Tetrahedron Letters No.29, pp. 2473-2478, 1965. Pergamon Press Ltd.
Printed in Great Britain.

# INTRAMOLECULAR CATALYSIS IN PHOTOLYSIS OF N-NITROSAMINES. AN OXIDATIVE DECARBOXYLATION OF α-AMINO ACIDS.

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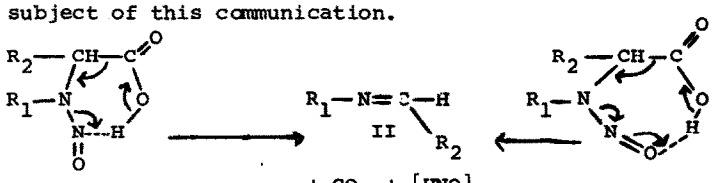
(Received 31 May 1965)

The requirement for an acid in the photolysis of N-nitrosodialkylamine has been established and a plausible mechanism has been proposed[1]. Although the way by which an acid participates in the photo-transformation[1] is yet to be proved, it was thought that a proton donating group suitably located near the nitrosamine moiety might faciliate the photo-transformation. In particular, N-nitroso derivatives of α-amino acids possess favourable steric arrangements of the nitrosamino and carboxylic groups required for hydrogen bonding and electronic disproportionation in the primary photo-elimination (see IA and IB). This hypothesis has been tested with a few model compounds and the results are the subject of this communication.



IA IB

N-Nitroso-N-phenylglycine[2] (I, $R_1 = C_6H_5$, $R_2 = H$) readily underwent photolysis alone in ether or methanol solution to give hexahydro-1,3,5-triphenyl-s-triazine[3]

(III, a singlet at τ5.06). It was apparent that III was formed from the trimerization of the primary photo-elimination product II ($R_1$ = $C_6H_5$, $R_2$ = H). In contrast, N-nitroso-N-methylaniline IV did not undergo the photolysis even in the presence of an acid catalyst.*

In view of the ready photolysis of N-nitrosamides[4], N-nitroso-N-acetyl-DL-phenylalanine** (I, $R_1$ = $COCH_3$, $R_2$ = $PhCH_2$), m.p. 65-70° (decomp.) was chosen as a model compound and prepared by means of $N_2O_4$ nitrosation[5]. Photolysis of the nitroso compound alone in aqueous methanol proceeds quickly to give, after recrystallization from cyclohexane, N-acetyl-1-phenyl-2-methoxyethylamine V (45%), m.p. 95-96°, $\gamma_{max.}$ 3300, 1650 and 1540 $cm^{-1}$, n.m.r. signals at τ7.04 (2 benzylic protons, doublet, J=5.5 cps), 4.48, 4.64 (1 proton, pair of triplets, J=10 and 5.5 cps) and 3.51 (amide proton doublet, J=10 cps), (Found: C, 68.63; H, 7.71; N, 6.99) and N-acetyl-β-styrylamine[6] VI (23%), m.p. 98-101°, $\lambda_{max.}^{EtOH}$ 287 and 221 mμ (ε, 21,200 and 13,800), $\gamma_{max.}$ 3290, 1640 and 1575, 1530 $cm^{-1}$ and n.m.r. signals each equivalent to one proton at

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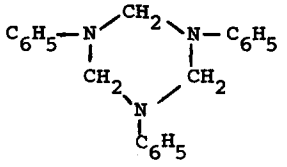
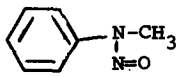
* The resistance to photolysis even in the presence of acid is surprising. This may be due to an electronic factor contributed by the benzene ring or the particular configuration as shown in IV. See G. J. Karabatsos and R. A. Taller, J. Am. Chem. Soc., 86, 4373 (1964).

** All the nitroso compounds used in this study has $\gamma_{max.}$ ca. 1720 $cm^{-1}$ and a carboxylic proton signal at τ ~1~0.4. Unless stated otherwise, the n.m.r. spectra were taken in $CDCl_3$ with Varian A-60 spectrometer using TMS as internal standard.

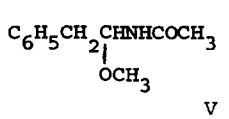
τ3.79 (doublet, J=15 cps), 2.13, 2.37(pair of doublets, J=10 and 15 cps) and 0 (doublet, J=15 cps). Further photolysis of VI in methanol solution did not yield V. It is apparent that V is formed from an nucleophilic addition of methanol to the intermediate II ($R_1$ = $COCH_3$, $R_2$=$C_6H_5CH_2$)[7]. The same photolysis



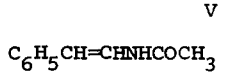
III



IV



V

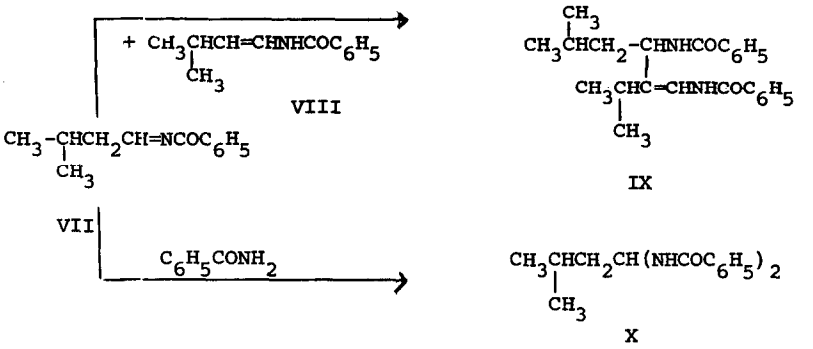


VI

in ether solution, however, gave, in addition to VI (27%), N-acetyl-DL-phenylalanine (38%). In both photolyses, amidoxime type compounds, frequently observed in the photolysis of N-nitrosodialkylamines[1], were not obtained. The C=N bond of the intermediate II is extensively delocalized with the substituent group $R_1$ ($CH_3CO$ or $C_6H_5$) and, therefore, is expected to be a powerful electrophilic center. Both the facile trimerization and the methanol addition are in agreement with this expectation. It also follows that in the assumed mechanism of amidoxime formation[1], the attack of the [NOH] species cannot be nucleophilic in nature.

The powerful electrophilic reactivity of the intermediate II, an N-acyl Mannich base, is further demonstrated in the photolysis of N-nitroso-N-benzoyl-DL-leucine (I, $R_1$ = $C_6H_5CO$, $R_2$ = $(CH_3)_2CHCH_2$). Among other products, compounds IX (40%) and X (13.8%) were isolated. The formation of IX and X is pictured as an electrophilic attack of the intermediate VII

on VIII (which was also isolated) and on benzamide, respectively.




Compound IX has m.p. 149-152° (Found: 76.16; H, 7.88; N, 7.38%), $\gamma_{max.}$ 3340, 1662, 1635, 1602, 1577, 1528 and 1490 $cm^{-1}$, n.m.r. signals (100 M c.p.s.), an AB quartet at $\tau$ - 0.53 and 3.12 (J = 9 c.p.s.) and a doublet at 3.20 (NH) coupled with a pair of triplets at 4.91 (J = 8 and 5.5 c.p.s.). Compound X has m.p. 208-208.5 (Found: C, 73.49; H, 7.24; N, 8.73%), $\gamma_{max.}$ 3295, 1642, 1600, 1555, 1520 and 1480 $cm^{-1}$, n.m.r. signals (in DMSO at 100 M c.p.s.)of quintet at $\tau$4.06 (J = 7.5 and 6 c.p.s.) coupled with a doublet at 1.49 (two equivalent NH).

N-Nitrosopipecolinic acid[8] (I.R., $R_1$, $R_2$ = $-(CH_2)_4-$), m.p. 93-95°, (Found: C, 47.87; H, 6.41; N, 17.56%) was photolysed in water to give $CO_2$ (87%) and an hygroscopic compound, $\gamma_{max.}$1635 $cm^{-1}$ and n.m.r. signals ($D_2O$) at $\tau$6.52 and 7.44 each approximately equivalent to 2 protons, which was readily isomerised either on heating or on treatment with hydrochloric acid to the known 2-piperidonoxime[1a] (65%), m.p. 121-123°. In ether solution the 345 mμ band disappears more than 10 times as fast to give the same 2-piperidonoxime

(56%) directly as well as the hygroscopic compound as the minor product. The latter is probably the geometrical isomer of the known 2-piperidonoxime[1a], m.p. 121-123°. The formation of 2-piperidonoximes follows from the proposed mechanism[1]. The rates in aqueous solution are not affected by the presence of 0.06N acetic or hydrochloric acid attesting to the preference for intramolecular over intermolecular catalysis.

In contrast, neither N-nitrosonipecotinic acid alone in ether nor N-nitrosopiperidine in the presence of one equivalent of acetic acid undergoes significant change on prolonged photolysis. The results establish that the intramoleculary hydrogen bonded species of N-nitroso-α-carboxylic acids I undergo photolysis leading to oxidative decarboxylation to give Mannich (or an N-acylated) bases II of the corresponding aldehyde. In view of the frequently proposed (and in some cases proved) biogenetic transformation of α-amino acids to such aldehydes (or the equivalent) as intermediates in alkaloids biosyntheses[9], the present phototransformation bears a degree of resemblance to the natural process.

Acknowledgement:

The Author thanks the National Research Council, Ottawa, for financial support and Mr. D. P. Horning for technical assistance.

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9. For a recent survey, E. Leete in "Biogenesis of Natural Products" edited by P. Bernfeld, Pergamon Press Ltd., Oxford, 1963, pp. 739