for two days. After removal of the solvent, ether was added to the residue and the suspension stirred at room temperature. The precipitate which formed was filtered and washed with ether. The impure dipeptide esters were recrystallized from normal propanol.

N-Substituted dipeptides. Three grams of the dipeptide methyl ester was added to a mixture of 50 ml. of acetone and 50 ml. of water. To this mixture was added approximately 8 ml. of 1*N* sodium hydroxide, and the solution was stirred for 1 hr. The reaction mixture was then neutralized with 6*N* hydrochloric acid and evaporated to dryness. The residue was extracted with several 5-ml. portions of hot absolute ethanol. The sodium chloride was filtered off and the filtrate evaporated to dryness *in vacuo*. The impure dipeptide was crystallized from propanol. In the case of benzoyl-*β*-alanyl-*l*-histidine, isopropanol was used as the solvent for crystallization.

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DEPARTMENT OF CHEMISTRY
ADELPHI COLLEGE
GARDEN CITY, N. Y.

DEPARTMENT OF CHEMISTRY
BROOKLYN COLLEGE
BROOKLYN, N. Y.

Reactions of Nitric Oxide. Synthesis of Salts of *p*-*N*-Nitrosohydroxylamino-*N'*-nitroso Substituted Anilines

MORRIS J. DANZIG[1] AND SALVATORE R. RICCITIELLO

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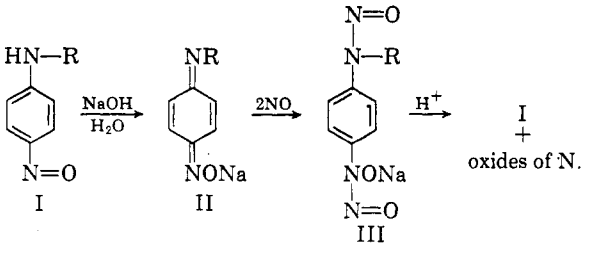
In a previous paper[2] we described the addition of nitric oxide to salts of quinonedioximes. We have extended this study to include the salts of quinonemonoxime imines (nitroso anilines).

In basic solution *p*-nitrosoanilines, I, tautomerize to quinone monoxime imines, II. This is analogous to the nitrosophenol–quinone monoxime system. The extent of formation of II is dependent on the solvent system and the concentration of the base. Under normal conditions I appears to have considerable stability as indicated by its green nitroso color and the large amount of base necessary to obtain a good conversion to III without impurities.

When a solution of I was dissolved in an excess of aqueous sodium hydroxide and treated with nitric oxide at 60 p.s.i., two moles of gas were absorbed to give the corresponding *p*-*N*-nitrosohydroxylamino-*N*-nitroso-*N'*-substituted anilines III. Using a methanol–methoxide system, a four molar absorption of nitric oxide was observed and an unstable diazonium compound was isolated and identified by infrared spectrum. The formation of this diazo compound is due to addition of nitric oxide to the nitroso group.[3,4]

Acidic decomposition of III (R = C_6H_5) resulted in the liberation of oxides of nitrogen, and 54% of I was isolated. Using precipitation techniques analogous to those of cupferron, the silver salt of III (R = C_6H_5) was prepared and converted to a methyl derivative. Because of reasons described previously[2] the exact structure of this compound is unknown.



EXPERIMENTAL

Apparatus. This reaction may be carried out in any type of stirred stainless steel pressure vessel or a Paar low pressure hydrogenator modified with a stainless steel tank and gauge. All tubing and valves are stainless steel. The nitric oxide was 99+ % pure (Olin Mathieson), and was passed through a stainless steel Kuentzel bomb (1 ft. long, 2 in. i.d.) packed with sodium hydroxide. Care must be taken that gas inlet and exit ports do not become clogged.

General Procedure. The *p*-nitroso-*N*-substituted aniline was dissolved in sodium hydroxide solution, filtered, placed in a reaction bottle, and cooled. The reaction bottle was placed in the Paar apparatus and the oxygen was removed by evacuation and flushing with oxygen-free nitrogen. The bottle was finally evacuated. Nitric oxide was admitted and the shaker started. When the absorption of gas was completed, the nitric oxide was removed by flushing with nitrogen and evacuation with a water aspirator. There is considerable foaming and care must be taken not to clog the exit ports. The product was isolated by filtration, washed, and dried. Compounds so prepared are listed in Table I.

Decomposition of III (R = C_6H_5). To 10 ml. of a stirred solution of concd. hydrochloric acid, 1.0 g. of III was added slowly. There was considerable foaming, and this was allowed to subside before additional III was added. One hour after all of the III was added, the solution was diluted with water and made alkaline with sodium hydroxide. Carbon dioxide was passed into this solution until precipitation was complete, and 0.70 g. of black solid, m.p. 110–113°, was isolated. The solid was redissolved in 20 ml. of 10% sodium hydroxide, filtered, and re-treated with carbon dioxide. The brown solid was collected by filtration, washed, and dried to give 0.38 g. (54%) of I (m.p. 141.5–143.5°). Infrared spectrum and mixed melting point were identical to that of an authentic sample.

Methyl ether of III (R = C_6H_5). To a filtered solution of 1.4 g. of III in 100 ml. of 50% aqueous methanol was added 0.90 g. of silver nitrate in 50 ml. of distilled water. The red precipitate was collected on a filter, washed, and dried to give 2.0 g. of the silver salt. To a suspension of this salt in 50 ml. of methanol was added 2 ml. of methyl iodide, and the mixture was stirred for 0.5 hour. The precipitate was collected on a filter and washed with methanol. Water was added to the

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TABLE I

Nitrosoanilines	Solvent	Formula	Carbon[a] Calcd.	Carbon[a] Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Metal Calcd.	Metal Found	Yield, %
N,N'-Diphenylethylenediamine	H_2O	$C_{14}H_{12}N_3O_6Na_2$	38.68	38.62	2.8	3.3	25.81	25.71	10.48	9.96	48
N-Phenyl-1-naphthylamine	H_2O	$C_6H_{11}N_4O_2Na$	60.90	61.23	3.34	3.58	—	—	6.3	6.78	24
β-Anilinopropionic acid sodium salt	H_2O	$C_9H_8N_4O_5Na_2$	36.25	36.08	2.69	3.09	18.79	19.08	15.42	15.31	42
2-Nitrodiphenylamine	H_2O	$C_{12}H_8O_5N_5Na$	44.30	44.87	2.49	2.84	—	—	7.0	6.78	40
Ethyl-1-naphthylamine	CH_3OH	$C_{12}H_{11}N_4O_3Na$	—	—	—	—	—	—	8.14	8.48	18
N-Ethyl-*m*-toluidine	H_2O	$C_9H_{11}N_4O_3Na$	—	—	—	—	—	—	9.34	9.43	23
N-Phenyl	H_2O	$C_{12}H_9N_4NaO_3$	51.43	51.53	3.24	3.58	20.0	19.93	8.21	8.09	58
N-Methyl	H_2O	$C_7H_7N_4NaO_3$	38.54	38.86	3.24	3.44	25.68	25.59	—	—	—
							Chlorine				
N-2-Chloroalkylaniline	CH_3OH	$C_9H_8N_4O_3ClNa$	—	—	—	—	12.85	12.43	8.25	8.08	31

[a] Galbraith Laboratories, Knoxville, Tenn.

filtrate until the cloud point was reached; the mixture was cooled, and 0.55 g. of crystalline solid was isolated. An analytical sample was prepared by recrystallization from methanol, m.p. 142–144° dec.

Anal. Calcd. for: $C_{13}H_{12}N_4O_3$; C, 57.35; H, 4.44; N, 20.58. Found: C, 57.40; H, 4.22; N, 20.48.

HUGH LORD LABORATORY
LORD MANUFACTURING CO.
ERIE, PA.

The Preparation of Some *N*-Alkylsydnones Containing a Functional Group in the Side Chain

F. H. C. STEWART

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Most investigations on the sydnones (I) have been concerned with derivatives in which the substituent R is an aromatic or heteroaromatic moiety.[1,2] *N*-Alkylsydnones, on the other hand, have been studied less extensively,[3] and the main interest in them has been their cleavage by strong acid to give otherwise rather inaccessible alkylhydrazines.[4,5]

A number of *N*-alkylsydnones have also been examined for biological activity. Brookes and Walker[7] prepared several *N*-methylsydnones (I. R = CH_3, R' = alkyl) as possible antagonists of the natural amino acids, while Daeniker and Druey[8] found that *N,N'*-ethylenebissydnone (II) exhibited slight antitumor activity. It has also been claimed that various simple sydnones possess ascaricidal action.[9]

The present work describes the preparation of several *N*-alkylsydnones of structure III, in which a short aliphatic side chain is terminated by a functional group R. Sydnones of this type have not been reported previously and could be of interest as potential biologically active agents, or as precursors of such agents.

The sydnones (III) have been obtained by the normal synthetic procedure,[10] that is, nitrosation

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