pearance of the above publications. Our results indicate that the reaction of one mole of N-bromosuccinimide, in the presence of benzoyl peroxide, with a mole of methylthiophene usually gives a mixture of roughly equal amounts of side-chain and nuclear bromination.[3] However, in several experiments, only nuclear brominated compounds could be isolated.[4] Since the original halogenation mixture was relatively clear and contained substantial amounts of the thenyl bromides, this was used without distillation to prepare a number of derivatives of 2- and 3-methylthiophenes. These are described in the experimental part.

Experimental

Reactions of 2-Methylthiophene with N-Bromosuccinimide.—One hundred and fifty grams of 2-methylthiophene[5] dissolved in 500 cc. of carbon tetrachloride was treated with 272 g. of N-bromosuccinimide and 1.0 g. of benzoyl peroxide. A vigorous exothermic reaction accompanied by the evolution of white fumes began. After the initial reaction subsided, the mixture was refluxed for 90 min. during which time the solid N-bromosuccinimide disappeared from the bottom of the flask.

After cooling to 10° the lachrymatory reaction mixture was filtered and distilled. The fraction boiling at 48–55° (3 mm.), was redistilled yielding 2-bromo-5-methylthiophene, b.p. 97° (67 mm.); yield 142 g. (53%). It formed a Grignard reagent which on carbonation gave 5-methylthiophene-2-carboxylic acid, m.p. 136°,[6] but would not react with piperidine.

The distillation residue consisted of 55 g. of a fuming, lachrymatory, viscous, black liquid which could not be distilled. It slowly evolved hydrogen bromide and became rock hard.

The Preparation of N-(2-Thenyl)-piperidine.—Fifty grams of 2-methylthiophene was slowly added, with constant stirring, to a mixture of 500 cc. of carbon tetrachloride, 1.2 g. of benzoyl peroxide and 105 g. of N-bromosuccinimide. The rate of addition was regulated so that the exothermic reaction maintained the temperature at 72–73°. After 60 minutes the heavy N-bromosuccinimide disappeared from the bottom of the flask. The reaction mixture was extremely lachrymatory. The solution was cooled and separated from the succinimide and added to three equivalents of piperidine in 100 cc. of carbon tetrachloride. Precipitation of piperidine hydrobromide occurred immediately, accompanied by the evolution of heat.

The reaction mixture was extracted with dilute mineral acid and the free amine was obtained by ether extraction after the addition of base. Under this treatment most of the excess piperidine remained in the water phase.

Distillation of the dried ether phase gave 54 g. (58%) of N-(2-thenyl)-piperidine, b.p. 139.5° (29 mm.); $n^{25}\text{D}$ 1.5373. *Anal.* Calcd. for $C_{10}H_{15}NS$: C, 66.29; H, 8.34. Found: C, 66.55; H, 8.51.

Picrate, m.p. 147–148. *Anal.* Calcd. for $C_{16}H_{18}O_7N_4S$: C, 46.82; H, 4.42. Found: C, 47.31; H, 4.85.

Methiodide, m.p. 59°. *Anal.* Calcd. for $C_{11}H_{18}SNI$: C, 40.88; H, 5.61. Found: C, 41.11; H, 5.85.

The identical tertiary amine was obtained by treating 2-chloromethylthiophene (obtained from Arapahoe Chemical Co., Boulder, Colorado), with piperidine in carbon tetrachloride, as shown by mixed melting points of solid derivatives.

Independent Synthesis of N-(2-Thenyl)-piperidine.—One gram of thiophene-2-carboxylic acid was converted to the acid chloride with thionyl chloride. After removal of excess thionyl chloride, a benzene solution of piperidine (excess) was added, and the mixture allowed to stand for an hour. The solution was then washed with dilute acid, to remove piperidine, and dried. The solution of amide was added directly to a solution of 0.3 g. (excess) of lithium aluminum hydride (obtained from Metal Hydrides, Inc., Beverly, Mass.) in anhydrous ether. The amine was isolated as the picrate, m.p. 148–149°; yield 2.3 g. (77% based on thiophenecarboxylic acid). The melting point was not depressed by the admixture of the tertiary amine picrate obtained from 2-halomethylthiophene.

Reaction of 3-Methylthiophene with N-Bromosuccinimide. The halogenation experiments described above were repeated, using 3-methylthiophene.

Treatment of the halogenation mixture with piperidine before distillation, as for the 2-methyl derivative, gave a 49% yield of N-(3-thenyl)piperidine; b.p. 141° (29 mm.); $n^{24}\text{D}$ 1.5373 (*cf.* 2-thenyl derivative).

Anal. Calcd. for $C_{10}H_{15}NS$: C, 66.29; H, 8.34. Found: C, 66.17; H, 8.42.

Picrate, m.p. 114–115°. *Anal.* Calcd. for $C_{16}H_{13}O_7N_4S$: C, 46.82; H, 4.42. Found: C, 46.80; H, 4.60.

The methiodide melted at 122–124°. *Anal.* Calcd. for $C_{11}H_{18}SNI$: C, 40.88; H, 5.61. Found: C, 41.41; H, 5.98.

Preparation of 3-Thenaldehyde.[1a]—Treatment of the halogenation mixture from 50 g. of 3-methylthiophene, as above, with 65 g. of hexamethylenetetramine for two hours with vigorous stirring gave a bulky precipitate, which was hydrolyzed by refluxing for three hours with 250 ml. of 50% ethanol. 3-Thiophenealdehyde was isolated by distillation; b.p. 78° (14 mm.), $n^{23}\text{D}$ 1.5810; yield 26.5 g. (47%). The odor is similar to that of benzaldehyde. It formed a 2,4-dinitrophenyldrazone, m.p. 235°.

Isolation of 3-Thenyl Bromide.[1a]—Direct distillation of the reaction mixture at 1 mm. gave a product which consisted of 3-thenyl bromide, plus substantial amounts of 2-bromo-3-methylthiophene.[1b] The mixture was redistilled, and the fraction, b.p. 66° (16 mm.), refractive index $n^{22}\text{D}$ 1.5712, was taken to be 2-bromo-3-methylthiophene. A second fraction was isolated at 92° (16 mm.), $n^{20}\text{D}$ 1.6048, which was intensely lachrymatory. It reacted instantly with piperidine to give N-thenylpiperidine, and thus was presumably 3-thenyl bromide. When pure it was quite stable; impure samples, darkened gradually, finally setting to a solid tarry mass after several days.

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[3] The experimental conditions were not strictly comparable to the prior investigators (ref. 1a) who obtained high yields of side-chain bromination by the use of smaller amounts of benzoyl peroxide catalyst.

[4] Similar results have been reported by other investigators (ref. 1b, footnote 8). Campaigne and Le Suer (ref. 1a) obtained only nuclear substitution in the absence of peroxide catalyst.

[5] Both 2- and 3-methylthiophene were obtained through the generosity of the Socony-Vacuum Oil Co.

[6] Confirming this melting point Rinkes, *Rec. trav. chim.*, **51** [4], 1141 (1932), and Hartough and Conley, THIS JOURNAL, **69**, 3096 (1947).

The Reaction of Aromatic Triazenes with Nitric Oxide

BY TOD W. CAMPBELL[1]

If a solution of an aromatic triazene, ArNH—N=NAr, in a hydrocarbon solvent is agitated in an atmosphere of pure nitric oxide, the nitric oxide is absorbed readily at a rate which increases with time, indicating a free radical reaction and possibly autocatalysis. If the absorption of nitric oxide in moles per mole of triazene is plotted against time, a curve similar to Fig. 1 is obtained. These curves are not reproducible, since repeating the experiment under identical conditions gives in each case a somewhat different absorption curve. The main difference is the position of the maximum with reference to the time axis. By examining the curve in Fig. 1, one can see that the reaction of a triazene with nitric oxide involves the absorption of more than two moles of nitric oxide, and probably three per mole of triazene, with the subsequent evolution of two moles of unidentified gas, probably nitrogen. The nature of the primary non-gaseous products was deduced from the following experiments: (1)

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One mole of triazene in an aromatic hydrocarbon was allowed to react with nitric oxide at 0° until maximum absorption was reached; at this point, the nitric oxide was displaced by nitrogen, and a coupling agent, either β-naphthol or dimethylaniline was quickly added. From the reaction mixture was obtained about two moles of azo dye. (2) This experiment was repeated, only the coupling agent was added at the end of the experiment, when the gas pressure in the system had attained a constant value. Only one mole of azo dye was produced; however, about 0.5 mole of a biaryl could also be isolated. (3) The experiment under (2) was repeated, only no coupling agent was added. From the reaction mixture a white solid was obtained which was recrystallized and identified as a diazonium nitrate. On the basis of the above observations, it would appear that a triazene reacts with nitric oxide to give two substances, one of which is much more stable than the other, and both of which react with passive couplers to give azo dyes. One of these substances is a diazonium nitrate, and the other, unstable product is probably a diazohydroxide. This latter substance would then be the source of hydroxyl radicals, which oxidize nitric oxide to the observed nitrate ion, and of phenyl radicals, which react with the solvent to give biphenyl.

Although we have insufficient experimental evidence, particularly with regard to the precise stoichiometry, to be able to postulate a rigorously acceptable mechanism for the reaction between a triazene and nitric oxide, we should like to point out the superficial similarity between this reaction and the autoxidation of olefins, and olefinic substances.[2,3,4]

Experimental Part

Materials.—Nitric oxide was prepared by the dropwise addition of 18 *N* sulfuric acid to a saturated solution of sodium nitrite. The gases were passed through a dry ice trap to remove most of the nitrogen dioxide, then through 6 *N* sodium hydroxide. The nitric oxide was stored in a 5-l. glass cylinder under a slight head of dilute aqueous alkali. Triazenes were synthesized by conventional methods.[5]

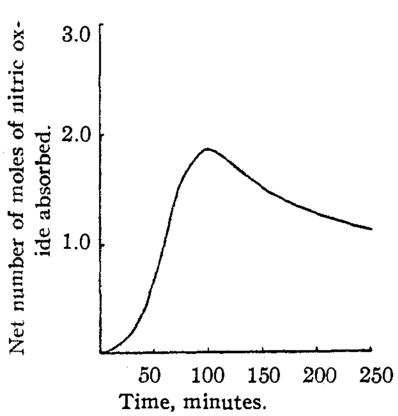

Fig. 1.

Apparatus and Methods.—The nitric oxide was transferred to a gas buret, which was connected to a reaction vessel held in a dewar flask containing cooling media. The flask and bath were vigorously agitated by a mechanical shaker. The course of the reaction was followed by observing the change in pressure in the system. All precautions were taken to deliver the gas to the reaction flask dry and free of other oxides of nitrogen.

Absorption of Nitric Oxide by 1,3-Di-*p*-tolyltriazene.—In a typical experiment, 1.004 g. of the triazene dissolved in 25.0 cc. of dry toluene at 0° was allowed to react with nitric oxide, with room temperature 23° and barometric pressure 758 mm. A typical absorption curve is shown in Fig. 1. The absorption curves are characteristic, showing an apparent maximum absorption of somewhat less than two moles, followed by evolution of gas to bring the net absorption of gas back to about 1 mole. Duplicate experiments under identical conditions gave similar, but not identical, curves, the principal difference being in the position of the maximum. In the experiment described above, a net absorption of 100 ml. of nitric oxide was observed; theory for 1 mole per mole of triazene was 110 ml.

The reaction flask was removed from the apparatus and the product examined. The solution had acquired a dark appearance, and a whitish precipitate had formed. The solid was filtered off, washed with benzene and hexane, dissolved in anhydrous isopropyl alcohol, and caused to crystallize by addition of anhydrous ether. The product crystallized as hygroscopic white needles, which exploded when struck with a hammer or when the temperature was raised to about 75°. This compound in methanol coupled readily with β-naphthol and dimethylaniline to give azo dyes which were isolated and identified as *p*-tolylazo-β-naphthol and *p*-tolylazodimethylaniline. It was surprisingly stable; samples were stored for six months at 0° without complete loss of coupling activity.

Dry combustion methods for analysis were unsatisfactory, because of the explosive nature of the compound. Use of a wet combustion method on a sample dried *in vacuo* over anhydrone for 24 hours gave better results, however.

Anal. Calcd. for $C_7H_7N_3O_3$: C, 46.9. Found: C, 44.4, 45.0.

Coupling Components Produced by Reaction of Nitric Oxide with Ditolyltriazene.—(1) Ditolyltriazene (0.7410 g.) was dissolved in 25 ml. of dry toluene and treated with nitric oxide as above. At 760 mm. and 21°, the pressure reached a constant value when 82 ml. of gas was absorbed. Theory for 1 mole NO per mole triazene was 82 ml. The nitric oxide was flushed from the system and to the cold solution was added 2 cc. of dimethylaniline and 5 cc. of methanol. After one-half hour, 0.65 g. of azo dye was isolated. Theory for 1 mole of azo dye per mole of triazene = 0.79 g.; recovery, 82%. A series of experiments using both dimethylaniline and β-naphthol as coupler gave yields of azo dye in the range of 75–90%, based on one mole of dye per mole of triazene.

(2) The above experiments were repeated except that the coupler (β-naphthol or dimethylaniline) was added to the reaction mixture at the time when the maximum gas absorption was observed. Thus 0.577 g. of ditolyltriazene in 25 cc. of toluene and 25 cc. of cyclohexane absorbed nitric oxide until the pressure ceased to drop. Then 2 cc. of dimethylaniline was added after flushing the system with nitrogen diluted with 15 cc. of methanol. From the reaction mixture was obtained 0.97 g. of azo dye, 80% based on 2 moles of coupling component per mole of triazene.

Coupling of β-Naphthol and Dimethylaniline with Ditolyltriazene.—To show that triazenes do not couple with β-naphthol rapidly to give azo dye in an approximately neutral solution, the development of the characteristic maximum of *p*-tolylazo β-naphthol in a solution of β-naphthol and ditolyltriazene was followed spectrophotometrically at 485 mμ. The results showed the reaction to be slow; at concentrations of about $5 \times 10^{-3}m$, the reaction was less than 1% complete in two hours at room temperature.

Reaction of Nitric Oxide with Ditolyltriazene in Methanol.—Ditolyltriazene (0.400 g.), β-naphthol (0.514 g., 2 equiv.) in 50 cc. of methanol was treated at room temperature with nitric oxide. No apparent absorption of nitric oxide resulted; however, the solution rapidly acquired the red color of the azo dye. In one hour, the reaction mixture was analyzed and found to contain 0.21 g. of β-naphthol, 0.15 g.

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(2) C. E. Frank, *Chem. Revs.*, **46**, 155 (1950).

(3) D. Swern, J. T. Scanlan and H. B. Knight, *J. Am. Oil Chem. Soc.*, **25**, 193 (1948).

(4) An interesting paper has recently appeared (K. H. Pausacker, *J. Chem. Soc.*, 3478 (1950)) in which the author interprets the autoxidation of certain phenylhydrazones, $ArCH{=}N{-}\underset{H}{N}{-}Ar$ in similar terms.

(5) K. H, Saunders, "The Aromatic Diazo Compounds," Longmans, Green, New York, N. Y., 1949; T. W. Campbell and B. F. Day, *Chem. Revs.*, **48**, 299 (1951).

of *p*-toluidine and 0.45 g. of *p*-tolylazo-*β*-naphthol. A quantitative recovery of azo dye was made assuming one mole of dye was produced from 1 mole of triazene. Furthermore, 79% of the expected toluidine and 80% of the excess *β*-naphthol was obtained. This experiment carried out in toluene rather than methanol resulted in a net absorption of one mole of nitric oxide; only a small yield of azo dye resulted, however. The principal product was an intractable tar. No apparent reaction occurred between ditolyltriazene and nitric oxide in methanol in the absence of passive coupler.

Fate of the Unstable Coupling Component Produced in an Inert Solvent.—Diphenyltriazene (5.0 g.) in 100 ml. of anhydrous thiophene-free benzene was treated at room temperature with nitric oxide in the usual way. When reaction had ceased, the solution was filtered to give 3.2 g. of dry solid. The dark solution was distilled to remove benzene, then steam distilled to give 1.9 g. (49%) of biphenyl, m.p. 69°. The residue was a dark tar, identical in appearance and odor to the usual "diazo resins" produced during typical biaryl syntheses by the Gomberg–Bachmann reaction.

The Reaction of Nitric Oxide with 1,3-Di-*p*-tolyl-1-methyltriazene.—In an attempt to isolate N-nitroso-N-methyltoluidine, the N-methyltriazene (8.80 g.) was treated with nitric oxide at 0°. The usual precipitate was obtained, which was identical to that from 1,3-di-*p*-tolytriazene. However, no N-nitrosoamine could be isolated. The absorption of nitric oxide, however, followed a somewhat different course. It was autocatalytic, but leveled off at a net absorption of about 2 moles.

Reaction of 1,3-Bis-(4-chlorophenyl)-triazene with Nitric Oxide.—One gram of this triazene in a mixture of 25 ml. of cyclohexane and 25 ml. of benzene was treated with nitric oxide at room temperature. (The reaction was too slow at 0°.) As above, a white solid was isolated (440 mg.) which contained 17.1% chlorine (Dumas) without further purification. A recrystallization from isopropyl alcohol-ether as described above gave *p*-chlorophenyldiazonium nitrate.

Anal. Calcd. for $C_6H_4N_3O_3Cl$: Cl, 17.6. Found: Cl, 17.4. Calcd. for $C_6H_4N_3O_3Cl\cdot H_2O$: C, 32.9. Found[6]: 32.1, 32.9, 31.9, 32.3, 32.3.

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(6) Wet carbon method. These samples were analyzed "as received" without additional drying, whereas the samples for Dumas halogen were dried *in vacuo* overnight over anhydrone.

(7) An earlier version of this manuscript was received on March 23, 1949.

Synthesis of 2,4-Dihydroxybenzohydrazide

BY BERNARD CAMBER[1] AND DOMINIC D. DZIEWIATKOWSKI

A new color test for aldehydes and ketones was introduced in 1949[2] based on the coupling of a diazonium salt with the naphtholic hydrazide derivative of an aldehyde or ketone to form a stable, intensely colored azo dye. The application of one reagent of this group, 2-hydroxy-3-naphthoic hydrazide, to histochemistry,[2–4] to the qualitative and quantitative study of urinary ketosteroids,[5] and to the isolation of estrone[6] has been reported. The usefulness of a phenolic hydrazide, 2,4-dihydroxybenzohydrazide, in the histochemical differentiation of active carbonyl groups and in the characterization of ketosteroids is now under study. No reference to the synthesis of 2,4-dihydroxybenzohydrazide has been found in the literature.

2,4-Dihydroxybenzohydrazide.—In a 100-ml. round-bottom flask with a ground glass joint 18.2 g. (0.1 mole) of ethyl 2,4-dihydroxybenzoate was dissolved in 10 ml. of absolute ethanol by warming. To the warm solution 8 ml. of 100% hydrazine hydrate was added slowly with mixing. Most of the ethanol was removed by distillation. The flask was attached to a reflux condenser and the reaction mixture refluxed for two hours. At the end of one hour an additional 4 ml. of hydrazine hydrate was added through the condenser. On cooling to room temperature the reaction mixture solidified. The flask with the reaction mixture was placed over anhydrous calcium chloride in an evacuated desiccator and kept therein for three days at room temperature to further remove the ethanol and thereby drive the reaction nearer completion. The solid was dissolved in a minimum volume, about 200 ml., of boiling 95% ethanol. A light tan crystalline precipitate was deposited on cooling to room temperature. The amount of precipitate increased further by placing the mixture at 0° for three hours. The precipitate was then isolated by filtration and washed repeatedly with small volumes of cold 95% ethanol. It was redissolved in slightly more than the required minimum volume of 95% ethanol and the solution was decolorized with activated carbon (Darco, Grade G-60). After 12 hours at 0° a nearly white crystalline product was isolated. It was dried briefly in air and then for 24 hours *in vacuo* over calcium chloride at room temperature. The yield was 5.7 g. (34%), m.p. 240–241° (uncor.). Two more recrystallizations from 95% ethanol gave colorless lath-like needles, m.p. 245–246° (uncor.).

Anal.[7] Calcd. for $C_7H_8O_3N_2$: C, 50.00; H, 4.76; N, 16.66. Found: C, 50.04; H, 4.82; N, 16.70.

Benzaldehyde 2,4-Dihydroxybenzoylhydrazone.—To 10 ml. of a saturated 95% ethanol solution of the hydrazide 0.1 ml. of freshly distilled benzaldehyde was added followed by 0.1 ml. of glacial acetic acid. The mixture was kept hot, short of boiling, for 20 minutes. After it had cooled, 10 ml. of distilled water was added and the reaction mixture was set aside at 0° for 24 hours. The resultant solid was isolated by filtration, washed with water and then with ether. One recrystallization from alcohol–water gave yellow needles in large part as burrs, m.p. 239° (uncor.).

Anal. Calcd. for $C_{14}H_{12}O_3N_2$: C, 65.62; H, 4.69; N, 10.93. Found: C, 65.61; H, 4.86; N, 11.08.

Cyclopentanone 2,4-Dihydroxybenzoylhydrazone.—The conditions of synthesis were as those for the benzaldehyde hydrazone. One recrystallization from alcohol–water gave colorless needles, m.p. 265° (uncor.) with decomposition.

Anal. Calcd. for $C_{12}H_{14}O_3N_2$: C, 61.53; H, 5.98; N, 11.96. Found: C, 61.62; H, 5.99; N, 12.36.

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(1) Advanced Medical Fellow of the Commonwealth Fund, 1949–1950.

(2) B. Camber, *Nature*, **163**, 285 (1949).

(3) R. Ashbel and A. M. Seligman, *Endrocrinology*, **44**, 565 (1949).

(4) R. S. Benua and E. Howard, *Bull. Johns Hopkins Hosp.*, **86**, 200 (1950).

(5) B. Camber, *Fed. Proc.*, **9**, 158 (1950).

(6) J. A. Ledogar and N. W. Jones, Jr., *Science*, **112**, 536 (1950).

(7) All analyses were performed by Mr. T. Bella, Rockefeller Institute for Medical Research, New York, N. Y.

Evidence that 1-Isopropyl-3-*t*-butylbenzene from Aluminum Chloride Alkylation of Benzene with Isobutene is Really 1,3-Di-*t*-butylbenzene

BY FRANCIS E. CONDON AND EDWARD E. BURGOYNE

That 20% of the product of aluminum chloride alkylation of benzene with isobutene was 1-isopropyl-3-*t*-butylbenzene,[1] or that this compound was formed by sulfuric acid or aluminum chloride "rearrangement" of 1,4-di-*t*-butylbenzene,[2] seems questionable because (1) treatment of the compound with aluminum chloride and benzene gave *t*-butyl-

(1) Legge, THIS JOURNAL, **69**, 2079 (1947).

(2) Legge, *ibid.*, **69**, 2086 (1947).