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The Structure of the Crystalline Adduct of Nitrosobenzene and 2,3-Dimethyl-1,3-butadiene

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The structure of the crystalline product obtained in up to an 18% yield in the reaction of nitrosobenzene with 2,3-dimethyl-1,3-butadiene in diethyl ether was determined to be the nitrone, II, by means of NMR, IR, and a series of reductions with lithium aluminum hydride and zinc–acetic acid, and by the ozonization of the reduction product.

Nitrosobenzene (NB) has been used as a dienophile in the Diels-Alder reaction with dienes. In the reaction with 2,3-dimethyl-1,3-butadiene (DMB) in diethyl ether, a white precipitate was obtained in a few minutes at from 0 °C to room temperature, in addition to the normal Diels-Alder adduct. This product was first reported by Arbuzov and his co-workers[1] although they did not give any structure, just the molar composition of 2NB: DMB. Hamer and Bernard[2] have carried out a very similar reaction of *p*-nitronitrosobenzene with DMB in nitromethane and obtained an orange precipitate at 0 °C in 15 min. They identified the product as 4,5-dimethyl-1,2-bis(*p*-nitrophenyl)-1,2,3,6-tetrahydropyridazine 1,2-dioxide. The present authors have now investigated the structure of the

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[1] Yu. A. Arbuzov, N. L. Fedyukina, V. V. Shavyrina, and R. I. Shepeleva, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, **1952**, 566; *Chem. Abstr.*, **47**, 4342f (1953).

[2] J. Hamer and R. E. Bernard, *J. Org. Chem.*, **28**, 1405 (1963).

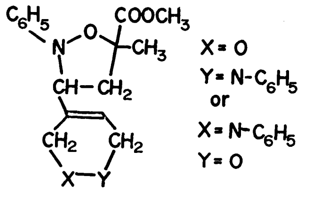
white product (**A**) of NB and DMB and determined it to have a nitrone structure.

Results and Discussion

The product, **A**, was obtained in a higher yield (up to 18%, based on 2 mol of NB and 1 mol of DMB) in diethyl ether and in a poor yield (5%) in benzene, but in nitromethane nothing but the normal Diels-Alder adduct was obtained. The thin-layer chromatography of **A** gave just one spot, indicating that the product was a pure material, not a mixture. The most striking characteristics of **A** were given in NMR, in which 18 protons, including 3 methyl protons, were found. This showed a clear difference in the phenyl and methyl region from the NMR of the Diels-Alder adduct of NB–DMB, 2-phenyl-4,5-dimethyl-3,6-dihydrooxazine (**B**), and from that of DMB–4,4′-dinitroazobenzene, 4,5-dimethyl-*N*,*N*-(4,4′-dinitrophenyl)-1,2,3,6-tetrahydropyridazine,[3] both of which contained 6 methyl protons. One methyl group per molecule of **A** means that one of the two initial methyl groups from DMB has reacted. This rules out a pyridazine dioxide structure. Eleven protons in the phenyl region were well observed in a $(CD_3)_2SO$ solution, as will be described in the Experimental section. The peak at δ 8.07 may be assigned to the aldo-nitrone structure, –CH=N(O)Ph.[4] These NMR analyses can give $C_{18}H_{18}N_2O_2$ as the molecular formula of the product; this formula is closer to the observed analysis that is $C_{18}H_{20}N_2O_2$ (2NB: DMB).

The nitrone structure was supported by the following experimental results. Irradiation with ultraviolet light yielded an isonitrile odor, reduced the strong peak at 1535 cm^{-1} assigned to N→O, and concurrently increased the peaks at 1665 and 1267 cm^{-1} attributed to C=O and $\underset{\diagdown\ \diagup}{\text{C–N}}\atop{\text{O}}$ respectively. The treatment with PCl_3 or $POCl_3$ in chloroform at room temperature overnight also reduced the peak at 1535 cm^{-1} and afforded a new peak at 1681 cm^{-1} which can be attributed to the amide group. These characteristics are generally observed in nitrone compounds.[5] One of the characteristic reactions of nitrone is the 1,3-dipolar addition to an alkene.[6] The treatment with an excess of methyl methacrylate gave colorless crystals. The NMR and elemental analyses are in good agreement with the structure of the isoxazolidine, I.

The formation of a nitrone from NB and alkene was reported long ago by Alessandri[7] in the reaction of NB with safrole and similar compounds; since then, however, very few articles have appeared.[5,8]



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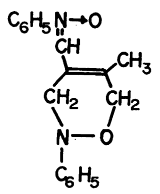

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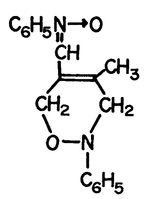

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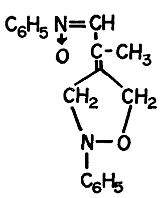

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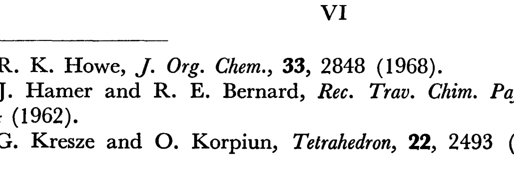
The possibility of the existence of a ring containing N–O from NB in **A** was indicated by the strong IR peaks at 1067 and 1082 cm^{-1}, since **B** has strong absorptions at 1047 and 1065 cm^{-1} attributable to the oxazine ring.[9] The existence of such a ring was supported by the fact that the reduction of **A** with zinc–acetic acid under conditions similar to those in the case of **B**[10] gave a solid whose IR showed no absorption at 1535 and markedly reduced absorptions at 1065 and 1082 cm^{-1}; subsequent treatment with acetic anhydride produced an acetylated solid whose IR had two carbonyl absorptions at 1735 (ester) and 1650 cm^{-1} (amide), the latter being remarkably decreased after hydrolysis with K_2CO_3 in methanol–water. The same behavior was observed in the case of **B**, and the IR absorptions of the acetylated product of **A** and **B** had nearly the same wave number and relative intensity. Furthermore, a structure which does not contain any cyclic N–O bond can not satisfy the elemental composition.

The double bond in **A** was detected with potassium permanganate and bromine.

All the foreging results obtained from the spectra, functional tests, and reduction suggest three probable structures, II, III, and IV, for **A**, but could not decide the correct structure. The final structure was determined by reduction with lithium aluminum hydride in tetrahydrofuran[8] and subsequently with zinc–acetic acid, followed by acetylation with acetic anhydride and the ozonization of the acetylated product in acetic acid. The colorless product thus obtained was identified as bis(*N*-acetylanilino)acetone, VIII. The acetoxyacetone, IX, was identified by gas chromatography.



VI

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[3] P. Baranger, J. Levisalles, and M. Vuidart, *C.R. Acad. Sci. Paris*, **236**, 1365 (1953).

[4] K. Koyano and H. Suzuki, *Tetrahedron Lett.*, **1968**, 1859; This Bulletin, **42**, 3306 (1969).

[5] J. Hamer and A. Macaluso, *Chem. Rev.*, **64**, 473 (1964).

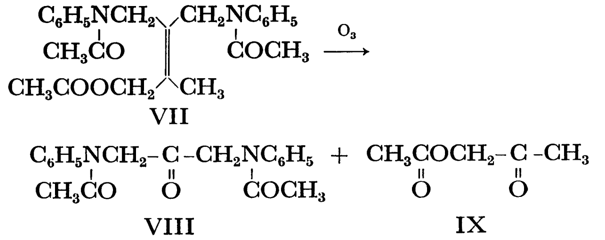
[6] R. Grashey, R. Huisgen, and H. Leitermann, *Tetrahedron Lett.*, **1960**, 9; R. Huisgen, R. Grashey, H. Hauck, and H. Seidl, *Chem. Ber.*, **101**, 2043, 2548, 2559, 2568 (1968).

[7] A. Angeli, L. Alessandri, and R. Pegna, *Atti Accad. Lincei*, **19**, I 650 (1910); L. Alessandri, *ibid.*, **24**, I 62 (1915); *Gazz. Chim. Ital.*, **51**, II 129 (1921).

[8] R. K. Howe, *J. Org. Chem.*, **33**, 2848 (1968).

[9] J. Hamer and R. E. Bernard, *Rec. Trav. Chim. Pays-Bas*, **81**, 734 (1962).

[10] G. Kresze and O. Korpiun, *Tetrahedron*, **22**, 2493 (1966).



VII

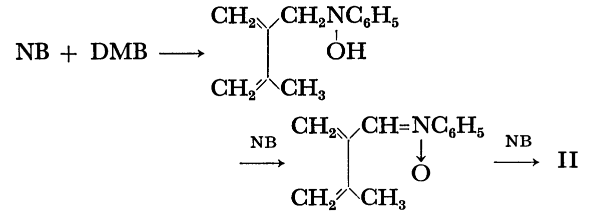
VIII

IX

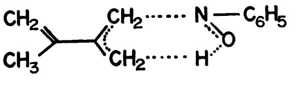
Consequently, the crystalline product, **A**, from NB and DMB was found to be the nitrone, II. This structure is also in accord with the results of catalytic hydrogenation, in which one mole of **A** consumed 6 mol of hydrogen, 3 mol for the nitrone part and the other 3 for the oxazine part.

The nitrone formation from DMB seems important because simple alkenes such as propylene, butenes, and octenes have not thus far given a nitrone.

The reaction may proceed *via* intermediate secondary hydroxylamine:[11)]



Since the first step is an "ene" reaction, the isopropenyl group may contribute to the stabilization of the transition state, facilitating the production of a nitrone in the reaction with NB:



Experimental

All the melting points were corrected.

Materials. The nitrosobenzene was prepared by the reduction of nitrobenzene;[12)] it was purified by sublimation before use. The 2,3-dimethyl-1,3-butadiene was prepared from acetone.[13,14)] A guaranteed grade of nitromethane was purchased and was used without further purification. The other organic solvents for the reactions and for recrystallization were distilled before use. The 4,5-dimethyl *N,N*-(4,4′-dinitrophenyl)-1,2,3,6-tetrahydropyridazine was prepared by the Diels-Alder addition of 2,3-dimethyl-1,3-butadiene and 4,4′-dinitroazobenzene;[3)] NMR ($(CD_3)_2SO$) δ 8.13 (d, 4, benzene ring), 7.04 (d, 4, benzene ring), 4.14 (q, J=16, 4, NCH_2), 1.67 (s, 6, CH_3).

Formation of Nitrone, II (A). A typical procedure was as follows; in a 100 ml, three-necked flask fitted with a thermometer, was placed 13.47 g (125.8 mmol) of NB and 80 ml of diethylether. After all of the nitrosobenzene had been dissolved with occasional warming, the solution was cooled to 5 °C and 9.91 g (120.5 mmol) of distilled DMB was added. The mixture was then stirred magnetically at room temperature (16 °C) for 6 hr. The white precipitate was formed within several minutes after the addition of the diene. The mixture was allowed to stand in a refrigerator overnight. The precipitate was filtered and recrystallized from ethanol or carbon tetrachloride into needles. Yield, 3.15 g (17.9% based on 2NB: DMB), mp 160.0—160.5 °C. Found: C, 73.50; H, 6.01; N, 9.29%; mol wt (cryoscopically in nitrobenzene), 294. Calcd for $C_{18}H_{20}N_2O_2$ (2NB: DMB): C, 73.00; H, 6.76; N, 9.12%; mol wt, 296; for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 10.87%; mol wt, 294. NMR ($CDCl_3$): δ 7.7—7.0 (m, 11), 4.75 (s, 2, OCH_2), 4.56 (s, 2, NCH_2), 1.86 (s, 3, CH_3). Phenyl region in $(CD_3)_2SO$: δ 8.07 (s, 1), 7.91—7.81 (m, 2), 7.58—7.47 (m, 3), 7.41—6.92 (m, 5).

The Diels-Alder adduct of NB–DMB, 2-phenyl-4,5-dimethyl-3,6-dihydrooxazine (**B**), was obtained from the filtrate; *i.e.*, the brown filtrate was concentrated and a small amount of ethanol was added. The solution was then cooled to about −20 °C. The white solid thus formed amounted to 9.34 g (40.9%) and was recrystallized from ethanol. Mp 37.5—38.5 °C; NMR ($CDCl_3$) δ 7.4—6.7 (m, 10, phenyl), 4.34 (s, 2, OCH_2), 3.67 (s, 2, NCH_2), 1.73 (s, 3, CH_3), 1.64 (s, 3, CH_3).

The reaction of 2 mol of NB with 1 mol of DMB and a nitrogen atmosphere did not increase the yield of **A**.

A similar treatment of 10.70 g (100 mmol) of NB and 8.10 g (98.8 mmol) of DMB in 60 ml of benzene gave 0.79 g (5.4%) of **A** and 5.84 g (31.1%) of **B**.

In nitromethane no precipitation occurred. A brown reaction mixture of 1.0 g (9.35 mmol) of NB and 0.80 g (9.73 mmol) of DMB in 40 ml of nitromethane was concentrated under reduced pressure, after which a large amount of diethyl ether was added. The solution was subsequently cooled to −10 °C, but no precipitate was formed. The evaporation of the solvent gave 0.33 g (18.7%) of **B**.

Measurements. The NMR spectra were recorded with a Japan Electron Optics Lab. Model JNM-4H-100 high-resolution spectrometer at 100 MHz at room temperature, with tetramethylsilane as the internal standard. The infrared spectra were recorded on a KRS-5 plate or by the KBr method with a Hitachi EPI-S2 double-beam spectrometer.

Thin-layer chromatography was carried out on silica gel (WAKOGEL B-5 UA) which was put on a glass plate (0.25 mm thick) and activated at 110 °C for 3 hr. A small drop of an about 1% chloroform solution of **A** was placed on the plate and developed with a mixture of chloroform–acetone (85 to 15 vol%) for 50 min. Coloring with sulfuric acid gave one spot with an R_f value of 0.59. A similar treatment with benzene–acetone (90 : 10 vol%) for 30 min gave one spot again, with an R_f value of 0.53.

Qualitative Tests of A. *Irradiation by Ultraviolet Light*: A small amount of **A** was placed in a quartz test tube, after which the test tube was stoppered and irradiated with a 100 W high-pressure mercury arc lamp for about half an hour. The initial white solid turned brown, and an isonitrile odor was perceived. The IR spectrum of the brown solid was recorded by the KBr pellet method.

Treatment with $POCl_3$ or PCl_3: 0.44 g of **A** was dissolved in 30 ml of chloroform, and then the mixture was ice-cooled. $POCl_3$ or PCl_3 (3 ml) was added to the cooled solution, which then turned red brown; the solution was allowed to stand overnight at room temperature. The subsequent evaporation of the solvent and an excess of the phosphorus compound gave a deep brown semisolid. It was dissolved in ethanol and cooled at −20 °C for 2 days, but no precipitate was yielded. The solution was then distilled at 60 °C under

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11) G. T. Knight and M. J. R. Loadman, *J. Chem. Soc.*, *B*, **1971**, 2107; G. T. Knight and B. Pepper, *Tetrahedron*, **27**, 6201 (1971).

12) G. H. Coleman, C. M. McCloskey, and F. A. Sturt, "Organic Syntheses" Coll. Vol. III, 668 (1955).

13) R. Adams and E. W. Adams, *ibid.*, Coll. Vol. I, 459 (1956).

14) C. F. H. Allen and A. Bell, *ibid.*, Coll. Vol. III, 312 (1955).

reduced pressure, and 0.38 g of a pale yellow liquid was obtained.

Detection of Unsaturated Group: To an acetic acid solution of **A** was added a few drops of a 0.5% potassium permanganate solution. The purple color was immediately lost. A carbon tetrachloride solution of bromine (1—2%) was added dropwise to 0.5 ml of a 1% acetic acid solution of **A**. More than two drops were needed before the color of bromine stayed.

Reaction with Methyl Methacrylate. In a 100 ml three-necked flask equipped with a condenser and a thermometer, was placed 0.50 g of **A** and an excess of methyl methacrylate (20 ml) containing a small amount of hydroquinone. The solution was then heated at 55 °C for 15 hr and at 80 °C for 2 hr. The excess methyl methacrylate was removed under reduced pressure, and the remaining pale yellow liquid was poured into petroleum ether. After a while, a white crystalline solid (I) was precipitated (0.39 g). The filtrate was concentrated, and another 0.23 g of the solid was obtained. Yield, 0.62 g (92.8%). It was recrystallized from methanol. Mp 118.0—118.5 °C. Found: C, 69.76; H, 6.29; N, 6.99%. Calcd for $C_{23}H_{26}N_2O_4$: C, 70.03; H, 6.64; N, 7.10%. NMR ($CDCl_3$): δ 7.37—6.90 (m, 10, phenyl), 4.75 (t, 1, CH), 4.39 (s, 2, OCH_2), 3.95 (s, 2, NCH_2), 3.58 (s, 3, OCH_3), 2.70 (q (two pairs), $J=13, 2$, CH_2(MMA)), 1.74 (s, 3, $CH_3C=$), 1.67 (s, 3, CH_3(MMA)).

Reductions and Acetylation. In a 100 ml Erlenmeyer flask was placed 2.14 g of lithium aluminum hydride and 60 ml of dry tetrahydrofuran; the stoppered flask was then cooled in an ice bath with magnetic stirring. To the flask was then added 3.14 g of **A** in small portions. The ice bath was removed, and the mixture was allowed to stand at room temperature for 4.5 hr with stirring. The excess of the hydride was then destroyed by adding water slowly. Diethyl ether was added to extract the product with shaking; the solution was collected by decantation. This procedure was repeated several times. The combined ether solution was dried over anhydrous sodium sulfate. The ether was removed under reduced pressure to give 2.55 g of an orange viscous liquid. About 30 ml of *n*-hexane was added to the liquid, and the mixture was heated. Because some of the liquid remained undissolved, ethanol was added with shaking until all the liquid had been dissolved. The solution was allowed to stand in a refrigerator (*ca.* 5 °C) for 2 days. The crystalline solid which formed at the bottom was removed by decantation and was found to be unreacted **A** by the measurement of the mp and IR spectra. The solution was subsequently evaporated to give 1.99 g of V.

In a 100 ml Erlenmeyer flask was placed 1.99 g of V and 25 ml of acetic acid; 6.08 g of zinc dust was then added slowly under water cooling (22 °C) and with magnetic stirring. Stirring was continued at room temperature (26 °C) for 5 hr. The mixture was then filtered, and the solid was washed with a small amount of acetic acid and then with diethyl ether. The filtrate and washings were combined, neutralized with a NaOH solution under ice cooling, and then extracted with diethyl ether. The extract was washed with water and dried over anhydrous sodium sulfate. The ether was then evaporated to give 1.42 g of VI. It was purified by distillation in a bent glass tube under highly reduced pressure. Yield, 1.28 g of a pale yellow semisolid. Found: C, 76.57; H, 7.67; N, 9.51%. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92%.

In a round-bottomed flask with a condenser was placed 1.28 g of VI, 80 ml of acetic anhydride, and about 0.2 g of anhydrous potassium acetate. The mixture was heated at 105 °C in an oil bath for 7 hr. The solution was then concentrated and neutralized with potassium carbonate. The brown crystals which came out were then dissolved in benzene. The solution was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness to give 1.76 g of crude VII. It was purified by recrystallization from *n*-hexane–diethyl ether as white crystals. Yield, 1.33 g; mp 106.0—106.5 °C. Found: C, 70.44; H, 6.61; N, 6.75%. Calcd for $C_{24}H_{28}N_2O_4$: C, 70.57; H, 6.91; N, 6.86%.

A (2.0 g) was also treated with zinc–acetic acid in a manner similar to that described above, yielding 1.1 g of a pale brown solid (softening point, 75 °C). Found: C, 77.72; H, 7.31; N, 8.51%. Calcd for $C_{18}H_{20}N_2O$: C, 77.14; H, 7.14; N, 10.00%. The subsequent acetylation of the reduction product (0.50 g) was carried out similarly, yielding 0.46 g of a brown solid (softening point, 85 °C). Found: C, 72.34; H, 6.57; N, 6.49%. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.53; H, 6.59; N, 7.69%. The hydrolysis of the amide group was carried out as follows; to a methanol solution of this solid was added an aqueous potassium carbonate solution until a slight cloudiness was observed. The mixture was then heated to boil for a few minutes, and then acidified with sulfuric acid. The white precipitate thus formed was filtered and dried *in vacuo*.

Catalytic Hydrogenation. **A** was hydrogenated over a Raney Ni or Pd–$BaSO_4$ catalyst. Raney Ni was used as an isobutyl alcohol suspension after the Raney Ni alloy (Ni: Al= 1:1) had been treated with an aqueous solution of sodium hydroxide. Pd–$BaSO_4$ was prepared from palladium chloride in hydrochloric acid and a water suspension of barium sulfate from barium hydroxide and sulfuric acid. Styrene was used in a control reaction for the calibration of the results.

In a 30 ml reaction flask was placed a stirring bar and 10 ml of isobutyl alcohol containing 0.4—0.5 g of the catalyst. About 15 mg of **A** was weighed accurately in a small aluminum basket and hung on a hook in the flask. After the complete absorption of hydrogen by the catalyst and the solvent (about 3 hr), the basket was dropped and stirring was continued for from 3 to 4 hr until the manometer showed no further change. The average absorption was 6.21 mol of hydrogen per mol of **A** (294 as mol wt). When α,*N*-diphenylnitrone and **B** were treated similarly, they absorbed 3 mol of hydrogen per mol of the sample. In the former case, a primary amine was detected in the reduction mixture by a carbylamine test and a diazo test.

Ozonization. The acetylated product, VII (0.60 g), was dissolved in 4 ml of acetic acid, and an oxygen stream containing ozone was bubbled through the solution at 0 °C. The reaction was continued for 16.5 hr until the color of the solution changed from the red-brown of the initial stage to a very pale yellow. Into the solution was then added 3.0 g of zinc dust with stirring. The solution did not change the color of KI-starch paper. A gas chromatogram of the solution, recorded by using a 75 cm column of SE-30 on celite at 176 °C, had a peak at the same retention time (1.4 min) as that of the solution containing acetoxyacetone obtained by the ozonization of acetylated **B**. The acetic acid solution was filtered, and the zinc was washed with a small amount of acetic acid and then diethyl ether. The filtrate and washings were then combined and evaporated to give a white crystalline solid, VIII. It was recrystallized from ethanol. Yield, 0.23 g (48.0%); mp 137.5—138.0 °C. Found: C, 69.72; H, 6.20; N, 8.41%. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64%. NMR ($CDCl_3$): δ 7.36 (m, 10, phenyl), 4.49 (s, 4, NCH_2), 1.91 (s, 6, CH_3). IR: 1744 (C–C=O), 1646 (N–C=O), 1418, 1382 (δ(C–H)), 1305 (ν(N–C=)), 1596, 1496, 740, 700 cm^{-1} (benzene ring).