[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

New Reactions Involving Alkaline Treatment of 3-Nitroso-2-oxazolidones. II

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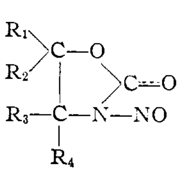
RECEIVED DECEMBER 5, 1953

A number of 4-substituted-3-nitroso-2-oxazolidones have been prepared. The products resulting from their treatment with alkali are listed in Table I. A mechanism for the reactions is proposed.

In a previous paper[2] the behavior of a number of 3-nitroso-2-oxazolidones (I) (in which R_1 and R_2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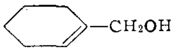
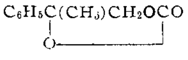
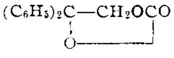
were alkyl and/or phenyl and R_3 and R_4 were hydrogen), on treatment with alkaline reagents was described. The products formed consisted of aldehydes, ketones, acetylenes and vinyl ethers. Inasmuch as good yields were generally obtained, these reactions were of interest because of their possible synthetic use. Mechanistically, these reactions were also of interest because they were postulated to involve an aliphatic carbonium ion having unsaturation at the electron deficient carbon. Such an intermediate does not appear to have been previously postulated.

In this paper we report on the behavior of 3-nitroso-2-oxazolidones (I) in which R_1 and R_2 are hydrogen and R_3 and R_4 are alkyl and/or phenyl. The results are summarized in Table I. In addition some work was done on the thermal decomposition of four nitrosoöxazolidones. This work is summarized in Table II.

TABLE I

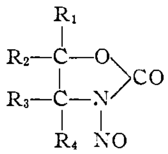
PRODUCTS FROM ALKALINE TREATMENT OF NITROSOOXAZOLIDONES[a]

	R_3	R_4	Products	Yield, %
I	$-(CH_2)_5-$		$C_6H_{11}CHO$	52^b
				45^c
II	CH_3	CH_3	$(CH_3)_2CHCHO$	38^b
			$CH_2{=}C(CH_3)CH_2OH$	54^c
			$(CH_3)_2C{=}CHOCOOCH_3$ ^{d}	29^c
			$CH_2{=}C(CH_3)CH_2OCOOCH_3$	33^f
III	C_2H_5	H	$CH_3CH_2CH_2CHO$	35^b
			$CH_3CH{=}CHCH_2OH$	46^c
			$CH_3CH_2CH{=}CHOCOOCH_3$ ^{d}	31^e
			$CH_3CH{=}CHCH_2OCOOCH_3$	40^f
IV	C_6H_5	H	$C_6H_5CHOHCH_2OH$	77^g
			$C_6H_5COCH_3$	12^b
			$C_6H_5CH(OC_2H_5)CH_2OCOOC_2H_5$ ^{d}	75^g
			$C_6H_5C(OC_2H_5){=}CH_2$	14^e
V	C_6H_5	CH_3	 $C_6H_5C(CH_3)CH_2OCO$	59^h
			$C_6H_5CH(CH_3)CHO$	22^b
VI	C_6H_5	C_6H_5	 $(C_6H_5)_2C-CH_2OCO$	51^h
			$(C_6H_5)_2CHCHO$	12^b
			$(C_6H_5)_2COHCH_2OH$	22^g

[a] See Experimental part for detailed description of identification and/or isolation of products. [b] Isolated as pure 2,4-dinitrophenylhydrazone. [c] Estimated by measuring catalytic hydrogen absorption after reduction of the aldehyde with lithium aluminum hydride. [d] Reaction carried out in anhydrous methanol or ethanol using the corresponding sodium alkoxide. [e] Hydrolyzed to the aldehyde or ketone and isolated as pure 2,4-dinitrophenylhydrazone. [f] Hydrolyzed and isolated as unsaturated alcohol after removal of aldehyde as 2,4-dinitrophenylhydrazone. [g] Isolated as reasonably pure compound by rectification. [h] Isolated by rectification in a not so pure form, see Experimental.

TABLE II

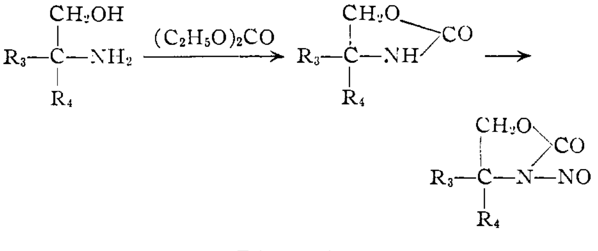
THERMAL DECOMPOSITION OF NITROSOÖXAZOLIDONES



R_1	R_2	R_3	R_4	Products	Yield, %
CH_3	C_6H_5	H	H	Parent oxazolidone	70^a
				$CH_3-C{\equiv}C-C_6H_5$	26^b
C_6H_5	C_6H_5	H	H	Parent oxazolidone	22^a
				$C_6H_5-CO-CH_2-C_6H_5$	10^c
				$(C_6H_5)_2CH-CHO$	56^c
H	H	C_6H_5	C_6H_5	Parent oxazolidone	87^a
H	H	CH_3	CH_3	Parent oxazolidone	4^a

[a] Isolated by crystallization. [b] Isolated as 2,4-dinitrophenylhydrazone of propiophenone after hydration. [c] Isolated as 2,4-dinitrophenylhydrazones directly from reaction mixture and separated by chromatography.

The oxazolidones required for nitrosation were prepared by treating the appropriate aminoalcohol with ethyl carbonate.[3] The nitrosations were carried out as previously described.[2]



Discussion

A. Alkaline Decomposition.—The results obtained previously in the alkaline treatment of 5,5-disubstituted-3-nitroso-2-oxazolidones were explained by the mechanism[2]

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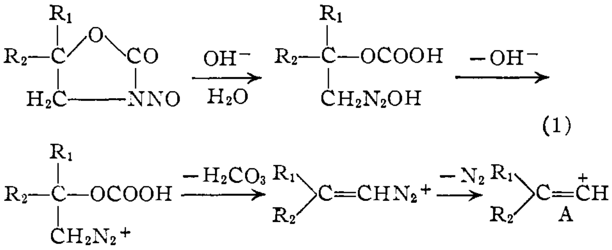
[1] The material herein presented was taken from the Ph.D. thesis of W. M. E., The Ohio State Univ., 1952.

[2] M. S. Newman and A. Kutner, THIS JOURNAL, **73**, 4199 (1951). Since the appearance of this paper a series of papers on the behavior of nitrosolactams has appeared. Some aspects of this chemistry have interest in connection with the proposed mechanism. See R. Huisgen and J. Reinertshofer, *Ann.*, **575**, 174, 197 (1952).

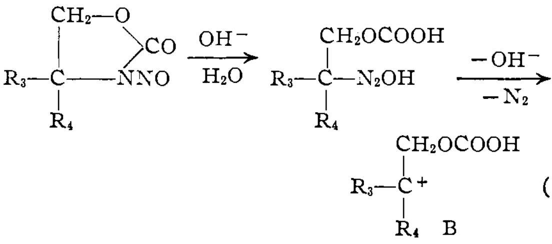
[3] A. H. Homeyer, U. S. Patent 2,399,118 (1946); *C. A.*, **40**, P4084 (1946).



(1)

No attempt was made to time proton addition or removal or to time the various steps. However, it was postulated that the base-catalyzed elimination of carbonic acid took place before the loss of diazonium nitrogen to yield the unsaturated carbonium ion, A. All of the products actually found could be accounted for by the further reactions of A.

In the study herein described, that of the decomposition of 4,4-disubstituted-3-nitroso-2-oxazolidones, different products were expected because it is impossible to have an unsaturated carbonium ion such as A since no hydrogen is available in the 4-position to participate in a base-catalyzed elimination of carbonic acid. However, the products obtained may be accounted for by a similar mechanism as



(2)

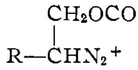
This mechanism is similar to that suggested for the alkaline decomposition of N-nitroso-N-cyclohexylurethan.[4]

The first step involves the opening of the oxazolidone ring by an attack of the base at the carbonyl carbon. The acyclic nitrosamine formed rapidly tautomerizes to an hydroxyazo compound which in turn assumes diazonium character. The loss of nitrogen from the diazonium hydroxide gives rise to the carbonium ion B. Throughout these changes it should again be stated that the timing of proton addition and removal is ignored.

The carbonium ion B can react in several ways to yield the products actually found. (1) It may eliminate a proton from the carbon bearing the bicarbonate group, to yield an enol bicarbonate which upon hydrolysis yields aldehydes, R_3R_4CHCHO (note compounds I, II, III, V and VI, Table I). (2) It may eliminate a proton from R_3 or R_4 to yield an allylic bicarbonate which upon hydrolysis yields allylic alcohols (note compounds I, II and III, Table I). (3) It may react with water in the solvent to yield a glycol, $R_3R_4COHCH_2OH$, after hydrolysis of the carbonate linkage. When the reaction medium is anhydrous a mixed dialkyl carbonate-ether is produced (see compound IV, Table I). (4) It may react internally with the bicarbonate group (or the corresponding anion) to yield a cyclic carbonate (note compounds V and VI, Table I).

It is noteworthy that in those cases where the carbonium ion B has only alkyl groups attached to the electron deficient carbon the products of reaction are those in which the ion reacts by loss of a proton. However, when one of the groups attached is phenyl the products of reaction are for the most part those in which the carbonium reacts by addition of some oxygenated group.

Two cases, namely III and IV, were included in which there remained a hydrogen on carbon 4. Here the hypothetical diazonium ion has the structure C and this could decompose into a carbonium ion of type A or B.

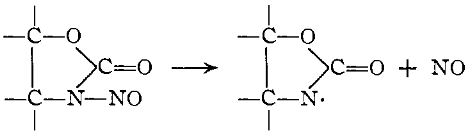


$$\begin{array}{l} \mathrm{CH_2OCOOH} \\ \quad | \\ \mathrm{R{-}CHN_2^+} \end{array}$$

C

The results indicate that when R is ethyl (compound III) the nitrogen is lost before any base-catalyzed elimination of carbonic acid takes place. The products are those formed by loss of a proton from the carbonium ion of type B. However, when R is phenyl (compound IV) the base-catalyzed elimination of carbonic acid to form a carbonium ion of type A takes place to an appreciable (12–14%) extent. It is noteworthy that the mechanisms operative seem to be little influenced by the change in solvent from aqueous alcoholic to absolute alcoholic. This is concluded from examination of the products formed under the varying conditions. The successful competition of the base-catalyzed elimination of carbonic acid from C when R is phenyl can be rationalized by pointing out that the hydrogen on carbon 4 should be more acidic in the phenyl compound IV than in the ethyl compound III.

B. Thermal Decompositions.—During the course of this and the previous[2] work it was noted that several nitrosoöxazolidones were unstable. It was therefore deemed of interest to examine the products of thermal decomposition. Accordingly four nitroso compounds were heated to decomposition. The results are summarized in Table II. In every case except one, the major product was the parent oxazolidone, in spite of the fact that precautions were taken to ensure the absence of any solvent of recrystallization. In these experiments no solvent was included and it should be interesting to carry out similar decompositions in the presence of solvents capable of participating in free radical reactions, especially in view of the reported substituted pyrrolidyl aromatics resulting from the pyrolysis of nitrosopyrrolidone in aromatic solvents.[5] The reaction leading to the recovery of parent oxazolidone probably involves a free radical dissociation similar to that postulated by Huisgen for nitrosopyrrolidone. Further work on thermal decomposition is under way.



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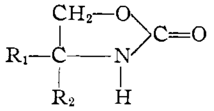
[4] F. W. Bollinger, F. N. Hayes and S. Siegel, THIS JOURNAL, **72**, 5592 (1950). See also H. R. Nace and M. H. Gollis, *ibid.*, **74**, 5189 (1952), for semipinacolic deamination studies.

[5] R. Huisgen and J. Reinertshofer, *Ann.*, **572**, 197 (1952).

TABLE III

2-OXAZOLIDONES



R_1	R_2	Yield, %	M.p., °C.	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
CH_3	CH_3[a]	86	55.6–56.4	$C_5H_9O_2N$						
H	C_2H_5[a]	74	Oil[b]	$C_5H_9O_2N$						
$-(CH_2)_5-$		89	81.0–82.0	$C_8H_{13}O_2N$					9.0	9.1[8c]
H	C_6H_5	92	136.8–137.8	$C_9H_9O_2N$					8.6	8.5[8c]
CH_3	C_6H_5	82	79.6–80.0	$C_{10}H_{11}O_2N$	67.8	67.7[8w]	6.2	6.5[8w]		
C_6H_5	C_6H_5	98	178.4–178.8	$C_{15}H_{13}O_2N$	75.3	75.5[8w]	5.4	5.5[8w]		

[a] A. H. Homeyer, U. S. Patent 2,399,118 (1946); *C. A.*, **40**, 4084 (1946). [b] Purified by low temperature crystallization from ether, $n^{20}\text{D}$ 1.4638.

Experimental

All melting points up to 200° were taken using Anschütz total immersion thermometers. No further correction was applied. Melting points over 200° were taken on a Fisher electrically heated block.

Aldehydes and ketones were determined as follows: a calculated excess of a 0.15 *M* stock solution of 2,4-dinitrophenylhydrazine in methanol (0.6 *N* with sulfuric acid) was added to the material to be analyzed and the mixture was refluxed gently for 30 minutes. After standing at least four hours in the cold, the derivative was collected and recrystallized. With known pure compounds this method afforded 85–95% yields of 2,4-dinitrophenylhydrazones.

Both 2-amino-2-methyl-1-propanol[6] and 2-amino-1-butanol[6] were commercial products.

1-Aminocyclohexanemethanol.—A mixture of 129 g. (1 mole) of nitrocyclohexane,[7] 36 g. of paraformaldehyde (1.2 moles of CH_2O) and 10 ml. of 30% methanolic potassium hydroxide was refluxed for 15 minutes and held at 30–40° for 24 hours. After acidification distillation afforded 148 g. (93%) of 1-nitrocyclohexanemethanol, b.p. 117–123° at 5 mm., $n^{20}\text{D}$ 1.4840, of sufficient purity for reduction. The analytical sample boiled at 113–114° at 3 mm., $n^{20}\text{D}$ 1.4853, d^{20}_{20} 1.1662.

Anal.[8c] Calcd. for $C_7H_{13}O_3N$: N, 8.8. Found: N, 8.7.

The 1-nitrocyclohexanemethanol (47.7 g., 0.3 mole) in absolute ethanol (125 ml.) was hydrogenated at 80° over Raney nickel at 1000 p.s.i. Reduction was complete within 30 minutes whereupon distillation afforded 31 g. (80%) of 1-aminocyclohexanemethanol,[9] b.p. 111–114° at 13 mm.

2-Amino-2-phenyl-1-ethanol.—To a slurry of 20.0 g. (0.5 mole) of finely powdered lithium aluminum hydride in 300 ml. of dry tetrahydrofuran there was added portionwise 60 g. (0.28 mole) of ethyl α-aminophenylacetate hydrochloride while stirring vigorously. After refluxing the mixture for one hour it was treated with 50 ml. of water. There was obtained 33 g. (85%) of 2-amino-2-phenyl-1-ethanol,[10] b.p. 104–106° at 1 mm. which solidified to a white solid, m.p. 48.0–49.5°. The amine reacted rapidly with carbon dioxide. The hydrochloride melted at 144–146°.

2-Amino-2-phenyl-1-propanol.—By reduction of α-aminohydratropic acid[11] with lithium aluminum hydride as described above, the amino alcohol was obtained as a colorless liquid, b.p. 103–105° at 1 mm., which solidified on standing to a colorless waxy solid, m.p. 49.0–50.0°.

Anal. Calcd. for $C_9H_{13}ON$: C, 71.5; H, 8.6. Found[8w]: C, 71.7; H, 8.6.

The hydrochloride melted with decomposition at 173–174°.

2-Amino-2,2-diphenylethanol.—In the best of several experiments a mixture of 45.6 g. (0.2 mole) of benzilic acid and 35.7 g. (0.3 mole) of thionyl chloride was allowed to stand at room temperature with occasional shaking for eight hours. The excess thionyl chloride was removed (without heating) at reduced pressure. The material was cooled (Dry Ice–acetone) and 50 g. (*ca.* 3 moles) of liquid ammonia was added. After one hour in the cold the excess ammonia was permitted to evaporate. Concentrated hydrochloric acid (100 ml.) was added and the mixture was evaporated to dryness on a steam-plate. The solids were dissolved in water (250 ml.) and pyridine was added dropwise until the material was neutral to congo red whereupon an additional 20 ml. (0.2 mole) of pyridine was added. The powdery white solid was filtered after standing several hours, and washed with water and alcohol. In this manner 29.5 g. (65%) of α-aminodiphenylacetic acid[12] was obtained, m.p. 244–246° dec.

For analytical and identification purposes, small quantities of the acid were esterified both with diazomethane and with methanol–hydrogen chloride, the products being identical. The methyl ester hydrochloride, recrystallized from methanol, melted at 202.0–203.5°.

Anal. Calcd. for $C_{15}H_{16}NO_2Cl$: N, 5.0; Cl, 12.8. Found[8c]: N, 5.1; Cl, 12.8.

The solid amino acid (23.1 g., 0.1 mole) was added portionwise to a slurry of 8 g. (0.21 mole) of lithium aluminum hydride in 250 ml. of tetrahydrofuran. After standing overnight, the mixture was hydrolyzed with 30 ml. of water and filtered. On concentrating the filtrate 14.5 g. (66.8%) of 2-amino-2,2-diphenylethanol precipitated in the form of white prisms, m.p. 132.4–133.2°.

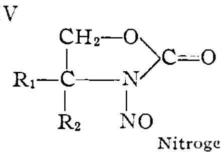
Anal. Calcd. for $C_{14}H_{15}ON$: C, 78.9; H, 7.0. Found[8w]: C, 78.7; H, 7.0.

The Oxazolidones.—These compounds were obtained by heating the appropriate aminoalcohol with diethyl carbonate[3] using sodium methoxide catalysis (see Table III).

The Nitrosoöxazolidones.—Nitrosation of the oxazolidones was effected as previously described[3] (see Table IV).

TABLE IV

3-NITROSO-2-OXAZOLIDONES



R_1	R_2	Yield, %	M.p., °C.	Empirical formula	Nitrogen,[d] % Calcd.	Nitrogen,[d] % Found[8]
CH_3	CH_3	70[a]	95.8–96.4	$C_5H_8O_3N_2$	19.4	19.1
H	C_2H_5	84[a]	Oil[c]	$C_5H_8O_3N_2$		[d]
$-(CH_2)_5-$		99[b]	107.5–108.5	$C_8H_{12}O_3N_2$	15.2	14.9
H	C_6H_5	80[b]	83.8–84.6	$C_9H_8O_3N_2$	14.6	14.0
CH_3	C_6H_5	98[b]	84.6–86.0	$C_{10}H_{10}O_3N_2$	13.6	13.6
C_6H_5	C_6H_5	91[b]	100.2–101.0	$C_{15}H_{12}O_3N_2$		

[a] Prepared with aqueous nitrous acid. [b] Prepared with nitrosyl chloride. [c] B.p. 110° at 1 mm. with decomposition; $n^{20}\text{D}$ 1.4720. [d] Analyses were usually low because of instability of nitroso compound.

Decomposition of Nitrosoöxazolidones by Aqueous Base.—Solutions of the nitrosoöxazolidones in aqueous alcoholic

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(6) We wish to acknowledge the generous gift of these products from the Commercial Solvents Corporation, New York, N. Y.

(7) We wish to acknowledge the generous gift of a sample of nitrocyclohexane from the du Pont Co.

(8) Analyses marked c by Clark Microanalytical Laboratories, Urbana, Ill.; marked g by Galbraith Laboratories, Knoxville, Tenn.; marked w by R. L. Warfel, O.S.U.

(9) H. Adkins and H. R. Billica, THIS JOURNAL, **70**, 3121 (1948).

(10) A. Kotz and H. Schneider, *J. prakt. Chem.*, [2] **90**, 137 (1914).

(11) A. McKenzie and G. W. Clough, *J. Chem. Soc.*, **101**, 390 (1912).

(12) H. Biltz and K. Seydel, *Ann.*, **391**, 215 (1912); S. A. Setlur, A. N. Kothare and V. V. Nadkarny, *J. Univ. Bombay*, **12A**, 68 (1943).

solvents (10–30% water) were treated dropwise with a solution of 5–10% aqueous potassium carbonate (mainly for purely aliphatic members) or with 20–50% potassium hydroxide. The evolution of nitrogen was always vigorous and immediate, especially with the dimethyl and ethyl compounds. The reaction was usually complete (theoretical amount of nitrogen collected) in one to four minutes. Less than the theoretical amount of base was added in all cases. After reaction was complete, the mixtures were made acid with hydrochloric acid. The individual analyses for products are described below.

4,4-Dimethyl-3-nitroso-2-oxazolidone.—The product of the decomposition of 14.4 g. (0.1 mole) of the nitroso compound with several drops of a saturated potassium carbonate solution, after neutralization, was diluted to 100 ml. with methanol. A 20% aliquot, treated with 2,4-dinitrophenylhydrazine stock solution as described above, yielded 1.91 g. (38%) of the isobutyraldehyde derivative, m.p. 180–181° (no depression with an authentic sample[13] m.p. 182–183°), accounting for 38% of the total product. By fractionating a 60-ml. aliquot in a 5–10 plate column, it was possible to remove most of the methanol and isobutyraldehyde (60–70°) before separating a fraction distilling as an azeotrope with water from 71–80°. Redistillation of the salted-out organic layer yielded 1.8 g. of β-methallyl alcohol, b.p. 100–115°, $n^{20}\text{D}$ 1.4211. That it was β-methallyl alcohol was shown by converting it to an α-naphthylurethan, m.p. 79.6–80.6° (from petroleum ether), which showed no depression with an authentic sample[14] m.p. 79.8–80.8°.

Anal. Calcd. for $C_{15}H_{15}O_2N$: N, 5.8. Found[8c]: N, 5.9.

In order to determine the amount of β-methallyl alcohol more accurately 5 g. (0.028 mole) of the nitroso compound in 30 ml. of ether was decomposed with 0.5 ml. of 50% potassium hydroxide by shaking for several minutes. The ether layer was dried (anhydrous sodium sulfate) and treated with excess lithium aluminum hydride (1 molar in ether) to reduce the aldehyde. On hydrogenating over platinum oxide at 60 p.s.i. 0.015 mole of hydrogen was absorbed, indicating 0.015 mole (54%) of the unsaturated alcohol. Distillation of the product afforded 1.9 g. (91%) total yield of isobutyl alcohol, b.p. 105–108°, $n^{20}\text{D}$ 1.3955.

4-Ethyl-3-nitroso-2-oxazolidone.—When the product from decomposing 2 g. (0.014 mole) of the oily nitroso compound was treated with 2,4-dinitrophenylhydrazine, there was obtained 1.23 g. (35%) of the *n*-butyraldehyde derivative, m.p. 122.0–122.5°, showing no depression with an authentic sample[13] m.p. 122–123°.

After decomposing 5.0 g. (0.035 mole) of the nitrosooxazalidone in 30 ml. of ether with 0.5 ml. of 50% potassium hydroxide, the ether layer was dried and distilled through a 24-inch packed column. Ether and *n*-butyraldehyde were removed after which there was obtained 1.0 g. (40%) of crotyl alcohol, b.p. 112–120°, $n^{20}\text{D}$ 1.4195. It formed an α-naphthylurethan, m.p. 91.2–91.8° (reported[15] m.p. 89°). A *p*-nitrophenylurethan was prepared, m.p. 81–82°, which showed no depression with an authentic sample.[16]

Anal. Calcd. for $C_{11}H_{12}N_2O_4$: N, 11.9. Found[8c]: N, 12.1.

In order to estimate the crotyl alcohol, the ether solution of products from 14.4 g. (0.1 mole) of nitroso compound in 50 ml. of ether treated with 5 ml. of 50% potassium hydroxide was dried and treated with lithium aluminum hydride. On hydrogenating the resulting solution at 60 p.s.i. over platinum oxide, 0.046 mole of hydrogen (indicating 46% crotyl alcohol) was absorbed. Distillation afforded 6.0 g. (86% total yield) of *n*-butyl alcohol, b.p. 117–120°, $n^{20}\text{D}$ 1.3998. The α-naphthylurethan, m.p. 70–71°, showed no depression of melting point when mixed with an authentic sample[17] m.p. 71°.

1-Nitroso-1-aza-3-oxaspiro(4,5)decan-2-one.—A solution of 9.2 g. (0.05 mole) of the nitroso compound in 75 ml. of methanol was stirred while 50% potassium hydroxide was added dropwise. After neutralization, a 20% aliquot yielded 1.48 g. (52% of the total) of the 2,4-dinitrophenylhydrazone of hexahydrobenzaldehyde, m.p. 169.0–169.5°, showing no depression with an authentic sample,[2] m.p. 168.5–169.5°. Distillation of a 50% aliquot afforded 1-cyclohexenylmethanol, b.p. 170–185°, which afforded a phenylurethan, m.p. 95.0–96.6° (reported[18] m.p. 96°).

When 2.50 g. (0.0136 mole) of the nitroso compound in 50 ml. of ether was decomposed, treated with lithium aluminum hydride and subsequently hydrogenated over platinum oxide as described above, 0.0061 mole of hydrogen was absorbed indicating 45% of the unsaturated alcohol, 1-cyclohexenylmethanol. The product, after removal of the ether, yielded 2.8 g. (74%) of the α-naphthylurethan of cyclohexanemethanol, m.p. 109.0–110.2°, showing no depression with an authentic sample[19] m.p. 110–110.5°. The authentic cyclohexanemethanol, b.p. 182–183°, was prepared in 95% yield by the lithium aluminum hydride reduction of ethyl hexahydrobenzoate. In high dilution the latter compound has an unusually offensive odor to some people and should therefore be handled with extreme precautions.

Anal. Calcd. for $C_{18}H_{21}O_2N$: N, 5.0. Found[8c]: N, 5.0.

4-Phenyl-3-nitroso-2-oxazolidone.—This nitroso compound (14.4 g., 0.075 mole) in 100 ml. of aqueous alcohol was decomposed by the dropwise addition of 20% potassium hydroxide. After neutralization a 20% aliquot afforded 0.54 g. (12%) of the 2,4-dinitrophenylhydrazone (recrystallized from ethanol) of acetophenone, m.p. 238–240°, showing no depression with an authentic sample[20] m.p. 239–240°. From a 30% aliquot, the ethanol was distilled and the residue taken into ether. On drying the ether solution and cooling it to −70°, there precipitated 2.33 g. (77%) of 1-phenyl-1,2-ethanediol which melted from 65–67°. When mixed with an authentic sample,[21] m.p. 65–67° (prepared in 70% yield by reducing mandelic acid with lithium aluminum hydride) no depression of m.p. was noted.

4-Methyl-4-phenyl-3-nitroso-2-oxazolidone.—A solution of 16.5 g. (0.08 mole) of the nitroso compound in 140 ml. of methanol was decomposed with 10% aqueous potassium hydroxide. After neutralization of a 10% aliquot there was obtained 0.55 g. (22%, after recrystallization from ethanol) of the 2,4-dinitrophenylhydrazone of hydratropaldehyde, m.p. 134–135°, which showed no depression when mixed with an authentic sample[22] m.p. 135–136°.

Anal. Calcd. for $C_{15}H_{14}O_4N_4$: N, 17.8. Found[8g]: N, 17.8.

The solvent was removed from a 25% aliquot and the residue was distilled at reduced pressure. Hydratropaldehyde (0.5 g., 15%) was collected from 100–107° at 7 mm. before a fraction which distilled from 125–130° at 2–3 mm., $n^{20}\text{D}$ 1.5165. Very little residue remained. The infrared spectrum of the distillate indicated two carbonyl compounds, one of which was hydratropaldehyde (absorption at 5.80 μ). As neither Girard's reagent P[23] nor oxidation with hydrogen peroxide was effective in removing the aldehyde, the material was fractionated through a 12-inch packed column to yield 4.2 g. of a colorless oil, b.p. 90–96° at 0.5 mm., $n^{20}\text{D}$ 1.5131. This material had a sharp absorption band at 5.60 μ (ethylene carbonate absorbs at 5.52 μ), a shoulder at 5.80 μ (probably due to hydratropaldehyde), and did not contain nitrogen or decolorize bromine. Saponification afforded 2-phenyl-1,2-propanediol,[24] m.p. 42–44°, in high yield. Analysis of the crude oil indicated a C:H:O ratio of 3:3:1 which would lead to a formula $C_9H_9O_3$ instead of the expected $C_{10}H_{10}O_3$ for 4-methyl-4-phenyldioxolane-2-one (the cyclic carbonate of 2-phenyl-1,2-propanediol). The 4.2 g. above mentioned represents a 59% yield of product if it consisted entirely of the dioxolane. A pure sample of the latter was synthesized (we wish to thank Mr. Roger Addor for this preparation) as follows.

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[13] E. H. Huntress and S. P. Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 46.

[14] We are indebted to the Shell Development Corporation for a sample of β-methallyl alcohol.

[15] K. Hess and W. Weistrow, *Ann.*, **437**, 256 (1924).

[16] Crotyl alcohol was prepared in 26% yield (polymers formed) by reduction of ethyl crotonate with lithium aluminum hydride.

[17] Reference 13, p. 436.

[18] E. P. Kohler, M. Tishler, H. Potter and H. T. Thompson, This Journal, **61**, 1057 (1939).

[19] Reference 13, p. 466.

[20] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 264.

[21] T. Zincke, *Ann.*, **216**, 293 (1883).

[22] Obtained from Van Ameringen-Haebler, Inc., Elizabeth, N. J.

[23] A. Girard and G. Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

[24] G. Darzens, *Compt. rend.*, **139**, 1216 (1904).

A solution of 5.0 g. of 2-phenyl-1,2-propanediol,[25] a small amount of potassium carbonate and 4.3 g. (10% excess) of diethyl carbonate in 10 ml. of benzene was refluxed gently into a small packed column. After three hours about 10 ml. of distillate, b.p. near 67°, had been collected. The product was distilled to yield 5.5 g. (93%) of colorless 4-methyl-4-phenyldioxolane-2-one, b.p. 135–137° at 1–2 mm., n^{24}_{D} 1.5215. A portion of this product was taken up in dry ether and passed through a column of alumina in order to remove traces of unreacted glycol (indicated by slight OH absorption on infrared analysis). Redistillation afforded pure dioxolanone, n^{25}_{D} 1.5202 with a sharp absorption at 5.60 μ.

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.4; H, 5.7. Found (crude): C, 66.2; H, 5.4. Pure: C, 67.8; H, 5.6.

4,4-Diphenyl-3-nitroso-2-oxazolidone.—In order to determine the quantity of aldehyde produced, 1.00 g. (0.0037 mole) of the nitroso compound in 10 ml. of 95% ethanol was decomposed with 3 drops of 50% potassium hydroxide. After neutralization the solution was treated as described above with 2,4-dinitrophenylhydrazine whereupon a mixture of derivatives was formed, m.p. 135–190°. To separate, they were dissolved in benzene and adsorbed on 100 g. of chromatographic alumina in an eight inch column. Elution with benzene afforded first 0.17 g. (12%) of a yellow-orange derivative, m.p. 154.0–155.5°, showing no depression with an authentic sample of diphenylacetaldehyde 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $C_{20}H_{16}N_4O_4$: C, 63.8; H, 4.3. Found[8w]: C, 63.9; H, 4.4.

There was also eluted 0.08 g. of an orange solid, m.p. 245.5–247.0°, which was not identified.

Decomposition of 2.00 g. (0.074 mole) of the nitroso compound in a similar manner led to a residue (from evaporation) which was washed with water. Recrystallization from petroleum ether (30–60°) afforded 0.35 g. (22%) of 1,1-diphenyl-1,2-ethanediol,[26] m.p. 119–121°, showing no depression when mixed with an authentic sample, m.p. 120–121° (prepared in 80% yield by the reduction of benzilic acid with lithium aluminum hydride). On distillation, the residue from the above petroleum ether filtrate afforded 0.9 g. of an oil, b.p. 200–235° at 1 mm. Infrared examination revealed strong absorption at 5.60 μ characteristic for the 5-membered ring carbonyl in cyclic carbonates. On the basis of a molecular weight of 240 for 4,4-diphenyldioxolane-2-one, the 0.9 g. represents a 51% yield. Oxidation of the dioxolanone with potassium dichromate in acetic acid led to benzophenone, showing that the carbon skeleton had remained intact during decomposition of the nitroso compound.

Decomposition of 3-Nitroso-2-oxazolidones with Anhydrous Alkali. 4,4-Dimethyl-3-nitroso-2-oxazolidone.—To a cooled (0°) solution of 4.1 g. (0.028 mole) of the nitroso compound in 30 ml. of absolute methanol, there was added several drops of a freshly prepared solution of sodium methoxide from 0.1 g. of sodium in 3 ml. of absolute methanol. The reaction was extremely vigorous. The volume of the reaction mixture was adjusted to 40 ml. with methanol and aliquots were used for the investigation of the products.

No formation of an aldehyde or ketone derivative was noted, even on prolonged reaction of a 25% aliquot under the usual acid conditions with 2,4-dinitrophenylhydrazine. This also indicated that no vinyl ether had been formed, for such a material would be expected to hydrolyze and yield the aldehyde derivative.

Most of the methanol was distilled from a 75% aliquot (0.021 mole) and the remaining material was taken into ether, washed free of base, dried and distilled to yield 1.8 g. of an oil, b.p. 135–155°, n^{20}_{D} 1.4170. A polymeric residue of 0.5 g. remained.

The distillate was unsaturated to bromine in carbon tetrachloride solution. The infrared absorption spectrum revealed a strong carbonyl band at 5.70 μ characteristic for the carbonyl band of diethyl carbonate. The remainder of the 1.8 g. of distillate was refluxed for one hour with 10% methanolic potassium hydroxide. After treatment with 2,4-dinitrophenylhydrazine reagent (0.015 mole) there was obtained (after recrystallization from ethanol) 1.5 g. (29%) of isobutyraldehyde 2,4-dinitrophenylhydrazone, m.p. 179.5–180.5°, showing no depression with an authentic sample.[13]

The filtrate from this preparation was taken into ether, dried and distilled to yield 0.4 g. (33%) of β-methallyl alcohol, b.p. 112–120°, from which was prepared an α-naphthylurethan, m.p. 79–80°, showing no depression with an authentic sample.

These observations indicate that in the original reaction mixture resulting from the alkaline treatment of the nitrosoöxazolidone there were at hand at least 29% of methyl 2-methyl-1-propenyl carbonate, $CH_3{-}C(CH_3){=}CH{-}O{-}CO{-}OCH_3$ and 33% of methyl β-methallyl carbonate, $CH_2{=}C(CH_3){-}CH_2OCOOCH_3$.

On this basis, the 1.8 g. of distillate represented 67% of the products. As these compounds might be expected to polymerize easily, the 0.5 g. of residue (19%) was probably derived from them.

4-Ethyl-3-nitroso-2-oxazolidone.—A solution of 4.1 g. (0.028 mole) of the oily nitroso compound in 25 ml. of absolute methanol was decomposed with sodium methoxide, as described in the preceding section. The mixture was diluted to 30 ml. and the solution used in the following experiments.

A 33% aliquot was treated with 2,4-dinitrophenylhydrazine reagent but no derivative was formed.

A 33% aliquot was refluxed with 10 ml. of a 20% methanolic potassium hydroxide for one hour. It was acidified, filtered and treated with 2,4-dinitrophenylhydrazine reagent. There was obtained (31%) of n-butyraldehyde 2,4-dinitrophenylhydrazone,[18] m.p. 120–122°.

The filtrate was concentrated somewhat and the oily residue taken into ether, washed and dried. On distillation, 0.26 g. (40%) of crotyl alcohol, b.p. 114–120°, was collected. From this material there was prepared an α-naphthylurethan, m.p. 88–89°, showing no m.p. depression with an authentic sample.[16]

4-Phenyl-3-nitroso-2-oxazolidone.—The nitroso compound (4.0 g., 0.021 mole), dissolved in 20 ml. of absolute ethanol, was decomposed by the dropwise addition of a solution of sodium ethoxide in absolute ethanol. The reaction was considerably milder than was the case with the aliphatic analogs. Most of the alcohol was removed and the residue was taken into ether. After washing and drying, the ether was removed and the material distilled at reduced pressure to yield 0.43 g. (fraction I) of a liquid, b.p. 85–100° at 10 mm., which decolorized bromine without liberating hydrogen bromide, and 3.75 g. (fraction II) of a colorless oil, b.p. 122–126° at 2 mm., n^{20}_{D} 1.4912. When half of fraction I was treated with a neutral saturated solution of 2,4-dinitrophenylhydrazine in ethanol no derivative was formed. The remaining 50%, when treated in the usual way with acidified reagent, yielded 0.44 g. (14%) of acetophenone 2,4-dinitrophenylhydrazone,[20] m.p. 238–241°. Acetophenone with neutral 2,4-dinitrophenylhydrazine gave a small quantity of derivative. This indicated that fraction I was probably the vinyl ether, α-ethoxystyrene.

On redistillation, fraction II boiled at 114–116° at 1 mm., n^{20}_{D} 1.4861.

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.6; H, 7.6; sapn. equiv., 238. Found: C, 65.6; H, 7.5; sapn. equiv. (titration to phenolphthalein end-point), 234.

The data indicate that fraction II was essentially 2-ethoxy-2-phenethyl ethyl carbonate, $C_6H_5{-}CH(OC_2H_5){-}CH_2{-}O{-}CO{-}OC_2H_5$.

The 3.75 g. constituting fraction II corresponds to a yield of 75%.

Thermal Decomposition of 3-Nitroso-2-oxazolidones. 5,5-Diphenyl-3-nitroso-2-oxazolidone.[2]—The solid nitroso compound (3.0 g., 0.011 mole) was placed in a previously dried 50-ml. flask which was connected to a gas collecting device. The flask was heated slowly in an oil-bath to 190–200° and maintained at that temperature until the evolution of gas had ceased (about 30 minutes). The decomposition was lively but never violent. After cooling, 5 ml. of petroleum ether (30–60°) and 1 ml. of ethanol was added and the material thoroughly mixed. On filtration there was obtained 0.6 g. (23%) of 5,5-diphenyl-2-oxazolidone, m.p. 199–201° (reported 199–200°) after recrystallization from ethanol.

The filtrate was evaporated and the residue treated with 2,4-dinitrophenylhydrazine. There was obtained 2.9 g.

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(25) We wish to thank the Dow Chemical Company for the gift of a sample of 2-phenyl-1,2-propanediol.

(26) C. Paal and E. Weidenkoff, *Ber.*, **39**, 2063 (1906).

of a mixture of carbonyl derivatives, m.p. 130–195°, 0.5 g. of which was separated by chromatography on alumina into 0.40 g. (56% based on total products) of diphenylacetaldehyde 2,4-dinitrophenylhydrazone, m.p. 153–155°, showing no depression when mixed with an authentic sample, and 0.07 g. (10%) of the desoxybenzoin 2,4-dinitrophenylhydrazone, m.p. 202–204°, not depressed when mixed with an authentic sample.[27]

The gas evolved, 350 ml. (theory for 1 mole, 246 ml.), was shown to contain carbon dioxide and carbon monoxide (precipitate of metallic silver on shaking the mixture with ammoniacal silver hydroxide).[28] Nitric oxide was present as judged by the fact that the gas turned brown on exposure to air.

5-Methyl-5-phenyl-3-nitroso-2-oxazolidone.[2]—The decomposition of this material was carried out as described above. During the decomposition of 5.0 g. (0.024 mole), 410 ml. of gas (corrected to standard conditions) was evolved. This is approximately 75% of theory for one molecular equivalent. The gas proved to be largely nitric oxide. The product was extracted with petroleum ether (30–60°) leaving 310 g. (70.5%) of 5-methyl-5-phenyloxazolidone, m.p. 145–147° (reported[2] 146–147°).

After evaporation of the petroleum ether, the residue was treated with neutral 2,4-dinitrophenylhydrazine reagent. As no precipitate formed on refluxing, there was added 0.5 g. of mercuric sulfate and 2 ml. of concentrated sulfuric acid. On gentle refluxing an orange precipitate formed. After recrystallization from ethyl acetate–methanol 1.96 g. of propiophenone 2,4-dinitrophenylhydrazone, m.p. 186.5–188°, was not depressed when mixed with authentic sample.[29] These facts indicated the presence of 1-phenylpropyne in at least 26% yield.

4,4-Diphenyl-3-nitroso-2-oxazolidone.—In the manner previously described 1.00 g. of 4,4-diphenyl-3-nitroso-2-oxazolidone which had been dried *in vacuo* was thermally decomposed. The product was dissolved in ethanol–petroleum ether (30–60°) and cooled. There crystallized 0.81 g. (87%) of 4,4-diphenyl-2-oxazolidone, m.p. 175–177°.

4,4-Dimethyl-3-nitroso-2-oxazolidone.—The freshly prepared and dried nitroso compound (20 g., 0.14 mole) was heated to 200°. When the evolution of gas (mostly nitric oxide) was complete, the product was recrystallized from a mixture of ether and petroleum ether (30–60°) at low temperatures. There was obtained 13.5 g. (84%) of 4,4-dimethyl-2-oxazolidone, m.p. 54–56°. From a small amount of material collected in a Dry Ice trap during the decomposition, there was prepared 1.3 g. of isobutyraldehyde 2,4-dinitrophenylhydrazone, m.p. 172–174°.

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(27) Reference 13, p. 365.

(28) G. Lunge and H. R. Ambler, "Technical Gas Analysis," Gurney and Jackson, London, 1934, p. 228.

(29) T. Thomson and T. S. Stevens, *J. Chem. Soc.*, 2607 (1932).

COLUMBUS, OHIO

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

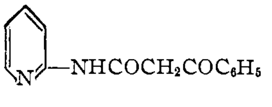
The Action of Alkali on Bromopyridopyrimidones

BY ROGER ADAMS AND IRWIN J. PACHTER

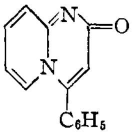
RECEIVED MAY 27, 1953

2-Substituted-3-bromo-4H-pyrido[1,2-a]pyrimidin-4-ones undergo rearrangement with ring contraction upon treatment with dilute alkali to yield imidazo[1,2-a]pyridine derivatives.

In a previous communication,[1] comparison of the ultraviolet absorption spectra of several pyridopyrimidones led to the conclusion that benzoylacetamidopyridine (I) does not cyclize in concentrated sulfuric acid to give 4-phenyl-2H-pyrido[1,2-a]pyrimidin-2-one (II), but instead rearranges and yields 2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one (III). A new reaction of some compounds of this series has now been discovered which provides chemical evidence to confirm this conclusion.



I



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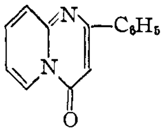
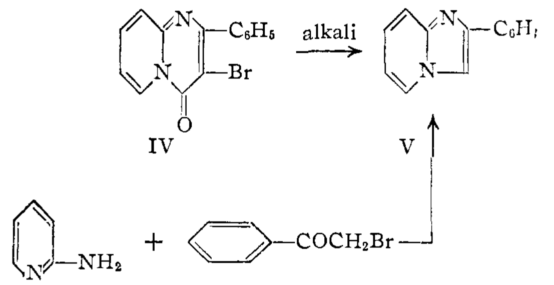


III

When 3-bromo-2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one (IV), obtained upon bromination of III with N-bromosuccinimide,[1] was heated with dilute aqueous sodium hydroxide, it was converted in 86% yield to a bromine-free base which was identical with 2-phenylimidazo[1,2-a]pyridine (V) prepared from 2-aminopyridine and phenacyl bromide.[2] The formation of V in this ring contraction reaction rather than the known 3-phenyl isomer[3] establishes unequivocally that the product obtained upon cyclization of I is III rather than II.



When 2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one is brominated with N-bromosuccinimide, an excellent yield of monobromo product results. This appears to be the 3-bromo-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one and not the possible isomeric 2-bromomethyl-4H-pyrido[1,2-a]pyrimidin-4-one. This conclusion is based on the fact that the 3-position in pyridopyrimidin-4-ones is highly reactive. The ease of bromination with NBS of the 2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one and the corresponding 2-chloro compound,[4] as reported in this communication, serves as an illustration. Khitrik[5] has demonstrated that nitration of the 2-methyl derivative results in substitution in the 3-position. It follows, therefore, that if the compound in hand were the 2-bromomethyl-4H-pyrido[1,2-a]pyrimidin-4-one, further bromination with NBS should convert the monobromo deriva-

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(1) R. Adams and I. J. Pachter, THIS JOURNAL, **74**, 5491 (1952).

(2) A. E. Chichibabin, *Ber.*, **59**, 2048 (1926).

(3) Y. A. Goldfarb and M. S. Kondakova, *J. Applied Chem.* (*U.S.S.R.*), **15**, 151 (1942) [*C. A.*, **37**, 2380 (1943)].

(4) H. R. Snyder and M. M. Robison, THIS JOURNAL, **74**, 4910 (1952); ref. 1.

(5) S. N. Khitrik, *J. Gen. Chem.* (*U.S.S.R.*), **9**, 1109 (1939).