium flow rate was 50 cc./min., the injection port temperature was 300°, and the detector temperature was 230°.

TABLE I

GAS CHROMATOGRAPHY DATA

Compound	Concn. in reaction mixture, mmole/ml.	Peak area (arbitrary units) Benzene	Phenol	Phenyl acetate
Benzene[a]	0.0113	1.82		
	0.0225	3.60		
		3.40		
Phenol[a]	0.0106		0.63	
	0.0212		1.22	
Phenyl acetate[a]	0.0079			1.61
				1.64
	0.0158			2.96
				2.99
Ia (14.70 mg.)[b]	0.0396	1.90	0.60	3.15
		1.82	0.70	3.06

[a] Calibration experiment. [b] Actual analytical experiment.

TABLE II

YIELDS OF AROMATIC PRODUCTS

Product	Yield,[a] mmole	Yield, %
Benzene	0.0121	30.0
	0.0116	
Phenol	0.0104	27.5
	0.0114	
Phenyl acetate	0.0163	40.7
	0.0159	

[a] From 0.0396 mmole of Ia.

Determination of Evolved Nitrogen.[6d]—The reaction was carried out in a small cell (capacity *ca.* 5 ml.) fitted near the top with a connection to the Dumas apparatus. The cell was also fitted with an inlet tube by which carbon dioxide gas was bubbled through the reaction mixture and a neck sealed with a syringe cap. A mixture of 4.040 mg. of Ia and 8.00 mg. of activated manganese dioxide[7] was sealed in the cell by means of the syringe cap, and the apparatus was swept for several minutes with a slow stream of carbon dioxide gas. The reaction was then started by injecting 1 ml. of a mixture of acetic acid and water (65% acetic acid) through the cap into the cell from a hypodermic syringe. Agitation of the reaction mixture was achieved by the bubbling action of the carrier gas which was passed through the train of the Dumas apparatus; the evolved nitrogen was measured by the usual Dumas technique. The reaction was allowed to continue until the evolution of nitrogen had ceased (30 min.). To determine the correction necessary for nitrogen absorbed onto the manganese dioxide a blank experiment (omitting Ia) was carried out as above. The following results were obtained: calcd. for phenylhydrazide nitrogen of Ia, 7.54%; found (corrected), 7.45% (98.8%).

Benzene, Detection and Yield.—A mixture of 14.70 mg. (0.0396 mmole) of Ia and 31.47 mg. of activated manganese dioxide[7] was sealed in a 2-ml. volumetric flask by means of a syringe cap. A mixture (1 ml.) of acetic acid and water (65% acetic acid) and 0.5 ml. of toluene were injected through the cap into the flask from a hypodermic syringe. Pressure was releaved through the hypodermic syringe. The reaction was allowed to proceed at room temperature for 40 min. with agitation. The contents of the flask were then thoroughly mixed and allowed to settle into two layers; 6 μl. of the top layer was removed with a microsyringe and injected into the gas chromatography apparatus. The initial column temperature was 80°, and it was programmed to increase at the rate of 5°/min. A peak, subsequently shown to be due to benzene, appeared at a retention time of 0.59 min. (relative to toluene). Benzene was identified as the compound responsible for this peak by the fact that, when benzene

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(4) In the case of each phenol, the color corresponded to that obtained by addition of a solution of benzenediazonium chloride to an alkaline solution of the phenol in question. Addition of the reaction mixture to a "blank" alkaline solution resulted in a faint pink coloration readily distinguishable from the more intense colors produced in the presence of phenols.

(5) In experiments where the carboxylic acid was isolated (ref. 2), the conditions of work-up would result in hydrolysis of any anhydride present.

(6) *Cf.* (a) H. A. Itano and E. A. Robinson, *J. Am. Chem. Soc.*, **83**, 3339 (1961), and references there cited; (b) D. J. Cram and J. S. Bradshaw, *ibid.*, **85**, 1108 (1963); (c) A. Nickon and A. Sinz, *ibid.*, **82**, 753 (1960). (d) NOTE ADDED IN PROOF.—The infrared spectrum of the gas collected directly from the reaction indicated the absence of oxides of nitrogen.

(7) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

was added to an aliquot of the reaction mixture before chromatography, the peak was enhanced without the appearance of an inflection or an additional peak, and, furthermore, when benzene was substituted for Ia and the experiment carried out as above, a peak with the same retention time resulted.

The yield of benzene was determined from the area of the peak by reference to a calibration curve constructed as follows. Appropriate, known amounts of benzene were substituted for Ia in reaction mixtures, chromatography was carried out as above, and the areas of the peaks due to benzene were plotted against the concentration of benzene in the mixture. Pertinent data are summarized in Table I; the yield of benzene is given in Table II.

Phenol and Phenyl Acetate, Detection and Yield.—The procedures used for the detection of these products and the determination of their yields were the same as those used for benzene with the exception that the column was kept at a constant temperature of 175°. Under these conditions the retention time for phenol was 5.55 min. and, for phenol acetate, it was 1.96 min. (both relative to toluene). Because of the slow rate of extraction of these products into toluene, due probably to adsorption onto solids in the reaction mixture, the yields were determined 5 hr. after the start of the reaction. Pertinent data are given in Table I and the yields in Table II.

Substitution of Benzenediazonium Ion for Ia.—A solution of 0.0396 mmole of aniline in 0.65 ml. of cold glacial acetic acid was treated with 0.35 ml. of cold, aqueous 0.11 *M* sodium nitrite solution and 31.47 mg. of activated manganese dioxide.[7] The mixture was agitated in a stoppered flask at room temperature for 40 min. It was then analyzed for aromatic products by gas chromatography as described above. Both phenol and phenyl acetate were found, but no benzene could be detected.

Valence Tautomerism of Vinyl-Substituted Three-Membered Heterocycles. I. Conversion of 1,2-Divinylethylene Oxide to 4,5-Dihydrooxepine

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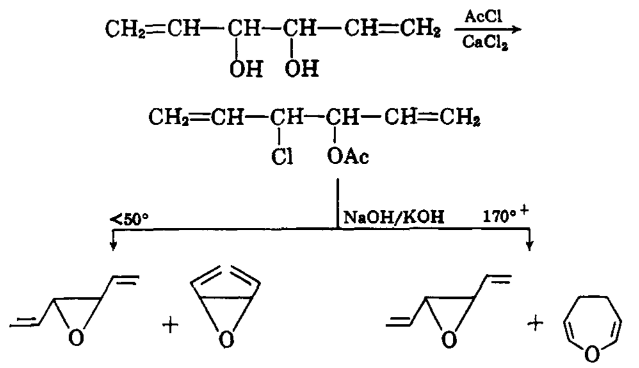
Received August 26, 1963

In recent years there has been considerable interest in the valence tautomerism of strained ring systems.[1-5] Until the work of Braun,[6] ring expansion of strained heterocyclic rings by a mechanism analogous to alicyclic systems had not been demonstrated. During the preparation of 1,2-divinylethylene oxide by the pyrolysis of *sym*-divinylethylene carbonate, Braun isolated its valence tautomer, 4,5-dihydrooxepine. Temperature requirements of cyclic carbonate pyrolysis precluded the isolation of *cis*- or *trans*-1,2-divinylethylene oxide free of 4,5-dihydrooxepine. We wish to report a convenient synthesis of *cis*- and *trans*-1,2-divinylethylene oxide together with the thermal requirements for conversion of each isomer to 4,5-dihydrooxepine.

The preparation of *cis–trans*-1,2-divinylethylene oxide and *trans*-1,2-divinylethylene oxide–4,5-dihydrooxepine was realized by the procedure shown.



In the absence of solvent, 1,5-hexadiene-3,4-diol was converted to 3-chloro-4-acetoxy-1,5-hexadiene in yields of 40–50%. Infrared spectra of the chloro ester exhibited C–Cl (12.7 μ), acetate (5.78, 8.15 μ), and terminal olefin absorption (6.1, 10.12, 10.7 μ)

Both high and low temperatures were used to accomplish ring formation from the chloro ester. The isomer distribution and ring size is a function of the ring closure temperature. At 170°+, only *trans*-1,2-divinylethylene oxide and 4,5-dihydrooxepine were formed in a ratio of 2:1. However, if the temperature was maintained at less than 50°, the *cis* and *trans* oxides were isolated in a ratio of 1:2. Under the latter conditions, only trace amounts (1–2%) of 4,5-dihydrooxepine were formed.

Neither the *trans*-1,2-divinylethylene oxide–4,5-dihydrooxepine nor *cis–trans*-1,2-divinylethylene oxide mixtures could be fractionated by distillation through a 75-plate concentric tube column. Pure *trans* and *cis–trans* oxides and 4,5-dihydrooxepine, for structural determination and thermal isomerization studies, were obtained by preparative g.c. separation.

Braun was unable to establish definitely the structure of the 1,2-divinylethylene oxide he isolated. Since we were able to isolate the *cis* and *trans* epoxide, structural assignment could be made on the basis of infrared and n.m.r. The infrared spectra of *trans*-1,2-divinylethylene oxide exhibits intense absorption at 11.51 μ.[7] In the *cis–trans* mixture, the presence of the *cis* isomer is indicated by a band at 12.1 μ and a decrease in intensity of the 11.51-μ absorption. 1,2-Divinylethylene oxide, *cis* and *trans*, give τ values of 6.85 and 7.15, respectively, for the methine protons. The chemical shifts[8] for the *cis* and *trans*-2-butene oxides exhibit this pattern; *i.e.*, the *cis* protons have a smaller τ value than the *trans* protons. The spin–spin splitting pattern of the oxide ring protons[8] also distinguishes between the *cis* and *trans* isomers.

Unequivocal evidence for the origin of 4,5-dihydrooxepine during high temperature 1,2-divinylethylene oxide preparation was obtained by the thermal isomerization of *trans*- and *cis–trans*-1,2-divinylethylene oxide. The *trans* oxide of 93% purity was heated in a sealed tube for 17 hr. at 230°. The composition after this heating period was 48.3% *trans*-1,2-divinylethylene oxide and 42.9% 4,5-dihydrooxepine. Under identical conditions, the 4,5-dihydrooxepine was recovered unchanged. However, a *cis–trans*-1,2-divinylethylene

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