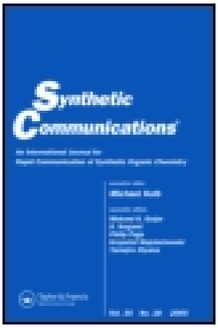

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HYPERVALENT IODINE OXIDATION OF HYDRAZONES OF SOME NITROGEN HETEROCYCLIC KETONES AND ALDEHYDES: AN EFFICIENT SYNTHESIS OF FUSED 1,2,3-TRIAZOLOHETEROCYCLES

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Abstract : Fused 1,2,3-triazoloheterocycles have been prepared by iodobenzene diacetate mediated oxidation of hydrazones of nitrogen heterocyclic ketones and aldehydes.

Introduction

The importance of organohypervalent iodine(III) compounds as versatile reagents in organic synthesis has been recognised in recent years.[1,2,3] Among important examples that may be cited are : (i) carbon-carbon bond formation[4], (ii) functionalization of carbonyl compounds[5], (iii) oxidation of phenolic compounds[6], (iv) synthesis of heterocyclic compounds[7], etc. During the course of our studies on the use of organoiodine(III) reagents, we have recently investigated the oxidation of nitrogen containing

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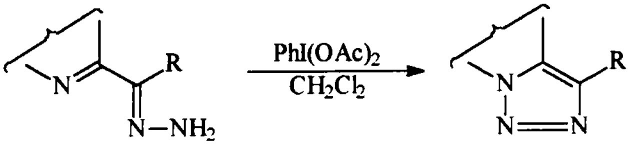
compounds such as rearrangement of *o*-aminochalcones[8], cleavage[9] and dimerization[10] of acid hydrazides with IBD. Iodobenzene diacetate (IBD) mediated cleavage of tosylhydrazones[11], semicarbazones[12] and oxidations of *N*-acylhydrazones and *N*-phenylsemicarbazones to 1,3,4-oxadiazoles and Δ^3-1,3,4-oxadiazolines[13] have also been reported by others. These studies find an extensive use in the synthesis of heterocyclic compounds including bridgehead heterocycles[14,15]. In continuation of these encouraging results, we have now developed a new, facile and efficient synthesis of fused 1,2,3-triazolo compounds by intramolecular cyclization of hydrazones of nitrogen heterocyclic ketones and aldehydes.

Discussion

The strategy for this work is based on the presumption that hydrazone moiety present at α-position in nitrogen heterocycle, on oxidation with IBD might afford fused triazoloheterocycles by intramolecular cyclization (Scheme-I).

To check the feasibility of this approach, 2-acetylpyridine hydrazone (**1a**) was treated with IBD (1 equivalent) in CH_2Cl_2 at room temperature. Interestingly, a rapid reaction occurred with the formation of desired product i.e. 1,2,3-triazolo-[1,5-a] pyridine (**6a**). Similarly, 2-benzoylpyridine hydrazone (**1b**) and 2-

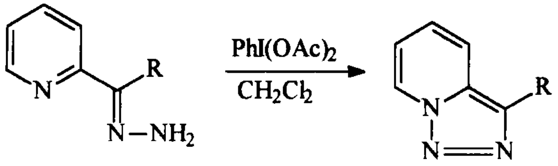


R = H, Me, Ph, etc.

Scheme - I.

pyridinecarboxaldehyde hydrazone (**1c**) underwent smooth cyclization to the triazolo compounds **6b** and **6c** respectively.

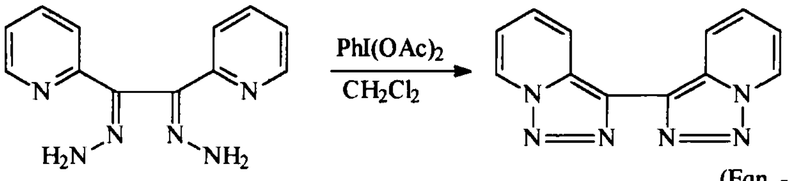
This method was further extended to synthesize various heterocycles as exemplified in equations **1-5**.



1 **6**

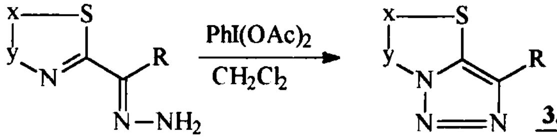
1, 6	**R**
a	Me
b	Ph
c	H

(Eqn. - 1)



2 **7**

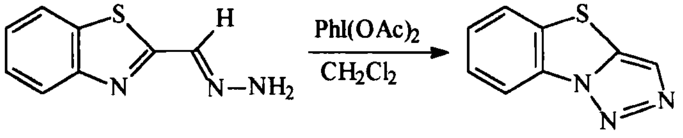
(Eqn. - 2)



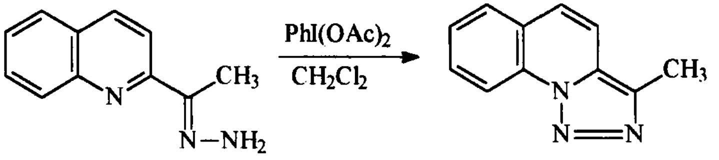
3 **8**

3, 8	**x - y**	**R**
a	$-CH=CH-$	Me
b	$-CH=CH-$	Ph
c	$-CH_2-CH_2-$	Me

(Eqn. - 3)



4 **9** (Eqn. - 4)



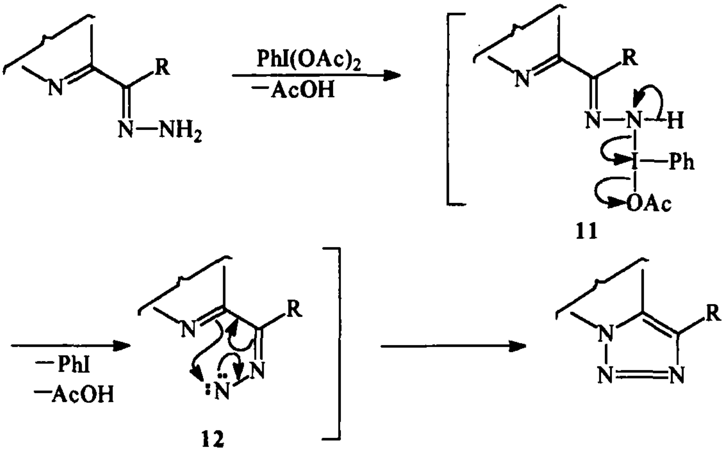
5 **10** (Eqn. - 5)

A plausible pathway for this IBD mediated cyclization is outlined in scheme-II. First of all, an electrophilic attack of IBD on the lone pair of terminal nitrogen of hydrazone gives intermediate **11** which then undergoes reductive elimination of iodobenzene along with expulsion of a molecule of acetic acid to give nitrene intermediate **12**. Finally, intramolecular cyclization of **12** gives the corresponding triazolo compound.

This IBD mediated cyclization has distinct advantages over the previously reported methods using lead tetraacetate[16], Ag_2O[17], $K_3[Fe(CN)_6]$[18], MnO_2[19], nickel peroxide[20] : (i) reaction is general, facile and efficient, (ii) experimental procedure is simple and no side products are obtained, (iii) IBD is less toxic than other oxidising agents used earlier.

Experimental

Melting points were taken in open capillaries and are uncorrected. ^1H NMR spectra were recorded on a Brucker 300 MHz



Scheme - II.

TABLE : Physical data of fused 1,2,3-Triazoloheterocycles 6a-10

Compound	*M.P. (Lit m.p.) °C.*	*Yield (%)*	*Solvent for recrystallization*
6a	84 (84–85)[20]	93	Ethanol
6b	111 (113–14)[20]	91	Ethanol
6c	33 (34–35)[17]	83	Ethanol
7	252 (254–55)[17]	79	Ethanol
8a	126 (126–28)[16]	71	Cyclohexane
8b	168 (167–68)[16]	75	Diethyl ether
8c	94–95	88	Methanol
9	113 (115)[21]	68	Hexane
10	91–92	72	Hexane

instrument using TMS as an internal standard. IR spectra were recorded on Perkin-Elmer 1800 IR spectrophotometer. Mass spectra were recorded on Kratos MS-50 mass spectrometer.

Hydrazones (**1–5**) were prepared by refluxing the corresponding aldehyde/ketone with hydrazine hydrate in EtOH, a well known method. Compounds **3c** and **5,** not known in literature, were identified by their spectral & analytical data:

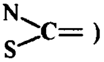
3c : m.p. 112-14°C. (Yield 72%) ^{1}H NMR ($CDCl_3$): δ 2.06 (s,3H,CH_3), 3.21 (t, 2H, J = 8.4Hz, S-CH_2), 4.36 (t, 2H, J = 8.3Hz, N-CH_2), 5.74 (bs, 2H, NH_2); IR (Nujol)-3354,3316, 3192, 2930, 2854, 1659, 1592, 1568; MS: m/z 143 (M^+); Anal. found : C 42.09, H 6.34, N 29.14, S 22.35 $C_5H_9N_3S$ requires C 41.96, H 6.29,N 29.37, S 22.38.

5 : m.p. 107-8°C. (Yield 68%) ^{1}H NMR ($CDCl_3$): δ 2.11 (s,3H,CH_3), 5.76 (bs, 2H, NH_2), 7.52-8.53 (m,6H,Ar-H) IR(Nujol)-3342,3314, 3175, 2942, 1652; MS: m/z 185 (M^+); Anal. found : C 71.57, H 6.06, N 22.32, $C_{11}H_{11}N_3$ requires C 71.35, H 5.94,N 22.70.

Cyclization of hydrazones (1-5) to 1,2,3-triazoloheterocycles (6-10)

General procedure : IBD (3.22g, 10mmol) was added in small portions to a suspension of hydrazone **1a** (1.35g, 10mmol) in CH_2Cl_2. A rapid reaction took place. Reaction mixture was stirred for about 30 min at room temperature.

After the completion of reaction, the solvent was evaporated *in vacuo* and the residual mass was washed with hexanes to give product **6a** as a colourless solid which was recrystallized with ethanol (m.p = 84°C, Lit. m.p. = 84-85°C[20], 93%). In a similar manner, compounds **6b, 6c** and **7-10** were also prepared. Physical data of the fused heterocycles obtained is listed in the Table. Compounds **6a, 6b, 6c, 7, 8a, 8b** and **9** were identified by comparing their physical properties with those reported in literature. The characterization and spectral data of new compounds **8c** & **10** are given as under:

8c : ^{1}H NMR ($CDCl_3$) : δ2.19 (s, 3H, C_3-CH_3), 3.97 (t, 2H,-S-CH_2, J = 7.5 Hz), 4.48 (t, 2H,-N-CH_2, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) : δ 10.6 (s,C_3–CH_3), 37.68 (s,-CH_2), 47.41 (s, -CH_2), 77.02 (t, C-CH_3), 134.7 (d,  $\overset{N}{\underset{S}{>}}C=$); IR (Nujol) : 3009, 1538, 1327, 1127; MS : (m/z) 141 (M^+); Anal. found : C 42.37, H 5.16, N 29,57, S 22.69. $C_5H_7N_3S$ requires : C 42.55, H 4.96, N 29.79, S 22.70.

10 : ^{1}H NMR ($CDCl_3$) : δ2.14 (s,3H,C_3-CH_3), 7.24-8.33 (m,6H,Ar-H); MS : m/z 183 (M^+); Anal. found : C 71.89, H 5.06, N 22.80, $C_{11}H_9N_3$ requires C 72.13, H 4.91, N 22.95.

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