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CONDENSATION OF IMINES WITH ACETYL CHLORIDE AND TRIETHYLAMINE : A REINVESTIGATION

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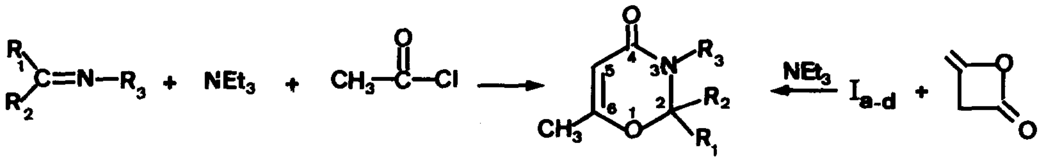
It has been established that the reaction of certain acid chlorides and an imine in presence of a tertiary amine led to a β-lactam[1]. Acetyl chloride has now been found to react in a different manner. Thus Bose and al.[2] reported that the mixture of acetyl chloride and triethylamine did not give a β-lactam with benzalaniline ; more recently Iwamura and al.[3] claimed the synthesis of 1,3-oxazetidine IV_d from this mixture and imine I_d. The structural assignment of IV_d was made on the basis of its elemental analysis, n.m.r. spectrum and isolated products from its methanolysis. As a part of a work concerning immonium salts[4], we reinvestigated this reaction with I_a (Scheme 1) : an oxazinone derivative III_a was obtained. We wish to report, herein, that it is a typical reaction and that the reported four membered heterocycle IV_d is in fact dihydrooxazinone III_d.

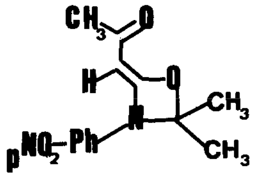
Scheme I



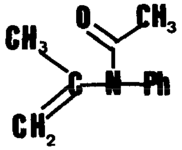
I_{a-d} III_{a-d} II

a : R_1 = Ph R_2 = H $R_3 = CH_2Ph$
b : R_1 = Ph R_2 = H R_3 = Ph
c : $R_1 = R_2 = CH_3$ R_3 = Ph
d : $R_1 = R_2 = CH_3$ $R_3 = p\text{-}NO_2Ph$

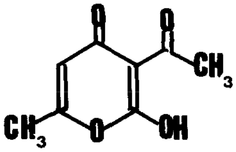
Following the reported procedure[3] (Method A), acetyl chloride (two equiv.) was slowly added to a stirred solution of imine I (1 equiv.) and triethylamine (2 equiv.) in anhydrous ether at room temperature. After three hours the mixture was filtered to remove the triethylamine hydrochloride. When the filtrate was concentrated, crystals of an oxazinone derivative



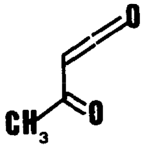
IV$_d$



V$_c$



VI



VIII

III was obtained and recrystallized from ether-hexane (2 : 1). Yields and physical constants of compounds III$_{a-d}$ derived from imines I$_{a-d}$ are listed in Table I. In contrast to published results[3], it was found that imine I$_c$ afforded III$_c$ (as well as V$_c$).

Table I - 4 H - dihydro-1,3-oxazine-4-ones obtained from imines

Imines	Adducts	mp ,°C	A[a*] Yields, %	B[b*]
I$_a$	III$_a$	77	55	56
I$_b$	III$_b$	90	4	22[d*]
I$_c$	III$_c$	76	27	62
I$_d$	III$_a$	138[c*]	76	37

[a*] From acetyl chloride (see text) - [b*] From diketene[12]
[c*] Ref. 3, mp : 137° - [d*] In this reaction I$_b$ was treated with four equivalents of diketene.

Structural assignments for these compounds were made by n.m.r. spectroscopy. The ^{1}H data are recorded in Table II. The spectrum revealed a doublet at δ = 1.83-2.02 (3H) and a quadruplet at δ = 5.32-5.42 (1H). The coupling constant between the two groups of protons is 0.8. Hz. The magnitude of the interaction can be easily interpreted as a long range allylic coupling between a methyl group and an olefinic proton accross a double bond $(CH_3-\overset{|}{C}=CH)$.

Table II - ^{1}H Chemical shifts

Compounds	CH_3^{c*} (d)	5-H[c*] (q)	R$_2$	R$_1$	R$_3$
III$_a$ [a*]	1.83 (d)	5.32 (q)	6,08 (s,1)	7,36(m,10);5,45(d,1)[d*];3,82(d,1)[d*]	
III$_b$	1.92 (d)	5.39 (q)	6.65 (s,1)	7.4 (m,10)	
III$_c$ [b*]	1.96 (d)	5.35 (q)	1.55 (s,6)		7.35(m,5)
III$_d$	2.02 (d)	5.42 (q)	1.63 (s,6)		7.42(m,2)8.33(m,2)

[a*] Chemical shifts (δ) in p.p.m. downfield from tetramethylsilane (internal). [b*] Ref. 3 : δ: 2.03 (s,3), δ 5.37 (s,1), δ 1.63 (s,6), δ 7.40 (d,2), δ 8.28 (d,2). [c*] J : 0.8-0.9 Hz. [d*] J = 15,4 Hz.

These structures were confirmed by the ^{13}C n.m.r. Fourier transform decoupled spectra of III_{a-d} : the chemical shifts are in good agreement with those reported recently for 2,3-dihydro-6-methyl-1,3-oxazine-2,4-dione $IX^{5,6}$. Moreover, from an off resonance decoupled experiment, we showed that the multiplicity of the observed signals are in accordance with peak assignements for III_a.

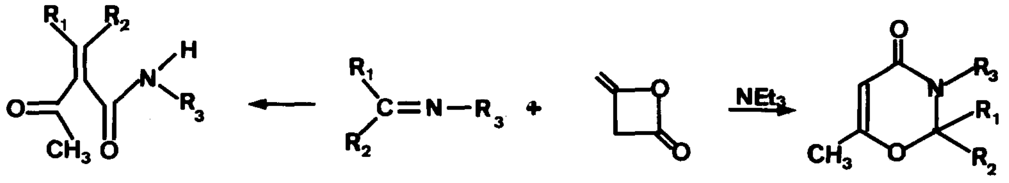
Table III - ^{13}C Chemical shifts ^{a*,b*}

Compounds	C_2	C_4	C_5	C_6	6-CH_3	2-CH_3
III_a^{c*}	87.2 (d)	164.2 (s)	99.5 (d)	162.7 (q)	18.94	-
III_b	89.5	164.3	101.2	162.3	19.28	-
III_c	92.4	163.5	98.4	162.7	19.31	25.59
III_d	92.5	164.7	98.2	162.6	19.47	25.65
IX^{d*}	148.5	166.4	100.9	162.5	18.59	-

^{a*} Chemical shifts (δ) in ppm downfield from tetramethylsilane (internal) - ^{b*} Chemical shifts of aromatic carbons, III_a- : 126.8 (d), 127.2 (d), 128.0 (d), 129.0 (d), 135.1(s), 136.8 (s) ; III_b : 124.1, 130.8, 143.8, 146.8 ; III_c : 127.6, 128.8, 128.6, 137.4 ; III_d : 124.7, 125.6, 126.8, 128.1, 128.6, 129.0, 136.6, 139.43. ^{c*} Chemical shift of CH_2 : 45.6. ^{d*} See ref. 5.

In order to explain the formation of oxazinone derivatives we suspected that diketene II was formed in a first step. This hypothesis was confirmed by a thorough investigation of the n.m.r. spectrum of the crude products, we found : (i) n.m.r. signals of diketene when acetyl chloride was in excess with respect to triethylamine, (ii) low yield formation of $VI^{7,8}$ (a dimer of diketene). It is well known that diketene reacts with imines.

Scheme II



VII_{a-b} I_{a-d} II III_{c-d}

Variations of reactivity with structure of imines have been noted in the litterature. Thus, Kato and al. reported that the reaction of diketene II gives α-alkyliden-acetoacetamides VII with Schiff bases[9] and 1,3-oxazine derivatives III with ketimines [10] (R_3=H) and imidates[11]. We reinvestigated this reaction (scheme II) and observed that diketene (1 equiv.) and imines $I_{a,b}$ (1 equiv.) afforded only acetamides $VII_{a,b}$ in good yields and that imines $I_{c,d}$ led to oxazinones $III_{c,d}$ very slowly (traces after several days). Nevertheless, when these reactions were conducted in presence of a catalytic amount of triethylamine (Method B)[12] we only obtained oxazinones III_{a-d} whatever the structure of the imine may be.

The above data are consistent with the following mechanism : formation of ketene from acetyl chloride, (ii) dimerization of ketene to diketene, this reaction is certainly faster than the cycloaddition to imines, (iii) heterolytic cleavage of the diketene ring through attack on the carbonyl by NEt$_3$ involving the formation of oxoketene VIII, (iiii) stepwise or concerted 1,4-addition of the C=N double bond to VIII; similar cycloadditions to oxoketeneshave recently been achieved[13].

Further examples of application of the above reaction will be presented in a forthcoming full paper.

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5. S. AHMED, R.LOFTHOUSE and G. SHAW, J.C.S. Chem.Comm., 959 (1974).
6. C_2 and C_4 assignments of ref. 5 have been reversed for compound IX, so, the C_4 chemical shift is consistent with the reported data for III_{a-d}.
7. mp 107-108, Litter. 109[8].
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12. Diketene II (1 equiv.) was added slowly to a stirred mixture of imine (1 equiv.) and triethylamine (0.2 equiv.) in anhydrous ether. After two hours the reaction mixture was concentrated and oxazinone derivative III recrystallized.
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    b) G. JÄGER, Chem. Ber., 105, 137 (1972).
14. VII_a = mp 108°, yield 65%, ms 279 (M^+) ; ^1H n.m.r. ($CDCl_3$) δ 2.40 (s, 3H), δ 4.55 (d, 2H), δ 6.15 (1H, >N-H), δ 7.25-7.65 (m,11H). ^{13}C n.m.r. ($CDCl_3$) δ 26.3 (q,CH_3) δ 43.4 (t,CH_2) δ 167.26 (s, -NH-CO-) δ 195.6 (s,-CO-). VII_b : traces were observed after six days at room temperature. This compound was obtained in poor yield by Kato and al.[9a].