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NOTE

Synthesis and Spectral Studies of Some Heterocyclic Azetidione Compounds

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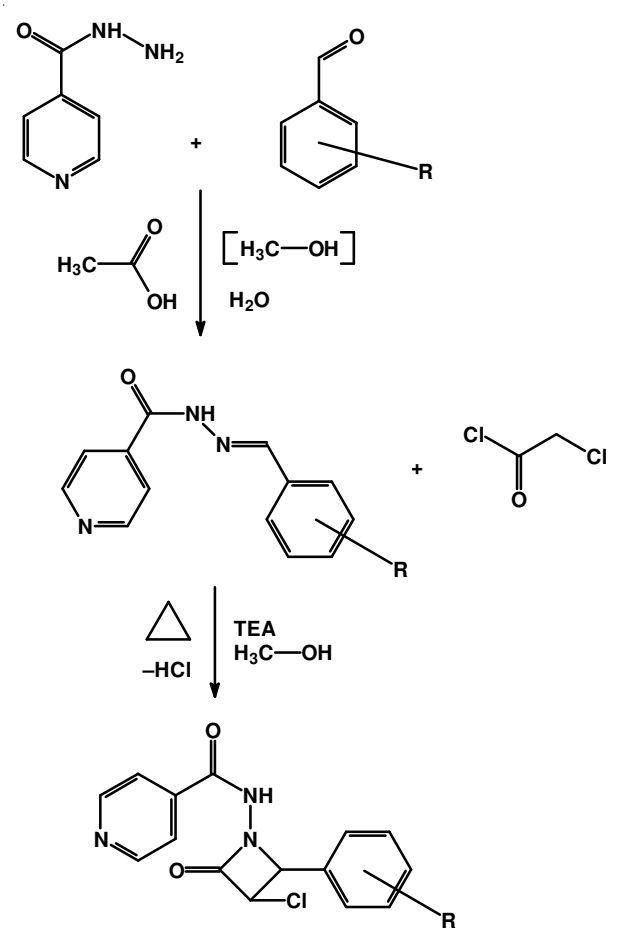
Some new heterocyclic azetidiones have been prepared by the reaction of various Schiff bases with chloro acetyl chloride. The intermediate Schiff bases were synthesized by the condensation of isoniazid with various aldehydes. The structures of compounds have been confirmed by elemental analysis and spectral analysis.

Key Words: Schiff bases, Heterocyclic azetidiones, IR and NMR Spectra.

The chemical intermediate used in the synthesis of the thiosemicarbazone was identified as highly potent anti-tuberculosis drug[1]. It was tested in Nemyork Hospitals and quickly became established as the most valuable antituberculosis drug ever discovered. It received the approved name of isoniazid and remains in use as an essential component of the combinations of drugs used to treat this deadly disease, which has reappeared with renewed virulence in recent year. Shortly after the announcement of this discovery of the activity of isoniazid both Kushner of Lederle Lab. and Solotorosky of Merck & Co., simultaneously reported the anti-tuberculosis properties of the nicotinamide analogue known as pyrazinamide. This remains an important drug because of its efficiency in meringue penetration in cases of meringue tuberculosis. The theraplix company in Paris subsequently introduced ethionamide, but it is now rarely used.

All the melting points were taken in melting point apparatus. The IR spectra were recorded with KBr pellets on Parkin-Elmer 783 spectrophotometer[2]. NMR Spectra were recorded ppm related to TMS[3]. Starting material [**1(a-j)**] were synthesized from the appropriate isoniazid and aromatic aldehydes according to known products and reaction monitoring by TLC method.

Synthesis of N-[(1Z)-(R) methylene] isonicotinohydrazide [2(a-j)][4]: A mixture of aromatic isoniazid (1 mol), acetic acid (0.7, v/w), H_2O (3 v) stirred well at 25-27 °C for 1 h. Add drop-wise aldehydes (1 mol) using addition funnel within 0.5 h under stirring and kept for 1 h. The product was filtered and washed by 1 volume of acetic acid (20 %). Finally, washed again by 2 volume of water. The solid obtained was collected and crystallized from methanol (Table-1).



Reaction Scheme

TABLE-1
ANALYTICAL DATA OF SCHIFF BASES [**2(a-j)**]

Substituents	m.w.	Yield (%)	m.p. (ºC)
Benzaldehyde	225	0.76	195-197
p-Cl benzaldehyde	260	0.73	212-215
Vaniline	271	0.72	210-214
Anisaldehyde	255	0.66	154-157
o-Cl benzaldehyde	260	0.62	206-210
Veratraldehyde	285	0.64	182-186
p-F benzaldehyde	243	0.53	216-220
Salicyaldehyde	241	0.59	192-196
P, *p*'-dimethyl amino benzaldehyde	268	0.66	202-204
m-Nitro benzaldehyde	270	0.58	182-186

IR (KBr, cm^{-1}): 1690-1630 ν(C=N), 3540-3300 ν(-NH) and 1870-1660 ν(-C=O), 1570-1510 δ(-NH).

Synthesis of N-[3-chloro-2-oxo-4-R- azetidin-1-yl] isonicotinamide [3(a-j)][5,6]: A mixture of Schiff base (0.02 mol) and methanol (10 v/w), chloro acetyl chloride (4.0 mL), triethylamine (2.5 mL) were heated under reflux on a water bath at 64-68 °C for 5 h cooled to 25 °C and isolated by 20 volume of water; filtered and washed by 2 volume of water and finally crystallized in methanol (Table-2).

TABLE-2
ANALYTICAL DATA OF NEW HETEROCYCLIC AZETIDIONES COMPOUNDS [**3(a-j)**]

Compd.	Substituent (R)	m.f. / (m.w.)	Elemental analysis %: Found (Calcd.)				m.p. / (Yield %)
			C	H	N	Cl	
2a	H	$C_{15}H_{12}O_2Cl$ (301.72)	59.69 (59.71)	4.00 (4.01)	13.91 (13.93)	11.75 (11.75)	191 (66.4)
2b	4-$N(CH_3)_2$	$C_{17}H_{17}N_4O_2Cl$ (344.79)	59.20 (59.22)	4.95 (4.97)	16.23 (16.25)	10.26 (10.28)	178 (62.8)
2c	3,4$(OCH_3)_2$	$C_{17}H_{16}N_3O_4Cl$ (361.78)	56.42 (56.44)	4.24 (4.46)	11.59 (11.61)	9.79 (9.80)	180 (57.4)

IR (KBr, cm^{-1}): 1750-1700 ν(N-C=O) and 1600-1590 ν(C=N). NMR: 7.2-7.3 (benzene ring, H), 8.0-8.5 (*sec*-amide), 7.3-8.5 (pyridine ring H) 5.2-6.8 (1H-ethelene in ring).

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