[CONTRIBUTION FROM THE ROHM AND HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION]

The Synthesis of Nitrosoalkane Dimers

BY WILLIAM D. EMMONS

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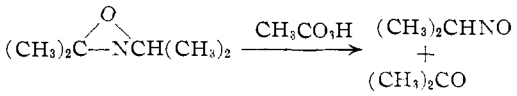
General methods for synthesis of nitrosoalkane dimers through use of oxazirane intermediates have been established. An improved preparation of cyclopropylamine is also described.

Satisfactory general methods for preparation of nitrosoalkanes or their dimers have not been previously described in the literature, and consequently their chemistry has not been investigated in any detail. The most suitable synthesis of these materials has been based on the vapor phase pyrolysis of alkyl nitrites.[1] However, this method is rather limited by the special apparatus required and by the rather small amounts of products which can be prepared conveniently. Furthermore, the

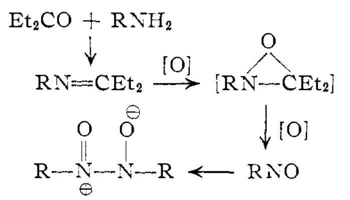
$$R_1R_2R_3ONO \xrightarrow{\Delta} R_1R_2CO + R_3NO$$

purification of nitrosoalkanes obtained in this manner is frequently tedious, and the method also is dependent on the availability of the parent nitrite. Other procedures which have been described for preparation of nitrosoalkanes involved the reaction of chlorine and nitric oxide with hydrocarbons in the presence of ultraviolet light[2] and the controlled oxidation of *t*-alkyl primary amines.[3] Both of these methods, however, suffer from limited applicability as well as from the very low yields obtained.

In connection with a general investigation of the chemistry of oxaziranes,[4] it was observed that these heterocycles react smoothly with one equivalent of peracetic acid to give fairly good yields of nitrosoalkane dimers. Thus 2-isopropyl-3,3-dimethyloxazirane was converted at room temperature in methylene chloride solvent to 2-nitrosopropane dimer in 33% yield. It subsequently was found that it was more convenient to prepare the nitrosoalkane by direct oxidation of an imine with two equivalents of peracetic acid. In most cases the crude imine was obtained by condensation of diethyl ketone with the appropriate amine in benzene solution using azotropic distillation to remove the water. Oxidation of the crude imine usually yielded the nitrosoalkane dimer in 30–90% yield. The reaction appears to be quite general and a summary of the compounds obtained along with the pertinent physical constants may be found in Table I. The availability of convenient laboratory procedures for preparation of the dimers should make the chemical investigation of these rather interesting compounds feasible.

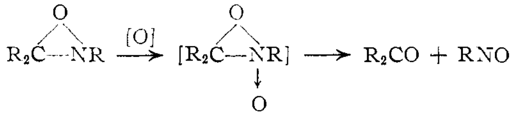


$$\overset{O}{(CH_3)_2C{-}NCH(CH_3)_2} \xrightarrow{CH_3CO_3H} (CH_3)_2CHNO + (CH_3)_2CO$$



With the exception of 2-nitrosoöctane dimer all of the compounds were solids. The structure and purity of the products was established by microanalytical data, by a comparison with the physical constants of those nitrosoalkane dimers prepared by other methods and finally by the intense ultraviolet absorption characteristic of nitrosoalkane dimers at 290 to 300 mμ.[1] Also the absence of any of the isomeric oximes in the products was confirmed by examination of the infrared spectra of these compounds which showed no absorption in the hydroxyl or imine regions. Nitrosocyclohexane also was characterized by its quantitative conversion to cyclohexanone oxime after heating in aqueous methanolic sulfuric acid.

The precise nature of this oxidation is uncertain. One possible formulation of the reaction is, however



$$\overset{O}{R_2C{-}NR} \xrightarrow{[O]} [\overset{O}{R_2C{-}\underset{\overset{\downarrow}{O}}{N}R}] \longrightarrow R_2CO + RNO$$

The nitrosoalkanes rapidly dimerize and only in the case of phenylnitrosomethane was any of the tautomeric oxime isolated. The stability of nitrosoalkane dimers has been commented on previously[5] and is, of course, the reason why oximes are not formed to any major extent in this reaction. Indeed the stability of some of the dimers was quite remarkable. Thus it was possible to obtain accurate measurements of the molecular weights of nitrosocyclohexane and 1-nitrosoöctadecane dimers ebullioscopically in acetone suggesting that very little if any dissociation of these compounds takes place in boiling acetone. It is also worth pointing out that the dimers obtained from this reaction are *trans* since the ultraviolet spectra of these compounds in solvents such as ethanol were not time dependent over several hour periods.[1]

Efforts to extend the imine oxidation to synthesis of *t*-nitrosoalkanes such as 1,1-dimethylnitrosoethane were not successful. The major reason for this was the extreme volatility of the monomeric *t*-nitrosoalkanes. The dimers are in this case relatively unstable because of steric factors and in solution the monomeric blue nitrosoalkanes are formed and codistil with even relatively low boiling organic solvents. Thus 1,1,3,3-tetramethylnitrosobutane codistilled with ethyl ether. It was found, however, that these nitrosoalkanes could be

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[1] B. G. Gowenlock and J. Trotman, *J. Chem. Soc.*, 1670 (1956).

[2] E. Müller and H. Metzger, *Ber.*, **88**, 165 (1955).

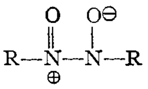
[3] E. Bamberger and R. Seligman, *ibid.*, **36**, 685 (1903).

[4] W. D. Emmons, THIS JOURNAL, **79**, 5739 (1957).

[5] H. T. J. Chilton and B. G. Gowenlock, *J. Chem. Soc.*, 3174 (1954).

TABLE I

PREPARATION OF NITROSOALKANE DIMERS,



$$R{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\oplus}{N}}{-}\overset{\overset{\displaystyle O^{\ominus}}{|}}{N}{-}R$$

R	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Yield, %	M.p., °C.	λ_{max}, mμ	ϵ_{max}
$(CH_3)_2CH$[1]	49.30	49.02	9.66	9.53	19.15	19.02	33	53–55	295	9300
$C_6H_5CH_2$[2]	69.40	69.39	5.83	5.60	11.56	11.40	37	116–118	296	8700
n-$C_{12}H_{25}$	72.31	72.56	12.64	12.83	7.02	6.96	37[a]	76–78	291	9740
n-$C_{18}H_{35}$	76.26	76.58	13.16	13.33	4.94	5.02	60	87–89	290	9100
C_6H_{12}[2]	63.68	64.01	9.80	9.86	12.38	11.86	68	86–88	297	10300
$CH_3(CH_2)_5CH(CH_3)$	67.09	67.43	11.97	12.00	9.78	9.74	83[b]	.....	295	9240
$C_6H_5CH_2CH_2$	71.09	71.80	6.71	6.80	10.36	9.83	71[b]	98–100	294	9100
$(CH_3)_3C$[3]	55.15	55.10	10.41	10.40	16.07	15.70	86	83–84	..	...
$(CH_3)_3CCH_2C(CH_3)_2$	67.09	66.83	11.97	11.90	9.78	9.60	87	63–64	..	...

[a] Recrystallized from hot ligroin. [b] Recrystallized from petroleum ether at −78°, $n^{20}D$ 1.4565.

prepared conveniently by reaction of aqueous alkaline hypobromite solutions with the corresponding hydroxylamines which are readily available from hydrolysis of 2-*t*-alkyl-3-phenyloxaziranes.[4] The nitrosoalkanes produced in the reaction dimerized at room temperature and the crystalline dimers

$$R_3CNHOH \xrightarrow{Br_2,\ OH^{\ominus}} R_3CNO$$

were filtered off in excellent yield from the aqueous solutions.

Finally it should be mentioned that it was possible to prepare nitrosocyclohexane dimer in 44% yield by oxidation of cyclohexylamine with two equivalents of peracetic acid. While the yield of product *via* the oxazirane was considerably higher, the availability of cyclohexylamine makes the direct oxidation a rather attractive synthesis for this nitrosoalkane. The oxidation of other amines was not a suitable preparative method for nitrosoalkanes, however. Also efforts to obtain nitrosocyclopropane from either cyclopropylamine or imines derived from cyclopropylamine were unsuccessful. A superior preparation of cyclopropylamine[6] based on the reaction of methyl cyclopropyl ketoxime and trifluoroacetic anhydride was, however, developed and is described in the Experimental section. The use of trifluoroacetic anhydride for Beckman rearrangements giving water-soluble amides apparently has not been reported previously and would appear to offer some advantages over other reagents.

Experimental

2-Isopropyl-3,3-dimethyloxazirane was prepared by reaction of peracetic acid with N-isopropylideneisopropylamine[7] as previously described.[4] There was obtained a 62% yield of the oxazirane, b.p. 60° (40 mm.), $n^{20}D$ 1.4072.

Anal. Calcd. for $C_6H_{13}NO$: C, 62.57; H, 13.10; N, 12.16. Found: C, 62.51; H, 13.00; N, 12.02.

2-Nitrosopropane Dimer.—To 20 ml. of methylene chloride was added fairly rapidly at 0° with efficient stirring 3.0 ml. (0.11 mole) of 90% hydrogen peroxide and one drop of sulfuric acid catalyst.[8] Acetic anhydride (13.5 g., 0.132 mole) then was added dropwise over a 10-minute period with continued cooling. The resulting mixture was stirred 15 minutes at room temperature and the clear solution so obtained was treated with 0.5 g. of sodium acetate to neutralize the acid catalyst. The resulting peracetic acid was added dropwise to an ice-cooled solution of 11.5 g. (0.1 mole) of 2-isopropyl-3,3-dimethyloxazirane in 30 ml. of methylene chloride. The mixture was allowed to stand overnight at room temperature. It was then washed with 100 ml. of cold 20% aqueous ammonia and the organic layer was dried over magnesium sulfate. Evaporation of the volatile solvent left an oil which was dissolved in 40 ml. of ether. The ethereal solution was chilled at − 78° for 2 hr. giving 2.4 g. (33%) of crystalline 2-nitrosopropane dimer, m.p. 53–55° (lit.[1] m.p. 52°).

α-Nitrosotoluene Dimer.—A solution of 53.5 g. (0.5 mole) of benzylamine and 60.4 g. (0.7 mole) of diethyl ketone in 200 ml. of benzene was azeotropically distilled until water removal was complete. The volatile solvent was evaporated at reduced pressure giving the crude imine in essentially quantitative yield. A solution of peracetic acid was then prepared as previously described from 30 ml. of methylene chloride, 6 ml. (0.22 mole) of 90% hydrogen peroxide, one drop of sulfuric acid and 27 g. (0.264 mole) of acetic anhydride. After neutralization with 0.5 g. of sodium acetate the peracid was added dropwise to 17.7 g. (0.1 mole) of the imine in 50 ml. of methylene chloride cooled in an ice–salt-bath. The reaction vessel was then kept at 0° overnight and subsequently washed with 200 ml. of ice-water and 200 ml. of cold 20% aqueous sodium bicarbonate. The organic extract was dried and the volatile solvent evaporated. To the mushy solid so obtained was added 25 ml. of ethanol and the mixture was kept in the refrigerator overnight. Filtration yielded 4.5 g. (37%) of fairly pure α-nitrosotoluene dimer, m.p. 114–115°. After recrystallization from acetone the product melted at 116–118° (lit.[2] m.p. 117°). The ethanol filtrate on evaporation gave 7.4 g. (60%) of oil which on the basis of its infrared spectrum was largely benzaldoxime.

1-Nitrosoöctadecane Dimer.—A solution of peracetic acid was prepared from 25 ml. of methylene chloride, 5.5 ml. (0.2 mole) of 90% hydrogen peroxide, one drop of sulfuric acid and 24.5 g. (0.24 mole) of acetic anhydride. After neutralization with 0.5 g. of sodium acetate this reagent was dripped into 33.8 g. (0.1 mole) of the crude imine obtained from condensation of *n*-octadecylamine and diethyl ketone in 50 ml. of methylene chloride at 0°. When addition was complete the reaction mixture was allowed to stand overnight at room temperature. A voluminous precipitate separated and was collected on a filter. The product was washed with a little cold methylene chloride, and there was obtained 25.1 g. (70%) of fairly pure 1-nitrosoöctadecane dimer, m.p. 82–84°. This was recrystallized from hot ligroin and melted at 87–89°. The characteristic blue color was observed in hot ligroin during the recrystallization, but it faded at room temperature.

Nitrosocyclohexane Dimer.—A peracetic acid solution was prepared in the usual way from 50 ml. of methylene chloride, 12.2 ml. (0.45 mole) of 90% hydrogen peroxide, one drop of sulfuric acid and 55 g. (0.54 mole) of acetic anhydride. This solution was then added dropwise to 19.8 g. (0.2 mole) of cyclohexylamine in 75 ml. of methylene chloride cooled in an ice–salt-bath. The mixture was allowed to stand overnight during which time the cooling bath

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[6] J. D. Roberts and V. C. Chambers, THIS JOURNAL, **73**, 3177 (1951).

[7] D. G. Norton, V. E. Hawry, F. C. Davis, L. J. Mitchell and S. A. Ballard, *J. Org. Chem.*, **19**, 1034 (1954).

[8] All preparations of peracetic acid were carried out behind a safety screen. For the hazards involved in handling 90% hydrogen peroxide, see E. S. Shanley and F. P. Greenspan, *Ind. Eng. Chem.*, **39**, 1536 (1947).

reached room temperature. The product was then washed with 200 ml. of water, 100 ml. of cold 15% aqueous ammonia and 100 ml. of 10% sulfuric acid. The organic layer was dried and evaporated at reduced pressure leaving an oily solid. This product was triturated with 50 ml. of cold ethanol and collected on a filter. There was obtained 10.0 g. (44%) of nitrosocyclohexane dimer, m.p. 119–120°. Recrystallization from ethanol raised the melting point to 120–121° (lit.[2] m.p. 120°). The same product was obtained in 68% yield by oxidation of the imine derived from condensation of cyclopentanone and cyclohexylamine.

1,1-Dimethylnitrosoethane Dimer.—A solution of 19.2 g. (0.12 mole) of bromine, 12 g. (0.3 mole) of sodium hydroxide and 75 ml. of water was stirred with ice cooling, and 8.9 g. (0.1 mole) of *t*-butylhydroxylamine[4] in 25 ml. of water was added dropwise over a 5-minute period. A blue color immediately developed. The mixture was stirred 2 hr. and the crystalline dimer was then collected on a filter. It was washed with water and dried to yield 7.5 g. (86%) of the nitrosoalkane dimer. The compound melted at 83–84° (lit.[3] m.p. 76°) to form a blue liquid.

Cyclopropylamine.—A solution of 190 g. (1.92 moles) of methyl cyclopropyl ketoxime in 400 ml. of 1,2-dimethoxyethane was heated to reflux (82°). At this temperature with stirring, 282 ml. (2.2 moles) of trifluoroacetic anhydride was added dropwise over a 1-hr. period. The mixture was then heated under reflux for one additional hour. The volatile solvents were distilled off at atmospheric pressure by slowly raising the pot temperature to 150°. The residue was then cooled and stirred in an ice-bath while a solution of 300 g. of potassium hydroxide in a mixture of 600 ml. of ethylene glycol and 300 ml. of water was added. The mixture so obtained was distilled overnight in a Todd column. The methylamine was vented off, and the cyclopropylamine was distilled over an 8-hr. period. This distillation was facilitated by the use of an automatic still-head which only collected product boiling below 51°. There was obtained in this manner 84.5 g. (77%) of cyclopropylamine, b.p. 49-51°.[6]

PHILADELPHIA, PENNA.

[CONTRIBUTION FROM THE FATTY ACID PRODUCERS' COUNCIL OF THE ASSOCIATION OF AMERICAN SOAP AND GLYCERINE PRODUCERS, INC., AND THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

Phosphorus Derivatives of Fatty Acids. III.[2] Trialkyl α-Phosphonates

BY BERNARD ACKERMAN,[3,4] ROSE MARIE CHLADEK[3] AND DANIEL SWERN

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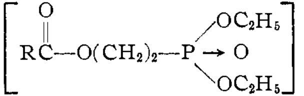
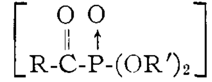
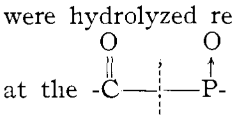
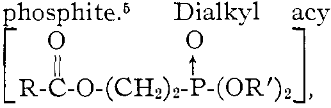
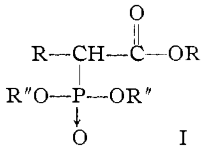
Triethyl α-phosphonates have been prepared in 60–96% yield from triethyl phosphite and the ethyl ester of the appropriate C_4–C_{18} straight chain α-bromocarboxylic acid (equation 1: R = C_2H_5, C_4H_9, $C_{10}H_{21}$, $C_{12}H_{25}$, $C_{14}H_{29}$ and $C_{16}H_{33}$). Mixed trialkyl α-phosphonates (formula I) have been similarly prepared in 30–90% yield from the appropriate trialkyl phosphite (trimethyl phosphite, tri-*n*-butyl phosphite or tri-*n*-hexyl phosphite) and alkyl ester of the α-bromocarboxylic acid (R′ = CH_3, C_2H_5, *n*-C_4H_9, *n*-C_6H_{13} and 2-ethylhexyl in formula I). The α-phosphonates are colorless, odorless, thermally stable liquids, insoluble in water and soluble in organic solvents. In contrast to the isomeric diethyl acyloxyethylphosphonates  $\left[RC(=O)—O(CH_2)_2—P(\to O)(OC_2H_5)_2\right]$ previously reported, the triethyl α-phosphonates are resistant to hydrolysis with 0.1 *N* hydrochloric acid, but they are converted to the tribasic α-phosphonocarboxylic acids (I, R′, R″ = H) when refluxed for 18–24 hr. with 20–35% hydrochloric acid. With dilute base in ethanol, the carboxylic ester group is preferentially hydrolyzed yielding α-diethylphosphonocarboxylic acids (I, R′ = H, R″ = C_2H_5).

In the first two papers of this series,[5,6] we described the preparation and properties of phosphorus-containing fatty acid derivatives which hydrolyzed in such a way as to separate the parent fatty acid from the phosphorus-containing group. Thus, dialkyl acylphosphonates  $\left[R\text{-}C(=O)\text{-}P(\to O)\text{-}(OR')_2\right]$ were hydrolyzed readily under neutral conditions at the  $\text{-}C(=O)\text{—}\vdots\text{—}P(\to O)\text{-}$ bond to regenerate the fatty acid and a fragment believed to be a dialkyl phosphite.[5] Dialkyl acyloxyethylphosphonates  $\left[R\text{-}C(=O)\text{-}O\text{-}(CH_2)_2\text{-}P(\to O)\text{-}(OR')_2\right]$, although considerably more resistant to hydrolysis under neutral conditions than the dialkyl acylphosphonates, hydrolyzed readily under mildly acidic conditions at the carboxylic ester group to give the fatty acid and dialkyl hydroxyethylphosphonate.[6]

An objective of the present investigation was to prepare phosphorus derivatives of fatty acids which on hydrolysis would yield a product having phosphorus attached to the fatty acid chain. The trialkyl α-phosphonates (I) are such a class of compounds. They were also of considerable interest because it would be possible to study the



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effect of variations in R, R′ and R″ on numerous physical and chemical properties under investigation. A few low molecular weight trialkyl α-phosphonates are described in the literature,[7] but aside from them there are no reports on the systematic preparation and study of the physical and chemical properties of trialkyl α-phosphonates.

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[1] A laboratory of the Eastern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article not copyrighted.

[2] Presented at the Fall Meeting of the American Chemical Society, September 8–13, 1957, New York, N. Y. Paper II is reference 6.

[3] Fellow of the Fatty Acid Producers' Council of the Association of American Soap and Glycerine Producers, Inc.

[4] Advance Solvents and Chemical Co., New Brunswick, N. J.

[5] B. Ackerman, T. A. Jordan, C. R. Eddy and D. Swern, THIS JOURNAL, **78**, 4444 (1956).

[6] B. Ackerman, T. A. Jordan and D. Swern, *ibid.*, **78**, 6025 (1956).

[7] G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 160–161.