Tetrahedron Letters No. 33, pp.3071-3074, 1971. Pergamon Press. Printed in Great Britain.

A NEW ENAMINE REACTION: SYNTHESIS OF 3-AMINO-1,2-DIAZETIDINES

L. Marchetti and G. Tosi
Istituto Chimico Facoltà di Ingegneria - Università di Bologna
40136 Bologna - Italy

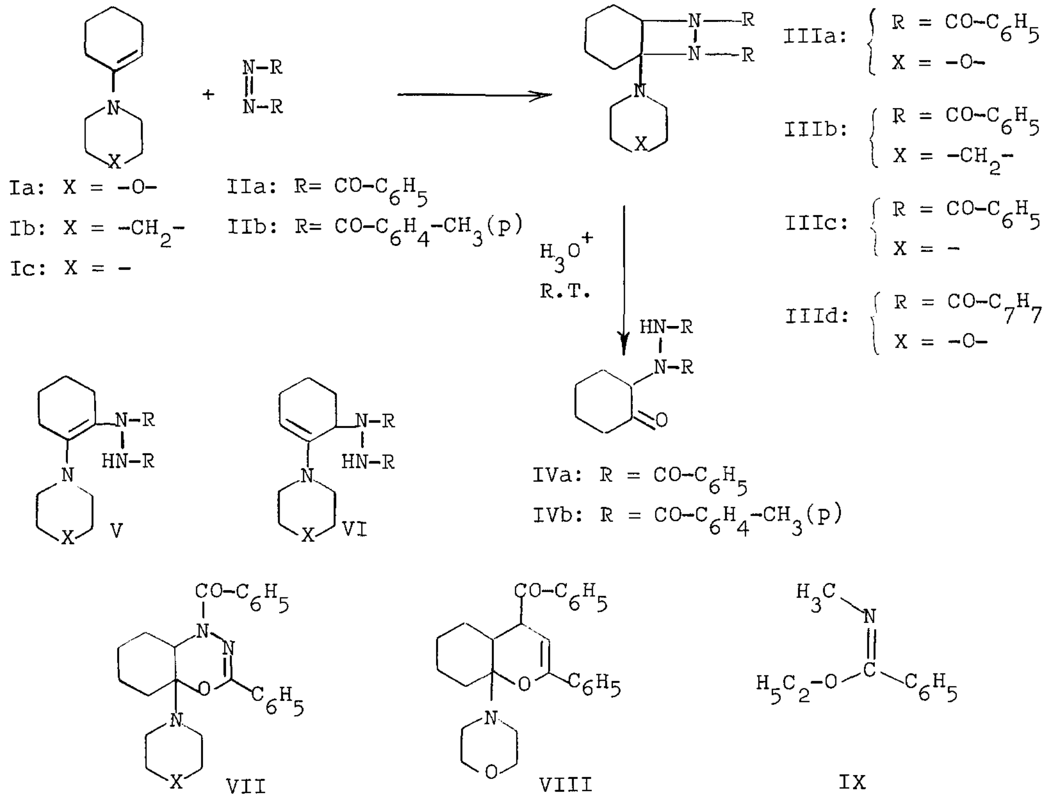
(Received in UK 7 July 1971; accepted in UK for publication 14 July 1971)

Cyclohexanone enamines react with dibenzoyldiimide (IIa) at room temperature leading to a 1:1 addition product in almost quantitative yield. This adduct, on mild acidic hydrolysis, gives 2-(N,N'-dibenzoyl)hydrazinocyclohexanone (IVa), identical with that obtained from cyclohexanone and (IIa) at 100°, in the presence of sulphuric acid.

Four structures, (III), (V), (VI) and (VII) could be postulated for the 1:1 adduct. The formation of these compounds should be analogous to that of cyclobutane derivatives (1,2), substituted enamines (3) and heterocyclic adducts (4) from the same enamines with electrophilic alkenes, ethyl azodicarboxylate (5) and α, β-unsaturated ketones, respectively.

I.R. and N.M.R. spectra are conclusive for the assignment of structure (III) to the reaction products. In the N.M.R. spectra there are no N-H bands and a signal appeared at τ 4.8-5.0, corresponding to only one hydrogen atom; enaminic structures such as (V) or (VI) are therefore excluded (3). I.R. spectra also showed no absorption in the N-H bond region, indicating that a cycloaddition occurred.

Cyclic structure (III), where the two phenyl groups are almost equivalent, is preferred to (VII), where they are not, because of the pattern of the N.M.R. spectra of the reaction products. These showed, in the aromatic hydrogen atom region, two well-separated multiplets centered at τ 2.15-2.25 and τ 2.60-2.65, respectively, with 4:6 integrated intensity ratio. Dibenzoyldiimide (IIa) and dibenzoylhydrazine N.M.R. spectra showed the same signal pattern: the lower field signal being attributable to the four hydrogen atoms in ortho position with respect to the carbonyl groups; the higher field signal to the hydrogen atoms in meta and para position. On the contrary, the N.M.R. spectrum of (IVa), whose carbonyl groups are not equivalent, showed, in the aromatic hydrogen atom region, a ten-proton complex multiplet from τ 2.2 to τ 2.8, not separable into two distinct signals.



Ia: X = -O-
Ib: X = $-CH_2-$
Ic: X = -

IIa: R= $CO-C_6H_5$
IIb: R= $CO-C_6H_4-CH_3$(p)

IIIa: R = $CO-C_6H_5$; X = -O-
IIIb: R = $CO-C_6H_5$; X = $-CH_2-$
IIIc: R = $CO-C_6H_5$; X = -
IIId: R = $CO-C_7H_7$; X = -O-

IVa: R = $CO-C_6H_5$
IVb: R = $CO-C_6H_4-CH_3$(p)

V

VI

VII

VIII

IX

Analogously, N.M.R. spectra of N,N'-di-(4-methyl)benzoylhydrazine and di-(4-methyl)benzoyldiimide (IIb) showed two well-separated multiplets, with 4:4 integrated intensity ratio, in the aromatic hydrogen atom region.

The reaction of (IIb) with cyclohexanone enamines led to a 1:1 addition product (IIId) whose N.M.R. spectrum showed two distinct multiplets in the aromatic hydrogen atom region, with 4:4 integrated intensity ratio, indicating that the aromatic rings are almost equivalent.

Mild acidic hydrolysis of the addition product gave (IVb), whose N.M.R. spectrum showed for the aromatic hydrogen atoms an eight-proton complex multiplet, analogous to that of (IVa) and not separable into two distinct multiplets.

A further argument favouring structure (III) rather than (VII) may be ob-

PHYSICAL PROPERTIES OF COMPOUNDS (III) AND (IV)

Compound	m.p. (solvent)	I.R.(Nujol) (cm^{-1})	N.M.R. (CDCl$_3$) (τ)
(IIIa)	154° (benzene/ ligroin)	1625-1637 No NH nor CO ketonic bands.	2.15 (m, 4, aromatic) 2.60 (m, 6, aromatic) 4.95 (broad, 1, $C\underline{H}$-N) 6.65 (m, 4, $C\underline{H}_2$-O-$C\underline{H}_2$) 7.25 (m, 4, $C\underline{H}_2$-N-$C\underline{H}_2$) 8-8.8(m, 8, aliphatic)
(IIIb)	156° (benzene/ ligroin)	1626-1636 No NH nor CO ketonic bands.	2.25 (m, 4, aromatic) 2.65 (m, 6, aromatic) 5.0 (broad, 1, $C\underline{H}$-N) 7.30 (m, 4, $C\underline{H}_2$-N-$C\underline{H}_2$) 8.2-8.7 (m, 14, aliphatic)
(IIIc)	100° (benzene/ ligroin)	1644 No NH nor CO ketonic bands.	2.25 (m, 4, aromatic) 2.75 (m, 6, aromatic) 5.15 (broad, 1, $C\underline{H}$-N) 7.2 (m, 4, $C\underline{H}_2$-N-$C\underline{H}_2$) 8.0-8.6 (m, 2, aliphatic)
(IIId)	149-51° (benzene/ ligroin)	1612-1620 No NH nor CO ketonic bands.	2.25 (two doublets, 4, aromatic) 2.80 (two doublets, 4, aromatic) 5.0 (broad, 1, $C\underline{H}$-N) 6.40 (m, 4, $C\underline{H}_2$-O-$C\underline{H}_2$) 7.25 (m, 4, CH_2-N-$C\underline{H}_2$) 7.55-7.60 (two singlets,6,methyl) 7.8-8.8 (m, 8, aliphatic)
(IVa)	142° (benzene/ ligroin)	3345 (NH); 1712 (CO Ketonic); 1676 - 1664 - 1648	1.55 (s, 1, NH) 2.5 (m, 10, aromatic) 4.65 (broad, 1, $C\underline{H}$-N) 7.3-8.3 (m, 8, aliphatic)
(IVb)	171-73° (benzene/ ligroin)	3215 (NH); 1720 (CO ketonic); 1640	1.70 (s, 1, NH) 2.7 (m, 8, aromatic) 4.60 (broad, 1, $C\underline{H}$-N) 7.63-7.68 (two singlets,6,methyl)

tained from inspection of N.M.R. spectra of 1,2-dibenzoyl-ethylene, of cromene (VIII) [whose structure has been unambiguously demonstrated (4)], and of iminoether (IX). The signal relative to the aromatic hydrogen atoms in N.M.R. spectrum of dibenzoylethylene showed two multiplets, analogously to (IIa), the hydrogen atoms in ortho position to carbonyl groups being more deshielded than meta and para hydrogens. Compound (VIII), where a carbonyl group only is present and phenyl groups are not equivalent, showed a quite different pattern in the aromatic hydrogen atom region, only two protons appearing at lower field ($\tau = 2.05$) set apart from a complex multiplet corresponding to the other eight protons ($\tau = 2.65$). The N.M.R. spectrum of the iminoether (IX), which structurally resembles (VII), showed in the aromatic hydrogen atom region, a narrow multiplet only corresponding to five protons, the ortho hydrogen atoms signal being not separated from meta and para hydrogens.

Finally, the high polarisability of the C=C enaminic bonds, according to Koerner (6), is in favour of the 1,2-cycloaddition, leading to diazetidines, and against the 1,4-cycloaddition, leading to dihydrooxadiazines.

This new enamine reaction appears to be a rather general synthetic route for 1,2-diazetidines, an heterocyclic system not well investigated (7).

Acknowledgement - This work was supported by a grant from the Consiglio Nazionale delle Ricerche (Rome).

References

(1) A.G.Cook, "Enamines", M.Dekker Inc., New York 1969, pg. 213, 230.
(2) M.Perelman and S.A.Mizsak, J.Am.Chem.Soc. 84 4988 (1962); G.Opitz and J.Koch, Angew.Chem.Int.Ed. 2 152 (1963).
(3) Such a signal may be due to a vinylic hydrogen or to a hydrogen of the group CH-N(R)-NHR: A. Risaliti and L. Marchetti, Ann.Chim.(Rome) 53 717 (1963); ibid. 55 635 (1965); F.P.Colonna, M.Forchiassin, G.Pitacco, A.Risaliti and E.Valentin, Tetrahedron 26 5289 (1970). In structure (V) no hydrogen atoms of this type are present, in structure (VI) there are two.
(4) F.P.Colonna, S.Fattutta, A.Risaliti and C.Russo, J.Chem.Soc. (C) 1970 2377.
(5) β-Disubstituted enamines were showed to give diazetidines in the reaction with methyl azodicarboxylate: J.Firl and S.Sommer, Tetr.Letters, 1969 1137.
(6) E.Koerner von Gustorf, D.V.White, B.Kim, D.Hess and J.Leitich, J.Org.Chem., 35 1155 (1970).
(7) J.A.Moore, in "The Chemistry of Heterocyclic Compounds", (A.Weissberger Ed.), Wiley Inc. New York 1964, vol. 19, Part. II, pag. 956-958.