described for the conversion of **7** into **6**. From 0.2 g of **8**, 2 ml of acetic acid, 0.2 g of sodium acetate, and a total of 6 ml of hydrogen peroxide (30%) there was obtained 0.1 g of product, mp 208–210°, the infrared spectrum of which was identical with that of **6**.

Registry No.—**1**, 16036-21-8; **2**, 17954-04-0; **3**, 17954-05-1; **4**, 17954-06-2; **5**, 6954-17-2; **6**, 17954-08-4; **7**, 17954-09-5; **8**, 17954-10-8; PhNCO, 103-71-9; PhNCS, 103-72-0; indole, 102-72-9.

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Nitrosoazomethine Derivatives. Oxidation of Amidoximes[1]

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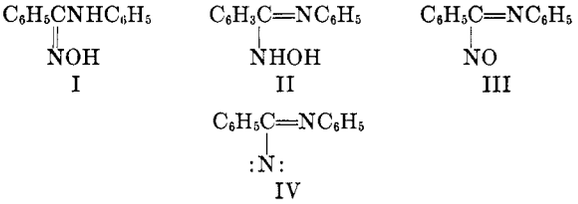
To investigate deoxygenation of nitrosoazomethine derivatives (III) as a method for the generation of azomethine nitrenes (IV), a preparation of these virtually unknown nitroso compounds[2a] by the oxidation and dehydrogenation of secondary amidoximes has been sought.

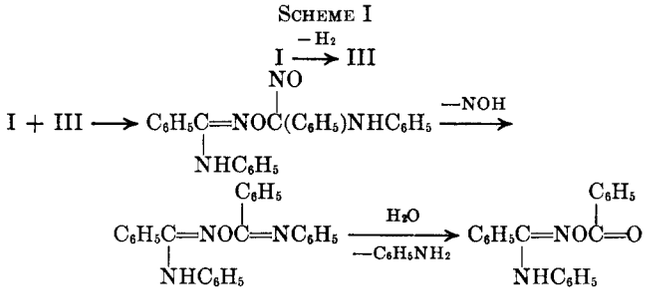


I II III IV

At room temperature or below, the oxime (I) of benzanilide reacts readily with lead tetraacetate, N-bromosuccinimide, or diethyl azodicarboxylate. The O-benzoyl derivative (V) of the oxime of benzanilide is produced in yields of 15.6, 13, and 57.7%, respectively. Its formation is consistent with an initial oxidation or dehydrogenation of the amidoxime into 1,2-diphenyl-2-nitrosoazomethine (III) and subsequent condensation between I and III followed by hydrolysis during the work-up (Scheme I).

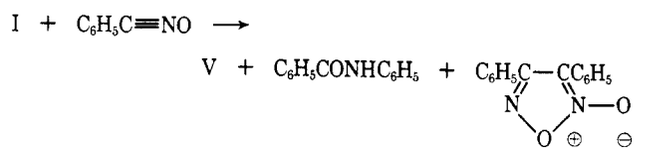
As alternative reactions leading to the formation of V, the condensation of I with either itself or benzanilide at the temperatures employed was eliminated by separate experiments which revealed no reaction in either event. A small amount of benzanilide isolated from each oxidation or dehydrogenation may be attributed to hydrolysis of anyone of the several derivatives of

SCHEME I



$C_6H_5C(NHC_6H_5)=N-$ which may be present during work-up of the reaction mixture.

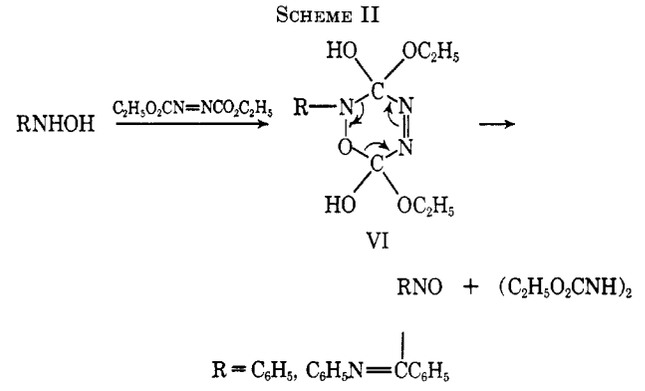
An independent synthesis of V (75.6% yield) was developed from a new reaction between benzonitrile oxide and the oxime (I). In addition to V, benzanilide



and diphenylfuroxan were formed. Although there is no direct positive evidence to support it, the possibility that benzonitrile oxide may be generated during an oxidation of I has been recognized.

Both oxidation and dehydrogenation may proceed from the tautomeric hydroxylamine (II). Facile oxidation of hydroxylamines to nitroso compounds is well established; however, dehydrogenation of the hydroxylamino function by ethyl azodicarboxylate was unknown heretofore. By this reagent phenylhydroxylamine has been dehydrogenated to nitrosobenzene in 71% yield.[2b] An explanation for the reaction is based upon a concerted or stepwise dissociation of a proposed cyclic adduct, VI (Scheme II). Ethyl hydrazocarboxylate is produced in a comparable yield of 72%. Conceivably this new preparation of a nitroso compound may be of value when carried out in the presence of other groups sensitive to oxidizing or reducing reagents. Closely related dehydrogenation of other compounds, *e.g.*, primary and secondary alcohols and primary amines and mercaptans, by diethyl azodicarboxylate has been reported.[3]

SCHEME II



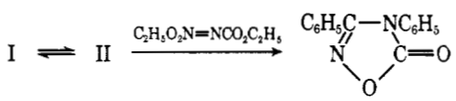
In low yield a by-product, 3,4-diphenyl-1,2,4-oxadiazolone-5 (VII), is also formed in the reaction between I $\rightleftharpoons$ II and ethyl azodicarboxylate. It was independ-

(1) Financial assistance was received from NASA Grant No. NGR 14-012-004.

(2) (a) P. A. S. Smith ["Open-Chain Nitrogen Compounds," Vol. II, W. A. Benjamin, Pasadena, California, 1966] discusses nitrosolic acids, RC(NO)=NOH (pp 356 and 384) and $CH_3C(=NOH)N(OH)N=C(NO)CH_3$ (p 92). J. H. Boyer in "Heterocyclic Compounds," R. C. Elderfield, Ed., John Wiley & Sons, Inc., New York, N. Y., 1959, Vol. 7, p 428] discusses $CH_3N(C_6H_5)N=C(CH_3)NO$. (b) Our work on the dehydrogenation of phenylhydroxylamine was carried out before a similar report appeared: E. C. Taylor and F. Yoneda, *Chem. Commun.*, 199 (1967).

(3) F. Yoneda, K. Suzuki, and Y. Nitta, *J. Amer. Chem. Soc.*, **88**, 2328 (1966).

ently established that VII is not produced under comparable conditions by the interaction of ethyl hydrazocarboxylate and I ⇌ II.



VII

Experimental Section

The oxime (I) of benzanilide was prepared by refluxing an alcoholic solution of thiobenzanilide, mp 98–100°, and equivalent amounts of hydroxylamine hydrochloride and sodium carbonate for 12 hr[4] or from an ether solution of benzonitrile oxide and a large excess of aniline on standing for 12 hr.[5] Average yields of 70% of colorless solid were obtained after recrystallization from hexane–benzene (2:1), mp 136–137°.

Addition of benzoyl chloride to I afforded the **O-benzoyl derivative (V)** as a colorless solid: mp 116–117°;[4] infrared absorption in chloroform, 3450, 3010, 1755 vs, 1620, 1610, 1580, 1510, 1455, 1400, 1260–1200, 1080, 1060 and 1025 cm^{-1}; in deuteriochloroform V gave nmr for two sets of aromatic protons at δ 8.10–7.86 and 7.60–6.69.

Oxidation of the Oxime (I) of Benzanilide. A. Lead Tetraacetate.—From a closed dropping funnel, a solution of 2.12 g (0.01 mol) of the oxime (I) in 50 ml of methylene chloride[6] was added slowly over a period of 2 hr with stirring to a solution of 4.43 g (0.01 mol) of lead tetraacetate[7] in 40 ml of methylene chloride in a closed 125-ml erlenmeyer flask in an ice bath to maintain the reaction mixture at 0°. As the addition progressed the solution turned dark and a colorless precipitate of lead acetate appeared and was removed by filtration after standing at room temperature for 12 hr, 2.9 g (0.0089 mol), 89.1%. After successively washing the dark filtrate with water and sodium bicarbonate solution, drying over magnesium sulfate, filtering, and evaporating, a dark tarry residue was obtained and chromatographed over silica gel. Following elution of an unidentified yellow oil by hexane and benzene mixtures, 100 mg (0.5 mmol) of benzanilide (5% yield) was eluted by benzene–chloroform (6:1) and recrystallized from carbon tetrachloride as colorless needles: melting point and mixture melting point with an authentic sample, 162–163°.

A very dark oil (1.0 g) was eluted with benzene–chloroform (2:3) and slowly solidified, mp 90–95°. With a Rodder streaker instrument 250 mg was deposited on a thin layer (2 mm thick) chromatographic silica gel plate. Plate development with benzene–ethyl acetate (5:1) produced eight colored bands, only one of which, R_f 0.5, consisted of an appreciable amount of material from which 80 mg of light yellow solid, mp 108–111°, was isolated and recrystallized from benzene–hexane (1:4) as colorless needles, mp 116–117°. Combined product from different tlc runs at this stage gave 248 mg (0.78 mmol) (15.6% yield) of the O-benzoyl derivative (V) of the oxime of benzanilide. Comparison with an authentic sample revealed an identical ir spectrum, an identical nmr spectrum, and undepressed mixture melting point. Hydrolysis of V in 5% sodium hydroxide produced the oxime I in 87% yield and benzoic acid in 81% yield.

B. N-Bromosuccinimide.—To a stirred solution of 1.6 g (7.5 mmol) of the oxime (I) in 50 ml of $CHCl_3$ cooled in an ice bath to 0° a solution of 1.35 g (7.5 mmol) of N-bromosuccinimide in 50 ml of carbon tetrachloride, mp 169–171°, was added dropwise as a brown color developed and colorless crystals separated. Stirring was continued for 1.5 hr at 0° and 12 hr at room temperature. Succinimide, 227 mg (2.3 mmol), 30.6%, mp 124°, was separated by filtration. Trituration with carbon tetrachloride of a dark oil obtained from the filtrate on evaporation brought about the separation of a colorless solid which after separation by filtration, was dissolved in water and treated with excess sodium carbonate. From an ether extract after drying over magnesium sulfate and evaporation, the colorless oxime (I) was recovered: mp 134–136°; yield 300 mg (1.4 mmol, 18.7%).

The carbon tetrachloride solution was extracted with 5% sodium carbonate, washed with water, dried over calcium chloride, filtered, and evaporated. A dark oil residue was chromatographed over silica gel. A small quantity of an unidentified yellow oil was eluted with benzene followed by a colorless solid which recrystallized from carbon tetrachloride as needles, mp 162–163°, 50 mg (0.25 mmol) of benzanilide (4.2% yield based on recovered I).

Benzene–chloroform (4:1) eluted a light yellow solid which recrystallized from hexane–benzene as fine colorless needles, mp 116–117°, 120 mg (0.379 mmol) of the O-benzoyl derivative (V) of the oxime of benzanilide (13% yield based on recovered I). In comparison with an authentic sample ir and nmr, respectively, were identical and a mixture melting point was undepressed.

Further elution gave a dark unidentified oil and ether–chloroform (1:1) eluted a brown solid which recrystallized from benzene–hexane as colorless I, mp 133–135°, 50 mg (0.23 mmol) (3%). Further elution with ether gave a dark tar.

C. Diethyl Azodicarboxylate.—An orange solution of 1.80 g (8.4 mmol) of the oxime (I) and 1.46 g (8.4 mmol) of diethyl azodicarboxylate[8] in 50 ml of chloroform was kept at room temperature in a 125-ml erlenmeyer flask for 12 hr as the color deepened to red-brown. Combined 2 *N* hydrochloric acid extracts were carefully neutralized by the addition of potassium hydroxide pellets. From the slightly basic solution a white solid separated from which ether extracted 0.16 g (0.75 mmol), mp 135–136°, of recovered oxime (I) (8.9%).

The chloroform layer gave a brown-red oil after drying over magnesium sulfate, filtering and evaporating. On addition of 50 ml of ether a light yellow solid separated which deposited as colorless needles, 340 mg (1.93 mmol) (25.2% based on recovered I), mp 129–131°, on recrystallization from carbon tetrachloride and identified as diethyl hydrazodicarboxylate.[8] An unidentified brown solid, 15 mg, mp 280–290°, remained insoluble in hot carbon tetrachloride and was separated.

The ether solution was chromatographed over 70 g of silica gel. A few milligrams of unidentified yellow oils were eluted by benzene–hexane. A colorless solid was then eluted with chloroform–benzene (1:6) and recrystallized from benzene–hexane as 3,4-diphenyl-1,2,4-oxadiazolone-5, mp and mmp 166–167°,[4] 35 mg (0.14 mmol), 1.9% yield. Its ir spectrum from chloroform was identical with that obtained from authentic material: 3060, 3020, 1785 vs, 1605, 1595, 1565, 1510, 1455, 1415, 1330, 1320, 1150, 1075, 1030, 1010, 1000, 975, 890, 610 cm^{-1}.

Next benzene–chloroform (6:1) eluted a colorless solid, mp 160–161°, identified as benzanilide, 75 mg (0.38 mmol, 4.9% yield). With an authentic sample the melting point was undepressed and an identical ir spectrum was obtained. Continued elution produced 0.70 g (2.21 mmol, 57.7%) of pale yellow needles, mp 112–115°, which recrystallized from benzene–hexane as colorless needles, mp 116–117°, of V. Comparison with authentic material produced identical ir spectra and an undepressed mixture melting point.

Chloroform–benzene (3:1) then eluted a brown oil, apparently a mixture of V and diethyl hydrazodicarboxylate according to tlc and ir, followed by a colorless solid, mp 130–132°, 450 mg (2.55 mmol, 33.3% yield based on recovered I), identified as diethyl hydrazodicarboxylate.[8] Ether eluted a dark red band as an unattractive black oil and ethyl acetate eluted an additional dark brown oil.

Oxidation of N-Phenylhydroxylamine by Diethyl Azodicarboxylate.—To an orange solution of 8.70 g (0.05 mol) of diethyl azodicarboxylate in 50 ml of ether externally cooled to −30° by a Dry Ice–acetone bath, a solution of 5.45 g (0.05 mol) of N-phenylhydroxylamine[9] in 50 ml of ether was added dropwise with magnetic stirring over a period of 1 hr during which time a green color rapidly developed and a colorless precipitate appeared. The solution was stirred an additional 2 hr at room temperature. Infrared absorption identical with that for an authentic sample and an undepressed mixture melting point identified the separate colorless solid as diethyl hydrazodicarboxylate, 6.4 g (0.0363 mol, 72% yield), mp 131–133°.

(4) H. Muller, *Ber.*, **19**, 1669 (1886).
(5) C. Grundmann, *J. Org. Chem.*, **31**, 157 (1966).
(6) Distilled from phosphorus pentoxide.
(7) Recrystallized from acetic acid and washed with hexane immediately before use.
(8) J. C. Kauer, "Organic Syntheses," Coll. Vol. IV, John Wiley & Sons, Inc., New York, N. Y., 1963, p 411. Commercial sample had $n^{20}D$ 1.4245.
(9) O. Kamm, "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1941, p 445.

A green solid remained after evaporation of the ether filtrate and was steam distilled. Combined ether extractions of the distillate were dried over calcium chloride, filtered, and evaporated leaving a green liquid which solidified to colorless crystals, mp 63–65° (green melt) of nitrosobenzene, 3.8 g (0.0356 mol, 71% yield). In comparison with authentic material, identical ir spectra were obtained and a mixture melting point was undepressed.

Benzonitrile Oxide and the Oxime (I) of Benzanilide.—After 12 hr at room temperature a solution of 2.12 g (0.01 mol) of the oxime (I) in 30 ml of chloroform and 0.0042 mol of benzoni rile oxide[10] in ether added dropwise became pale yellow. Combined 2 *N* hydrochloric acid extracts were carefully neutralized by the addition of potassium hydroxide pellets whereupon a colorless precipitate separated and was extracted with ether. The ether extracts were dried over magnesium sulfate, filtered, and evaporated leaving a residue of 1.60 g (0.0075 mol) of recovered I, mp 135–136°.

The ether–chloroform substrate after acid extraction was dried over magnesium sulfate, filtered, and evaporated to leave a brown oil which was chromatographed over silica gel. Hexane–benzene (3:1) eluted a colorless solid, mp 112–114°, 110 mg (0.46 mmol, 21.9%) identified as diphenylfuroxan.[11]

Next benzene–chloroform (6:1) eluted 45 mg (0.22 mmol) of benzanilide, mp 160–161° (8.8% yield based on recovered I or 5.2% based on benzonitrile oxide).

Continued elution with benzene–chloroform (6:1) removed 0.60 g (1.89 mmol) of V, mp 114–116°, as colorless needles (75.8% yield based on recovered I or 45.0% based on benzonitrile oxide). A brown band remained on top of the column.

Registry No.—I, 3488-57-1; lead tetraacetate, 546-67-8; N-bromosuccinimide, 128-08-5; diethyl azodicarboxylate, 1972-28-7; N-phenylhydroxylamine, 100-65-2; benzonitrile oxide, 873-67-6.

(10) From 0.65 g (0.0042 mol) of benzhydroxamoyl chloride and alkali according to P. Rajagopalan and B. G. Advani, *J. Org. Chem.*, **30**, 3369 (1965).

(11) A. Werner and H. Buss, *Ber.*, **27**, 2193 (1894).

Synthesis of (−)-(1*R*)-*cis*- and (+)-(1*S*)-*trans*-2-Isopropylidene-(5*R*)-N,N-trimethylcyclopentanemethylamines and Their Dideuterio Derivatives[1]

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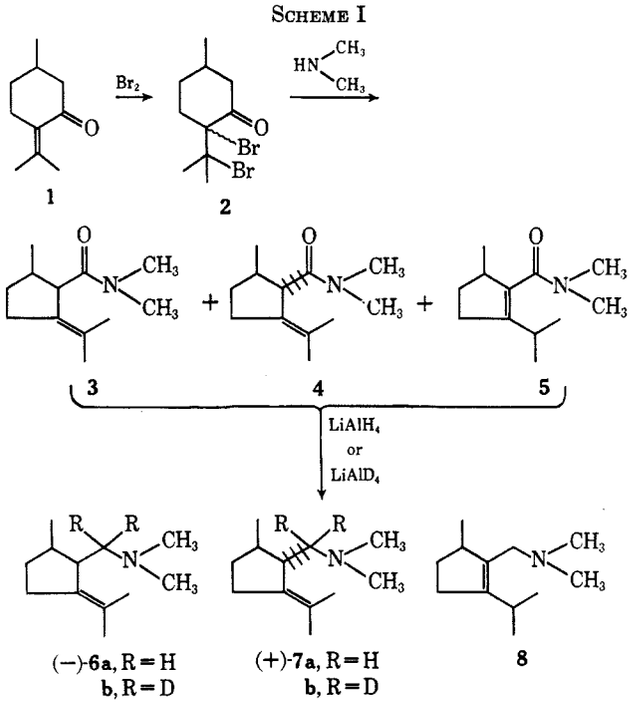
(−)-(1*R*)-*cis*-2-Isopropylidene-(5*R*)-N,N-trimethylcyclopentanemethylamine (**6a**) and (+)-(1*S*)-*trans*-2-isopropylidene-(5*R*)-N,N-trimethylcyclopentanemethylamine (**7a**) and their dideuterio derivatives (**6b** and **7b**) provided excellent model compounds for instrumental and chemical reaction comparisons with the elimination products obtained from Hofmann elimination reactions applied to α-, β-, γ-, and δ-skytanthines.[3] We now report the preparation of **6a**, **6b**, **7a**, **7b**, and **8** from (+)-pulegone (**1**) as shown in Scheme I.

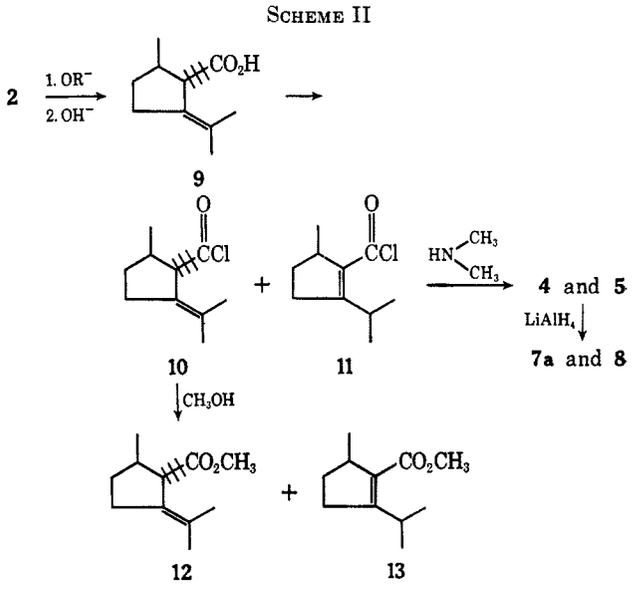
Scheme I is a useful alternate route to the earlier synthesis of **7a** and **8** shown in Scheme II.[4] The major

SCHEME I



advantages in using Scheme I are a low yield of **8** and the formation of **6a** as the major product (**6a**:**7a**:**8** = 11:7:1) in three steps from **1**. In comparison, Scheme II requires five steps, and if carried out on pure **9**, does not provide **6a** in significant yield and does produce considerable unwanted **8**. In our hands, Scheme II provided **7a**:**8** = 5:1.

SCHEME II



We used Scheme II to prepare authentic (+)-*trans* **7a** to serve as a reference compound in the assignment of stereochemistry and absolute configuration to (−)-**6a**, **6b**, (+)-**7a**, and **7b** from Schemes I and II. A stereochemical and absolute configuration assignment to (+)-*trans* **7a** had not been made. However, the data obtained from Schemes I and II are adequate to make this assignment. The major product of Favorskii rearrangement of **2** with aqueous alkali has been shown to be *cis*-pulegenic acid.[5] By analogy, the

(1) Supported by the National Science Foundation Grant GB-5607.

(2) Address correspondence and reprint requests to this author at the Department of Chemistry.

(3) H. Auda, H. R. Juneja, E. J. Eisenbraun, G. R. Waller, W. R. Kays, and H. H. Appel, *J. Amer. Chem. Soc.*, **89**, 2476 (1967).

(4) J. Wolinsky, B. Chollar, and M. D. Baird, *ibid.*, **84**, 2775 (1962).

(5) S. A. Achmad and G. W. K. Cavill, *Aust. J. Chem.*, **16**, 858 (1963).