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A NOVEL SYNTHESIS OF 1H-1,2-BENZODIAZEPINES

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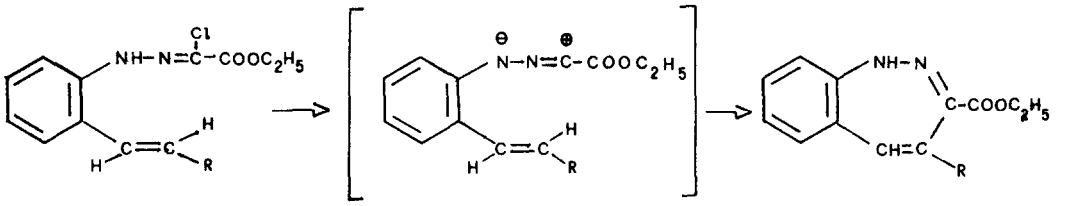
Reports on fully unsaturated 1H-1,2-benzodiazepines are rare in the literature. To our knowledge, only the unsubstituted compound and its 5-methyl derivative have been synthesized by photoinduced ring expansion of N-iminoquinolinium ylides.[1,2] We now wish to report that phenylhydrazoyl chlorides 1, bearing an α,β unsaturation in the ortho position, are useful intermediates for the synthesis of 1H-1,2-benzodiazepines 3.



1 2 3

a, R = $COOC_2H_5$; b, R = CN; c, R = C_6H_5

Compounds 1a-c were prepared by diazotization of the properly substituted anilines and subsequent coupling with ethyl α-chloroacetoacetate. All of them exhibited correct elemental analyses, IR and NMR spectra.[3]

Treatment of 1a-c with triethylamine (1.2 moles) in boiling benzene at 0.1 M concentration gave orange red crystalline compounds of general formula 3. Reaction times, yields and properties of the products are collected in the table.

Interestingly, compound 3c was also obtained (22% yield) starting from the

cis isomer corresponding to 1c; the reaction time, however, was longer (6h).

TABLE[4,5]

Compd	Time (h)	Yield (%)	M.p. (°C)	IR (nujol) (cm^{-1})	NMR (CD_3COCD_3) (δ)
3a	0.5	66	114	3310(NH), 1740 and 1720(CO)	1.25,1.28(6H,two t,CH_3), 4.22(4H, q,CH_2), 6.9-7.4(4H,m,ar), 7.86 (1H,s,CH=), 8.1(1H,broad s,NH)
3b	0.25	58	168	3300(NH), 2220 (CN), 1740(CO)	1.30(3H,t,CH_3), 4.29(2H,q,CH_2), 6.8-7.5(4H,m,ar), 7.66(1H,s,CH=), 8.3(1H,broad s,NH)
3c	2	25[6]	131	3310(NH), 1730 (CO)	0.91(3H,t,CH_3), 3.96(2H,q,CH_2), 7.0-7.45(10H,m,ar and CH=), 8.0 (1H,broad s,NH)

Since the treatment of 1-chlorohydrazones with triethylamine is a well known procedure for generating in situ nitrile imines, it seems reasonable to posit that intermediates 2 are initially formed in the course of the above reaction. These intermediates could then evolve according to one of the following alternative pathways: a) intramolecular cycloaddition to the olefinic function to give strained tricyclic species, which should rearrange quickly to the final products; b) 1,7-electrocyclic ring closure, followed by prototropic shift.

Work is in progress to provide further mechanistic informations, particularly by varying the olefinic substituents.

References and notes

(1) T. Tsuchiya, J. Kurita, H. Igeta, Chem.Comm., 640 (1974).

(2) J. Kurita, T. Tsuchiya, Chem.Comm., 936 (1974).

(3) Compounds 1a,b show for the olefinic protons J = 16 Hz. In the case of 1c, the signal of these protons is masked by that of the aromatics; however, the assigned structure was proved to be correct through the independent synthesis of the cis isomer (J = 12 Hz).

(4) Satisfactory elemental analyses were obtained for all the compounds listed.

(5) NMR spectra were taken at 60 MHz with tetramethylsilane as the internal standard. Melting points are uncorrected.

(6) After chromatography on silica gel column.