Tetrahedron Letters No. 44, pp 3877 - 3878, 1975. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF FUSED ISOQUINOLINONES BY THERMAL CYCLIZATION OF β-PHENYL-α-SUBSTITUTED AMINO HETEROCYCLIC COMPOUNDS

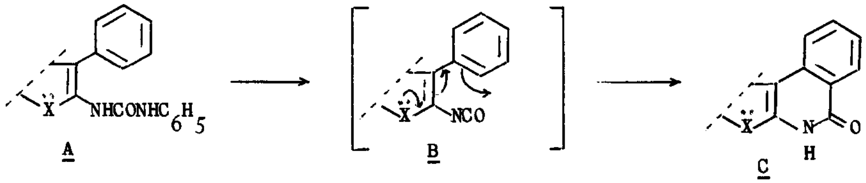
G.Winters *) and N. Di Mola

Research Laboratories of Gruppo Lepetit S.p.A., Milan, Italy

(Received in UK 9 September 1975; accepted for publication 22 September 1975)

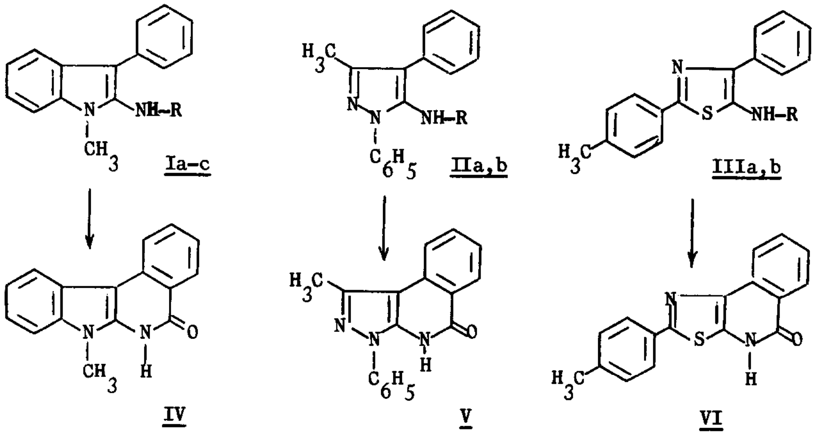
o-Biphenylylisocyanate and ethyl N-o-biphenylylcarbamate are known to undergo a cyclization reaction to phenanthridone in the presence of Friedel-Crafts reagents 1), with polyphosphoric acid 2) or photochemically 3).

We found that a number of ureas of electron-rich heterocyclic compounds (A) undergo a thermal cyclization on the vicinal phenyl group giving rise to the hitherto unknown heterocyclic fused isoquinolinones (C). The reaction is carried out simply by heating A-type ureas until aniline begins to form (270-280°C).



A few examples are listed in Fig. 1. Starting materials have been obtained from the known amines Ia 4), IIa 5) and IIIa 6) by classical methods. The chemico-physical properties are collected in Table I.

Fig. 1



a) R = H; b) R = $CONHC_6H_5$; c) R = $COOC_2H_5$

Table I

Compound	m.p. °C	(solvent)	Yield %	Molec. formula	Analysis
I b	230 modif.	(AcOEt)	87	$C_{22}H_{19}N_3O$	C, H, N
c	159-161	(Et.ether)	80	$C_{18}H_{18}N_2O_2$	C, H, N
II b	225	(EtOH)	82	$C_{23}H_{20}N_4O$	C, H, N
III b	247-263	(EtOH)	78	$C_{23}H_{19}N_3OS$	C, H, N, S
IV	350 dec.	(DMF)	61 * 95 **	$C_{16}H_{12}N_2O$	C, H, N
V	302-304	(DMF)	85	$C_{17}H_{13}N_3O$	C, H, N
VI	314-316	(DMF)	75	$C_{17}H_{12}N_2OS$	C, H, N, S

* from Ib; ** from Ic

The compounds of type C share the following characteristics: high melting point, a very low solubility in common organic solvents, a fair solubility in aqueous alcoholic alkali and fluorescence under U.V. irradiation. In the I.R. spectrum they show a broad band at 3100-2500 cm^{-1} and a carbonyl band at 1670-1660 cm^{-1}. N.M.R. and Mass Spectra are in agreement with the assigned structures.

As demonstrated by further experiments, thermal ring closure could be achieved also by heating ethyl carbamates (e.g. Ic), by melting the starting amine Ia with urea or treating it with phosgene in boiling toluene. The reaction seems to be greatly facilitated by the unshared electron pair of the hetero-atom since N-o-biphenylyl-N'-phenylurea does not cyclize under the same conditions.

Scope and limitations of the reaction are presently under investigation.

References

1. a) J.M.Butler, J.Am.Chem.Soc., 71, 2578 (1949)
   b) A.Pictet, A.Hubert, Chem.Ber., 29, 1188 (1896)
2. E.C.Taylor Jr., N.W.Kalenda, J.Am.Chem.Soc., 76, 1699 (1954)
3. a) J.S.Swenton, Tetr.Lett., 30, 2855 (1967)
   b) N.C.Yang, Arnon Shani, G.R.Lenz, J.Am.Chem.Soc., 88, 5369 (1966)
4. G.A.Golubeva, Yu.N.Portnov, A.N.Kost, Khim.Geterotsikl.Soedin., 4, 511 (1973)
5. C.Alberti, Gazz.Chim.Ital., 89, 1017 (1959)
6. K.Gewald, H.Schönfelder, U.Hain, J.prakt.Chem., 361, 299 (1974)