gold, *et al.*,[5] have reported both these as liquids; possibly their method gave sterically homogeneous material. However, their measurement of the position of the prototropic equilibrium point by refractometric means is open to some doubt, in view of the unknown stereoisomer composition of their reference compounds and their equilibrium mixtures.

During crystallization of 3-anisyl-1-phenylpropene, a small amount of the less soluble β-anisylpropiophenone was isolated and identified by its melting point 67.5–67.9° and its oxime, m.p. 87–89°.[15]

1-Phenyl-3-*p*-anisylpropane.—In hopes of obtaining a solid for derivative purposes, a sample of solid 1-phenyl-3-*p*-anisylpropene was hydrogenated in methanol at 1 atm. pressure over 5% palladium–charcoal. Absorption of hydrogen was very rapid and quantitative. The methanol was evaporated and the residue recrystallized from petroleum ether (b.p. 30–40°). It melted at 2–4°. It was then distilled, b.p. 184–185° (10 mm.), n^{26}_D 1.5578.

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 85.00; H, 7.74.

No picrate could be formed.[16] An attempt to prepare a sulfonamide[17] gave solid material which was alkali-soluble, but which could not be purified. It melted at 130–140°, depending on the rate of heating, then immediately solidified, to remelt at 180–183°.

Acknowledgment.—The author is indebted to Miss Kathleen Hsu, Mr. Richard Scribner, Mr. Moe Wassermann and Mr. Max Boudakian for preparing some of the chalcones and for some preliminary experiments.

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(15) P. Pfeiffer, *J. prakt. Chem.*, [2] **108**, 350 (1924), reports melting points of 69° and 89°, respectively.

(16) Ref. 13, p. 190, Proc. 32.

(17) *Ibid.*, p. 189, Proc. 31.

ANN ARBOR, MICHIGAN RECEIVED MARCH 22, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

The Reaction of Menthofuran with *p*-Toluenediazonium Sulfate[1]

BY RICHARD H. EASTMAN AND FRANCIS L. DETERT

Menthofuran (I) reacts with *p*-toluenediazonium sulfate in acetate-buffered methanol to yield an unstable intermediate containing a molecule of methanol. Treatment of the unstable intermediate with aqueous acid causes loss of the molecule of methanol and conversion to N-(2-azabicyclo[4,3,0]3-keto-4,8-dimethyl-4,9-nonadienyl-2)-*p*-toluidine. The structure of the latter has been established by autohydrogenolysis to *p*-toluidine and 3,6-dimethyloxindole, and by comparison of its ultraviolet absorption spectrum with that of a model compound. An unambiguous synthesis of 3,6-dimethyloxindole is reported, and a mechanism for the reaction of furans with diazonium salts in buffered alcoholic media is proposed.

In an earlier communication[2] we have described the course of the reaction between *p*-nitrobenzenediazonium chloride and 2,5-dimethylfuran. The present communication deals with the reaction between *p*-toluenediazonium sulfate and menthofuran (I), and proposes a mechanism for the reaction.

When menthofuran (I) and *p*-toluenediazonium sulfate were permitted to react in an aqueous, methanolic solution of potassium acetate there was obtained a bright-yellow, crystalline substance, $C_{18}H_{24}N_2O_2$ (II) which was converted to N-(2-azabicyclo[4,3,0]3 - keto - 4,8 - dimethyl - 4,9-nonadienyl-2)-*p*-toluidine (III) on treatment with acid. The evidence for the structure of III is as follows: (1) Treatment of III with nitrous acid gave a pale-yellow nitroso compound (IV) which was an N-nitroso derivative since treatment of it with ammonium sulfide regenerated III. (2) III showed one active hydrogen on treatment with methylmagnesium iodide. (3) When III was heated with palladized charcoal there was obtained, in good yield, *p*-toluidine and 3,6-dimethyloxindole (V). The identity of 3,6-dimethyloxindole was established by comparison with an authentic sample and by its ultraviolet absorption spectrum (Fig. 1). (4) The ultraviolet absorption spectrum of III (Fig. 2) is nearly identical with that of IX (Fig. 2), prepared as described below, and with the calculated sum (Fig. 2) of the absorptions of VII[3] (Fig. 3) and *p*-toluidine.

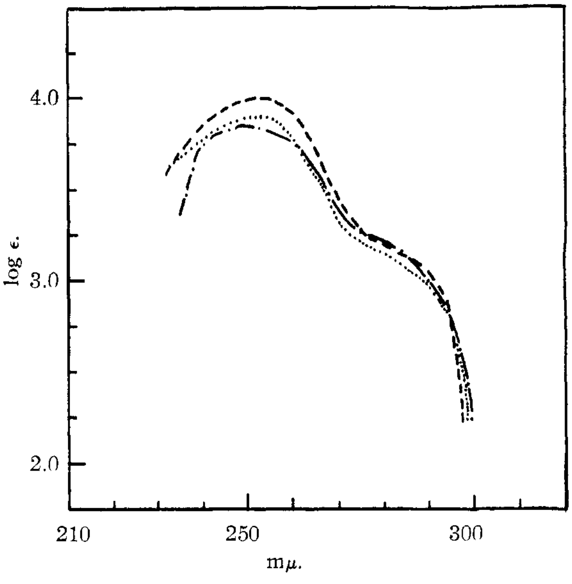

Fig. 1.—Ultraviolet absorption spectra in alcohol: — —, 3,6-dimethyloxindole (V); — · —, 1,3,3-trimethyloxindole [Ramart-Lucas and Biquard, *Bull. soc. chim.*, 2, 1387 (1935)]; ...., 3,4-dimethyloxindole.

The results of this investigation, taken with the earlier work on 2,5-dimethylfuran,[2] make it possible to propose a scheme for the coupling of furans with diazonium salts in alkaline alcoholic media which is based upon the accepted mechanism of aromatic substitution, and which accounts for the participa-

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(1) The work reported here is taken from the Dissertation of Francis L. Detert for the degree of Doctor of Philosophy in Chemistry at Stanford University, and was presented in part at the 1949 Spring Meeting of the American Chemical Society in San Francisco, Calif.

(2) Eastman and Detert, THIS JOURNAL, **70**, 962 (1948).

(3) VII has been prepared by dehydration of the autoxidation product VI of menthofuran (I) (Woodward and Eastman, *ibid.*, **72**, 399 (1950). Desoxypatulin which possesses the same chromophoric system as VII has λ_{max} 273, log ε 4.17 (Woodward and Singh, *ibid.*, **71**, 758 (1949).

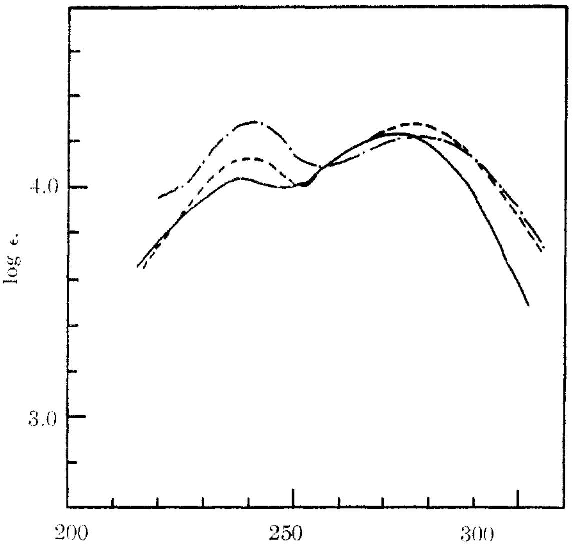


Fig. 2.—Ultraviolet absorption spectra in alcohol: ——, III; — — —, sum of VII and *p*-toluidine; —·—·, IX.

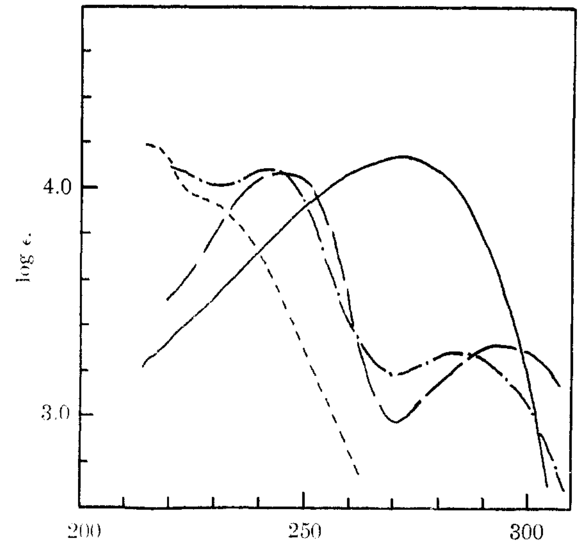
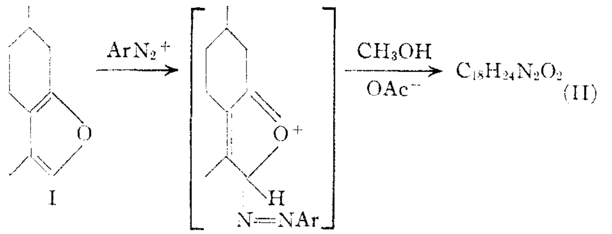
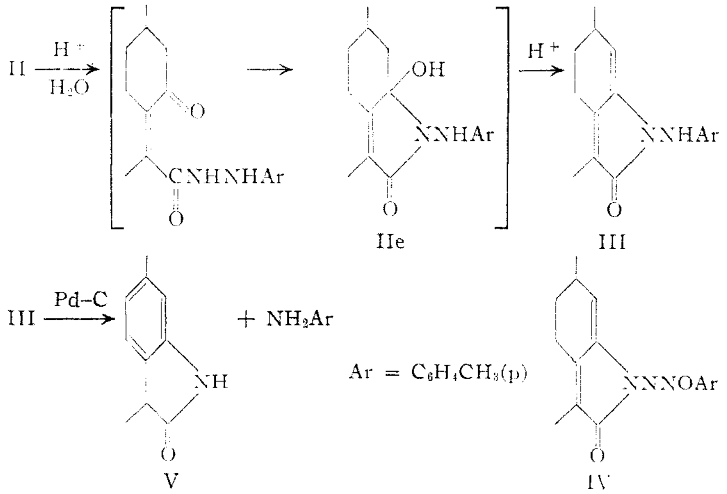


Fig. 3.—Ultraviolet absorption spectra: ——, VII in alcohol; —·—·, VIII in alcohol, — — —, VIII in 6 *N* hydrochloric acid; ————, methylaniline in alcohol.

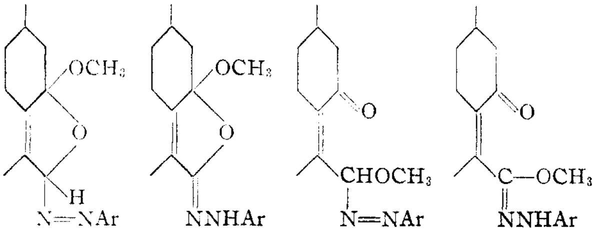
tion of the alcohol solvent in the reaction. In the case of the furan I, which has an α-position available for substitution, the following is proposed.





Evidence bearing on the structure of II is at a minimum. The substance was isolated in only one experiment, apparently fortuitously, and repeated attempts to obtain more of the compound for study failed. For II the structures IIa, b, c and d may be considered.

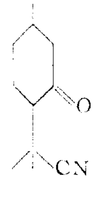
All of these substances would be expected to show the deep yellow color and smooth conversion by acid to III characteristic of II. However, IIa and IIc would not be expected to persist under the strongly basic reaction conditions for the preparation of II, since they are, respectively, the azo



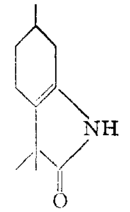
IIa IIb IIc IId

tautomers of the phenylhydrazone types IIb and IId. Experimental evidence is not at hand to distinguish between IIb and IId for the structure of II, and in the absence of such evidence the structure of II remains undetermined. In all experiments III was readily obtained by dissolving the crude, non-crystallizable coupling product in dilute alcoholic acid. A somewhat similar situation arises in the hydrolysis of XII which produces XIII directly[4] rather than the expected keto amide.

The conversion of IIe to III is analogous to the facile conversions of VI to VII[3] and of VIII to IX on distillation from a trace of potassium bisulfate. VIII was prepared by heating the



XII



XIII

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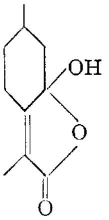
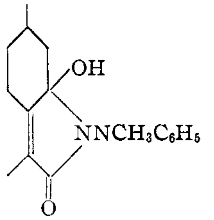
(4) Lapworth and Clarke, *J. Chem. Soc.*, **89**, 1869 (1906).

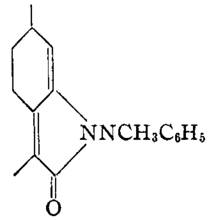
autoxidation product (VI) of menthofuran with α-methylphenylhydrazine. Its absorption spectrum in alcohol (Fig. 3) is nearly identical with that of methylaniline (Fig. 3) which is the expected result since VI shows no absorption down to 220 mμ in alcoholic solution.[8]



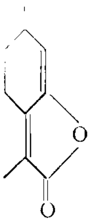
VI



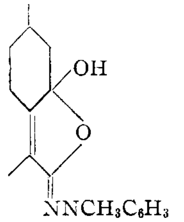
VIII



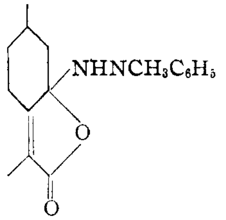
IX



VII



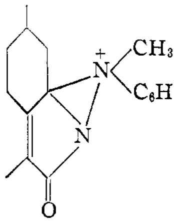
X



XI

VIII is similar in properties to VI in that it dissolves in sodium hydroxide but not in sodium bicarbonate solution. Surprisingly, VIII is a weak base also, being soluble in 6 *N* hydrochloric acid but insoluble in 3 *N* hydrochloric acid. The low basicity of VIII rules out alternative structures X and XI which would be least as strongly basic as methylaniline. The solubility of VIII in strong acid is somewhat difficult to reconcile with the insolubility of IX and III under the same circumstances. The ultraviolet absorption spectrum of VIII in 6 *N* hydrochloric acid (Fig. 3) shows no maxima characteristic of a benzene nucleus although such is present. This result can only be explained on the basis that in the salt of VIII the unshared pair of electrons on the anilino nitrogen atom is involved in covalent bond formation. Salt formation of this type causes a pronounced shift to shorter wave lengths and a great decrease in intensity of absorption in the analogous case of aniline[5] and, in the case under discussion, a similar shift could result in maxima which would be concealed by non-specific absorption at short wave lengths. The presence of the hydroxyl group in VIII may be expected to enhance the solubility of the compound in water and hence favor formation of a soluble salt.[6] Alternately, VIII may show pseudo-base behavior with XIV as the structure of the salt.[7]

Thus, simple protonation of the anilino nitrogen or formation of the anhydro-base XIV would account for the disappearance of the aniline absorption shown by VIII (*cf.* Fig. 3). Evidence is not at hand to distinguish between the two possibilities.



XIV

Considerable effort was devoted to establishing beyond doubt that the autohydrogenolysis product (V) was 3,6-dimethyloxindole.[8] The ultraviolet absorption spectrum of the autohydrogenolysis product V was identical with those reported for various oxindoles (see Fig. 1), and after several other syntheses failed, an authentic sample of 3,6-dimethyloxindole which showed no melting point depression when mixed with V was obtained on catalytic hydrogenolysis of the benzoyl derivative of 3-formyl-6-methyloxindole according to the method of Horner.[9] 3-Formyl-6-methyloxindole was prepared by condensation of ethyl formate with 6-methyloxindole[10] and the latter was obtained by standard procedures from *p*-xylene. Nitro-*p*-xylene[11] was condensed with ethyl oxalate in the presence of sodium ethoxide to yield 2-nitro-4-methylphenylpyruvic acid which was oxidized with hydrogen peroxide to 2-nitro-4-methylphenylacetic acid.[12] Reduction of the latter with tin and hydrochloric acid or with hydrogen in the presence of platinum gave 6-methyloxindole.

We wish to express our appreciation to the American Chicle Company, Long Island City, New York, for their support of a portion of this work.

Experimental[13]

Reaction of Menthofuran with *p*-Toluenediazonium Sulfate.—Three and two-tenths grams of *p*-toluidine in 60 ml. of water containing 4.5 g. of concentrated sulfuric acid was diazotized at 5° by the rapid addition of 2.10 g. of sodium nitrite in 6 ml. of water. The solution of *p*-toluenediazonium sulfate was added during 15 minutes to a well-stirred solution of 4.5 g. of menthofuran and 12 g. of anhydrous sodium acetate in 100 ml. of 95% methanol kept below 10°. Fifteen minutes after addition was complete an orange oil separated from the reaction mixture. The reaction mixture was stirred for a total of 1.5 hours while keeping the temperature below 10°, 40 ml. of absolute methanol being added in two equal portions at 1.5 hours of reaction time. The mixture was then allowed to come to room temperature during 1.5 hours during which time the oil which had separated partially solidified. The mixture was filtered, the oily residue was washed with water and then with a small amount of cold methanol. Trituration of the gummy residue with

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[5] Doub and Vandenbelt, THIS JOURNAL, **69**, 2716 (1947). Methylaniline shows λ_{max} 255 mμ, log ε 2.19 in 6 *N* hydrochloric acid solution.

[6] This suggestion was made by R. B. Woodward, Harvard University. For a similar case, see Gates, Woodward, Newhall and Kunzli, THIS JOURNAL, **72**, 1141 (1950).

[7] One of the referees made this excellent suggestion.

[8] Boehringer and Sohne (*Chem. Zentr.*, **81**, 781 (1910)) reported the preparation of 3,6- and 3,4-dimethyloxindole from β-propionyl-*m*-tolylhydrazine by pyrolysis with lime. In repeating this work we obtained a dimethyloxindole, m.p. 145–146°, presumably identical with their isomer of m.p. 148–149°. Since our material had the absorption spectrum of a dimethyloxindole (see Fig. 1) and was not identical with an authentic sample of 3,6-dimethyloxindole (m.p 137–138°) prepared in the unequivocal synthesis reported here, the material of m.p. 148–149° was presumably 3,4-dimethyloxindole. We were unable to obtain the substance of m.p. 113° reported to be 3,6-dimethyloxindole, and in view of our work their material must have been impure.

[9] Horner, *Ann.*, **548**, 117 (1941).

[10] Julian, Pikl and Boggess (THIS JOURNAL, **56**, 1797 (1934)) prepared 1-methyl-3-formyloxindole by condensation of ethyl formate with 1-methyloxindole.

[11] Jannasch, *Ann.*, **176**, 55 (1875).

[12] Reissert, *Ber.*, **30**, 1036 (1897).

[13] Melting points are not corrected.

cold methanol and dilution of the trituration liquor after filtration yielded 1.5 g. of a bright yellow solid which on crystallization from a small volume of methanol gave 1.25 g. of bright-yellow needles, m.p. 77.8–79°. Two further crystallizations from methanol raised the m.p. to 78–79°. A sample was dried *in vacuo* over sodium hydroxide and calcium chloride at room temperature.

Anal. Calcd. for $C_{18}H_{24}N_2O_2$: C, 72.0; H, 7.93; N, 9.24. Found: C, 72.3; H, 8.00; N, 9.34.

When a solution of 0.1 g. of the compound in 1 ml. of alcohol was treated with 1 ml. of 1 *N* hydrochloric acid, a bright red color flashed through the solution and a gummy, red solid separated. The mixture was warmed to boiling and heated for a few minutes to yield a nearly colorless solution from which, after addition of water to incipient precipitation, there separated on cooling, 0.05 g. of white cubes of m.p. 132–133°. A sample was crystallized from aqueous alcohol giving material of the same melting point.

Anal. Calcd. for $C_{17}H_{20}N_2O$: C, 76.1; H, 7.54; N, 10.4. Found[14]: C, 76.2, 76.5; H, 8.29, 7.40; N, 10.9.

This substance has been shown, as described below, to be N-(2-azabicyclo[4,3,0]3-keto-4,8-dimethyl-4,9-nonadienyl-2)-*p*-toluidine (III). In subsequent experiments the crude II from the coupling reaction was converted directly to III by acid treatment. In a typical experiment, 1.29 g. of III of m.p. 132–133°, which showed no depression in melting point on mixture with III obtained from purified II, was obtained from 3.8 g. of menthofuran. III showed $[\alpha]^{23}\text{D}$ +71° (0.01 molar solution in alcohol).

Nitrosation of III.—To 0.09 g. of III was added 0.175 g. of sodium nitrite in 1 ml. of water. Sufficient alcohol was added to give a solution and then 0.8 ml. of 6 *N* hydrochloric acid was added. After allowing the mixture to stand at room temperature for 15 minutes, water was added to effect the separation of 0.08 g. of bright-yellow needles, m.p. 101–102° after crystallization from alcohol.

Anal. Calcd. for $C_{17}H_{19}N_3O_2$: C, 68.7; H, 6.46. Found: C, 68.8; H, 6.43.

This compound is formulated as IV. A solution of 0.08 g. of IV in 6 ml. of alcohol plus 2.5 ml. of 15 *N* ammonia was saturated with hydrogen sulfide during 90 minutes and then reduced to a volume of 3 ml. at the hot plate. The sulfur which separated was removed by filtration, and water was added to the filtrate to effect the separation of a yellow oil which subsequently solidified. Trituration of the crude solid with alcohol and several crystallizations from alcohol gave white crystals of m.p. 128–131°. A mixture of this material with III had m.p. 128–133°.

Zerewitinoff Determination with III.—To one millimole of III (0.268 g.) dissolved in 5 ml. of dry pyridine was added an excess of methylmagnesium iodide in butyl ether solution. At the conditions of measurement (21°, 767 mm.) 25.6 ml. of methane was collected, after correction for blank, showing 1.07 active H per $C_{17}H_{20}N_2O$.

Autohydrogenolysis of III.—The catalyst prepared from 1.0 g. of palladium chloride by the method of Linstead[15] was mixed with 2.0 g. of III in a small distilling tube. The distilling tube was swept with carbon dioxide which was led to a nitrometer filled with 20% sodium hydroxide. The lower part of the distilling tube was heated in an air-bath to 205° at which temperature a distillate which solidified on being cooled appeared in the neck of the distilling tube. This material (0.15 g.) was shown to be *p*-toluidine by comparison of its acetyl derivative, m.p. 147–148° with an authentic sample of acet-*p*-toluidide, m.p. 148–149° in a melting point determination on the mixture, m.p. 147–149°.

During the distillation of the *p*-toluidine no gas was collected in the nitrometer. Distillation of the remaining material in the tube was carried out at 185–190° (20 mm.). An oily product (0.65 g.) was obtained which solidified on being cooled. Crystallization from aqueous alcohol gave 0.23 g. of white crystals, m.p. 139–140°. This material was soluble in alkali and insoluble in acid.

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.5; H, 6.89; N, 8.69. Found: C, 74.3; H, 6.99; N, 9.06.

This compound was shown to be 3,6-dimethyloxindole (V) by comparison with an authentic sample as described below. The ultraviolet absorption spectrum is reported in Fig. 1.

Synthesis of 3,6-Dimethyloxindole (V). A. 2-Nitro-4-methylphenylacetic Acid.—A mixture of 36 g. of ethyl oxalate and 18.9 g. of nitro-*p*-xylene[11,16] was slowly added to a solution of 11.5 g. of sodium in 187 g. of absolute ethanol. The deep-red solution which resulted was held at 35° for 72 hours during which a red solid separated. The greater portion of the ethanol was removed at the steam-bath after acidification of the suspension with 6 *N* hydrochloric acid, and the acidic residue was extracted with ether. The ether extract was repeatedly extracted with 5% sodium hydroxide solution until the alkaline extract was no longer red. Acidification of the alkaline extract produced a brown oil which solidified on being permitted to stand. Trituration of the crude solid with ethanol and crystallization from benzene yielded 9.6 g. of crude **2-nitro-4-methylphenylpyruvic acid**, m.p. 120–135°. Thirty per cent. hydrogen peroxide solution was added dropwise to a stirred solution of 2.6 g. of crude 2-nitro-4-methylphenylpyruvic acid in 25 ml. of 5% sodium hydroxide solution until the red color of the solution disappeared. Upon acidification of the solution a yellow solid separated. Crystallization of it from aqueous methanol gave 2.0 g. of **2-nitro-4-methylphenylacetic** acid, m.p. 168–169°.

Anal. Calcd. for $C_9H_9NO_4$: C, 55.40; H, 4.61. Found: C, 55.17; H, 4.61.

B. **6-Methyloxindole.**—Reduction with hydrogen at 50 pounds pressure of 3.3 g. of 2-nitro-4-methylphenylacetic acid dissolved in 50 ml. of glacial acetic acid took place during one hour in the presence of 0.04 g. of platinum oxide (Adams). The catalyst was removed by filtration and acetic acid was taken off at reduced pressure. Trituration of the residue with potassium carbonate solution left 2.0 g. of white needles, m.p. 176–180°. Crystallization of this material from aqueous alcohol yielded **6-methyloxindole** in the form of white needles, m.p. 179–180°.

Anal. Calcd. for C_9H_9NO: C, 73.48; H, 6.11. Found: C, 73.23; H, 6.17.

C. **3-Formyl-6-methyloxindole.**[10]—One gram of 6-methyloxindole and 0.68 g. of ethyl formate were added all at once to a hot solution of 0.23 g. of sodium in 5 ml. of absolute ethanol. The suspension which resulted was heated under reflux for 30 minutes and then poured into 200 ml. of hot water. The aqueous solution was decolorized with Darco and acidified to produce 0.94 g. of crude product. After several crystallizations from methanol, **3-formyl-6-methyloxindole** was obtained as yellow-orange plates, m.p. 221–222° (dec.).

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.58; H, 5.14. Found: C, 68.72; H, 5.16.

The compound was soluble in alkali hydroxide, and gave a green coloration with ferric chloride solution.

D. **Enol Benzoate of 3-Formyl-6-methyloxindole.**[9]—While assuring a slightly alkaline solution by the addition of 5% sodium hydroxide, a mixture of 0.5 g. of 3-formyl-6-methyloxindole and 0.4 g. of benzoyl chloride suspended in 10 ml. of water was shaken until the odor of benzoyl chloride disappeared. The benzoyl derivative separated and when crystallized from acetone was obtained in the form of thread-like, yellow needles, 0.57 g., m.p. 231–232° (dec.).

Anal. Calcd. for $C_{17}H_{13}NO_3$: C, 73.12; H, 4.66; N, 5.02. Found: C, 73.01, 72.35; H, 4.91, 4.62; N, 4.74.

Hydrolysis of this material (0.08 g.) by boiling it with 10% sodium hydroxide solution gave 3-formyl-6-methyloxindole (0.02 g.).

E. **Catalytic Reductive Cleavage of the Enol Benzoate of 2-Formyl-6-methyloxindole.**[9]—One-tenth gram of the enol benzoate of 3-formyl-6-methyloxindole was dissolved in 6 ml. of glacial acetic acid and hydrogenated in the presence of 0.03 g. of platinum oxide (Adams) with hydrogen at atmospheric pressure and at room temperature until two molar equivalents of hydrogen had been absorbed. (The hydrogenation had to be stopped at this point since if carried further about six molar equivalents were absorbed without the production of any crystalline product.) The catalyst was removed by filtration, the solvent was removed by dis-

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[14] Analyses by Microchemical Specialties Co., Berkeley, California.

[15] Linstead, *J. Chem. Soc.*, 1127 (1940).

[16] We wish to thank Shell Development Company, Emeryville, California, for providing us with a sample of 98 mole per cent. *p*-xylene for use in this work.

tillation at reduced pressure, and the resulting brown, crystalline residue was washed with dilute sodium bicarbonate solution. Acidification of the bicarbonate washings yielded benzoic acid, m.p. 121°, the identity being confirmed in a mixture melting point with an authentic sample. The residue left after bicarbonate washing was extracted with 20 ml. of hot water, decolorized with Darco and concentrated by evaporation to a small volume. The crude solid so obtained was twice crystallized from small volumes of aqueous ethanol to yield 0.02 g. of **3,6-dimethyloxindole**, m.p. 137–138°. A mixture of this material and that obtained as described above under autohydrogenolysis of III (m.p. 139–140°) had m.p. 138–139°.

Preparation of Model Compounds. Preparation of VII.—VII was prepared according to the method of Woodward and Eastman.[3] The sample used for the ultraviolet absorption spectrum reported in Fig. 3 had m.p. 31–32°.

Preparation of VIII.—Seventy-five hundredths of a gram of VI[3] was heated with 0.70 g. of α-methylphenylhydrazine in a sealed tube filled with nitrogen at 140° for 16 hours. The mixture crystallized on being permitted to stand for two days at room temperature. The crystals were separated by filtration and washed with benzene to yield 0.65 g. of material, m.p. 108–109°. Crystallization from aqueous methanol gave 0.60 g. of white needles, m.p. 108–109.5°.

Anal. Calcd. for $C_{17}H_{22}O_2N_2$: C, 71.34; H, 7.68. Found: C, 71.14; H, 7.73.

VIII was soluble in warm 5% potassium hydroxide solution. Acidification of the alkaline solution with 3 *N* hydrochloric acid regenerated the compound in nearly quantitative yield. The compound VIII was also soluble in 6 *N* hydrochloric acid but not appreciably so in 3 *N* acid. Addition of excess sodium bicarbonate to the acid solution caused precipitation of VIII unchanged. The ultraviolet absorption spectrum is reported in Fig. 3.

Preparation of IX.—Two-tenths of a gram of VIII was heated with a tiny crystal of sodium bisulfate in a small distilling tube over a free flame while maintaining a pressure of 1 mm. Gas evolution commenced soon after the mixture melted and continued for 15 minutes of gentle heating. The product was finally distilled over an indentation in the distilling tube and after being cooled consisted of a greenish-yellow glass. This material was dissolved in purified ether and the solution was extracted three times with 3 *N* hydrochloric acid, three times with 5% sodium hydroxide and washed with water. Evaporation of the ether, finally at 1 mm., left a faintly yellow, very viscous oil. A sample was prepared for analysis by sublimation at 1 mm. and 130°.

Anal. Calcd. for $C_{17}H_{20}N_2O$: C, 76.1; H, 7.53; N, 10.30. Found: C, 75.72; H, 7.63; N, 10.30.

This material was insoluble in 6 *N* and 12 *N* hydrochloric acid, hot or cold, and insoluble in hot or cold 5% sodium hydroxide. The ultraviolet absorption spectrum is reported in Fig. 2.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectra were determined with a Beckman Model DU Quartz Spectrometer. The sensitivity knob was kept three and one-half turns from the extreme clockwise position and the instrument was balanced by varying the slit width from 0.3 to 2.0 mm. as necessary. Readings were taken at 5 mμ intervals.

STANFORD, CALIF.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

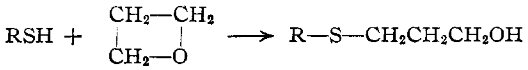
The Reactions of Trimethylene Oxide with Mercaptans, Thiophenol and Some Inorganic Sulfur Compounds[1]

BY SCOTT SEARLES

Trimethylene oxide is cleaved by sulfur anions in the same manner as is ethylene oxide although at a much slower rate. The reaction of thiophenol and aliphatic mercaptans proceeds smoothly in alkaline solution to give good yields of 3-hydroxypropyl sulfides, whereas no reaction occurs with tetrahydrofuran. The reactions of trimethylene oxide are strongly catalyzed by acids. A kinetic study of the reaction with aqueous sodium thiosulfate showed that acid catalysis is more effective with trimethylene oxide than with ethylene oxide in this reaction, as expected from the more basic nature of the four-membered cyclic ether.

Previous work has shown that trimethylene oxide is very similar to ethylene oxide in its reaction and reactivity with the Grignard reagent.[2] In order to obtain evidence on whether the four-membered cyclic ether is generally as reactive as the three-membered one, the reactions of the former with several mercaptans, thiophenol and certain inorganic sulfur anions have been investigated.

In contrast to the observations with the Grignard reaction, it is found that trimethylene oxide reacts with thiols much more slowly than does ethylene oxide; the course of the reaction, however, is analogous.



$$RSH + \begin{array}{l} CH_2—CH_2 \\ | \quad\quad | \\ CH_2—O \end{array} \longrightarrow R—S—CH_2CH_2CH_2OH$$

The uncatalyzed reaction requires prolonged heating, and even when catalyzed with strong acids such as sulfuric acid or aluminum chloride the reaction gives poor yields. This is quite different from the easy reaction of mercaptans and thiophenol with ethylene oxide.[3]

The trimethylene oxide reaction proceeds smoothly in aqueous alkali, however, to give the expected sulfide alcohols in 60–75% yields (Table I). The faster reaction in the basic solution may be ascribed to the more nucleophilic character of the mercaptide anion, compared to the mercaptan.

The reaction of mercaptide ion, however, is much slower with trimethylene oxide than with ethylene oxide or propylene oxide, as shown by the time required and the products from competition experiments. Tetrahydrofuran, on the other hand, reacted much more slowly than trimethylene oxide, indicating that the ease of nucleophilic attack parallels the strain in the ring.

In view of the very easy reaction of thiosulfate,[4,5] bisulfite[6] and sulfide[5,7] ions with ethylene oxides, the reaction of these salts with trimethylene oxide was investigated. Trimethylene oxide reacted

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[1] Most of this material was presented before the Division of Organic Chemistry at the 118th Meeting of the American Chemical Society, Chicago, Ill., September 5, 1950.

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