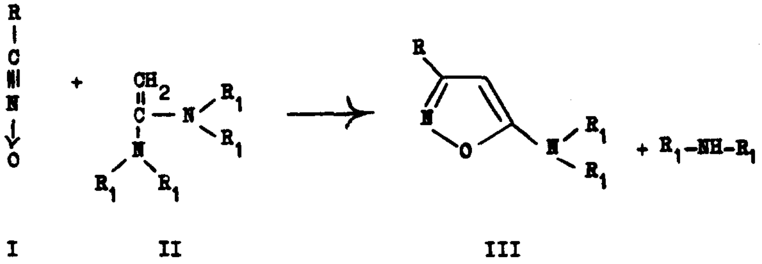
Tetrahedron Letters No.38, pp. 4537-4539, 1966. Pergamon Press Ltd.
Printed in Great Britain.

DIPOLAR ADDITION REACTIONS OF NITRILEOXIDES. IV.*
THE CYCLOADDITION OF NITRILEOXIDES TO KETENE AMINALS.

P. Rajagopalan and C.N. Talaty
CIBA Research Centre, Goregaon, Bombay 63, India

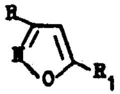
(Received 6 July 1966)

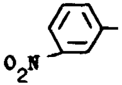
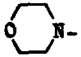
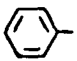
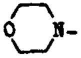
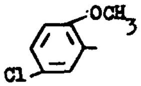
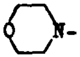
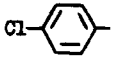
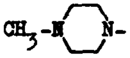
Nitrileoxides (I) react vigorously with ketene aminals (II) to furnish 5-substituted-aminoisoxazole derivatives (III) directly in good yields. Since ketene aminals can be prepared readily from triethyl orthoacetate and secondary amines (1), this cycloaddition reaction affords a new, one-step approach to the isoxazole system.



---

* Contribution No.65 from CIBA Research Centre, Bombay 63.
For Part III of this series *cf*. P. Rajagopalan and C.N.Talaty, Tetrahedron Letters, 1966, 2101.



Compd.	R	R_1	Mol.formula	M.P.		Analysis C	H	N
a	$(CH_3)_3C$-		$C_{12}H_{20}N_2O$	67-70°	Calcd. Found	69.19 69.36	9.68 9.63	13.45 13.09
b			$C_{13}H_{13}ClN_2O_2$	127-130°	Calcd. Found	58.99 59.05	4.95 5.03	10.59 10.79
c			$C_{13}H_{13}N_3O_4$	188-192°	Calcd. Found	56.72 57.14	4.76 4.56	15.27 15.10
d			$C_{13}H_{14}N_2O_2$	98-100°	Calcd. Found	67.81 67.81	6.13 6.13	12.17 12.66
e			$C_{14}H_{15}ClN_2O$	109-111°	Calcd. Found	64.00 63.57	5.76 5.80	10.67 10.59
f			$C_{14}H_{15}ClN_2O_3$	91-93°	Calcd. Found	56.96 57.05	5.27 5.13	9.51 9.44
g			$C_{14}H_{16}ClN_3O$	132-134°	Calcd. Found	60.53 60.81	5.81 5.79	15.13 14.61

The general procedure for the preparation of compounds of the type III is as follows: A solution of the ketene aminal in absolute ether (0.5 mole) is added in one lot, with agitation, to a solution of freshly liberated nitrileoxide (0.5 mole) in absolute ether. In many cases, precipitation of the product occurs within a few minutes. The mixture is then refluxed for 30 minutes, cooled, filtered and the residue recrystallised from a suitable solvent. In case there is no separation of the product, the mixture, after being refluxed for 30 minutes, is evaporated to dryness under reduced pressure and the residue triturated with 1N hydrochloric acid, filtered and recrystallised from an appropriate solvent.

A few of the substituted-aminoisoxazole derivatives thus prepared are listed in the Table. They are extremely, if at all, weak bases and exhibit I.R. absorption characteristic of isoxazoles. At least in two cases the secondary bases liberated during the reaction were isolated and identified by conversion into substituted ureas by treatment with 4-chlorophenylisocyanate and comparison of the latter with authentic samples.

Acknowledgement: We thank Professor T.R. Govindachari for his interest in this work and Dr. S. Selvavinayakam and his associates for the elemental analyses and spectra.

Reference

1. H. Baganz and L. Domaschke, Chem.Ber., 95, 2095 (1962).