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Reaction of N-(1-Cyanoalkyl)alkylideneamine N-Oxide with Carboxamides

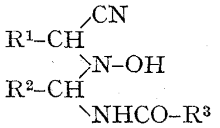
It is known that nitrones react as a 1,3-dipole with many unsaturated compounds to give cycloadducts, and with Grignard reagents and hydrogen cyanide to give hydroxylamines.[1]

However, all these reactions, except the cycloadditions of isocyanate, isothiocyanate,[1] and N-sulfinylaniline,[2] involve a carbon nucleophile which attacks on the carbon atom of a nitrone group.

In this communication, we wish to report the first example of a non-cyclic 1,3-addition reaction of a nitrogen nucleophile with a nitrone.

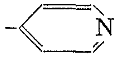
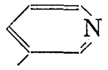
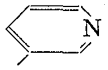
When N-(1-cyanoalkyl)alkylideneamine N-oxide was dissolved in excess formamide at room temperature and the mixture was allowed to stand for 3—10 days, a crystalline product, consistent with the expected 1:1 adduct (I), was separated from the solution.

Table I. N-(1-Cyanoalkyl)N-(1′-carbonamidoalkyl) Hydroxylamine



$$\begin{array}{l} \quad\;\;\diagup CN \\ R^1\text{–}CH \\ \qquad\;\; \rangle N\text{–}OH \\ R^2\text{–}CH \\ \quad\;\;\diagdown NHCO\text{–}R^3 \end{array}$$

I

(I)	R¹	R²	R³	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
a	Pr^n	Pr^i	H	148.5—149.0	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.29	8.98	19.58
b	Pr^n	Pr^n	H	145.0—146.5	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.56	8.83	19.77
c	Pr^i	Pr^n	H	134.0—135.0	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.14	8.91	20.02
d	Pr^i	Pr^i	H	121.5—122.0	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.51	8.91	19.46
e	Pr^n	Et	H	151.5—152.0	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.10	8.55	21.71
f	Pr^i	Et	H	138.0—139.0	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.21	8.52	20.71
g	Et	Pr^n	H	140.0—140.5	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.48	8.59	21.05
h	Et	Pr^i	H	154.0—154.5	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.21	8.65	21.16
i	Pr^i	Me	H	137.0—137.5	$C_8H_{15}O_2N_3$	51.87	8.16	22.69	52.16	8.44	22.69
j	Pr^i	Pr^i		155.5—156.0	$C_{15}H_{22}O_2N_4$	62.12	7.65	19.32	61.91	7.55	19.13
k	Pr^i	Pr^i		146.0—148.0	$C_{15}H_{22}O_2N_4$	62.12	7.65	19.32	62.24	7.47	19.37
l	Pr^n	Pr^i		150.0—150.5	$C_{15}H_{22}O_2N_4$	62.12	7.65	19.32	61.81	7.62	18.98

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1) J. Harmer and A. Macaluso, *Chem. Rev.*, **64**, 473 (1964).
2) O. Tsuge, M. Tashiro, and S. Mataka, *Tetrahedron Letters*, **1968**, 3877.

The reaction proceeds also in dry ethanol at room temperature and is catalized by sodium ethoxide.

Nicotinamide and isonicotinamide also add to the nitrone in dry ethanol to give the expected 1:1 adduct. The structure of the adduct was confirmed by elemental analysis (shown in the Table) and the following spectral evidences. The infrared (IR) spectrum of (I-d) (KBr disk) exhibits strong absorptions at 3350 and 3210 cm^{-1} (NH and OH), and two characteristic absorptions of secondary amide at 1526 and 1216 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum of (I-d) (in DMSO-d_6 with tetramethylsilane as an internal reference) shows a broad singlet at τ 1.88 (1H, CHO), a singlet at 1.62 (1H, OH), a broad doublet at 1.69 (1H, NH), and a triplet at 5.76 (1H, Pri–$\underline{\mathrm{CH}}$–NHCO).

Many runs carried out on both aromatic and cyclic nitrones, which have no α-cyano group, failed to give the similar adduct.

The studies on the additional chemical and physical properties of the adduct, and the reaction of other amides with nitrones are now being in progress.

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Structures of Tracheloside and Nortracheloside from *Trachelospermum asiaticum* Nakai var. *intermedium* Nakai

During our investigation on the constituents of the stems of *Trachelospermum asiaticum* Nakai var. *intermedium* Nakai (Apocynaceae), three lignan glucosides, arctiin (I), matairesinoside (II) and tracheloside have hitherto been isolated.[1,2]

In addition, we have isolated a new lignan glucoside named nortracheloside from the ethyl acetate-soluble fraction of the methanol extracts by silica gel column chromatography.

This paper deals with the structures of tracheloside and nortracheloside.

In a previous paper, we suggested the structure of tracheloside as IX or X.[2] We have now proposed X for tracheloside and XI for nortracheloside.

XI, $C_{26}H_{32}O_{12}\cdot H_2O$, mp 95—100°, was obtained as a white powder from chloroform–ethanol, $[\alpha]^{19}_{D}$ -47.9 ($c=1.02$, EtOH), UV $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε): 229 sh (4.07), 282 (3.70), $\lambda^{\mathrm{EtOH+NaOH}}_{\mathrm{max}}$ mμ: 247, 284, 298, IR $\nu^{\mathrm{KBr}}_{\mathrm{max}}$ cm^{-1}: 1770 (C=O), 1605, 1515 (aromatic C=C).

On hydrolysis with dil. H_2SO_4, XI gave D-glucose and amorphous nortrachelogenin (XIII) which was already isolated from the ether-soluble fraction and elucidated to be 4,4′,8′-trihydroxy-3,3′-dimethoxy-lignan-olid(9,9′).[3]

On methylation with excess diazomethane, XI gave X, $C_{27}H_{34}O_{12}\cdot 1/2H_2O$, mp 168—170°. Enzymatic hydrolysis of X with β-glucosidase gave D-glucose and trachelogenin (XII). Hence, XI is mono–glucoside of XIII.

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1) I. Inagaki, S. Hisada and S. Nishibe, *Chem. Pharm. Bull.* (Tokyo), **16**, 2307 (1968).

2) I. Inagaki, S. Hisada and S. Nishibe, *Phytochemistry*, **10**, 211 (1971).

3) S. Nishibe, S. Hisada and I. Inagaki, *Phytochemistry*, in press.