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HYPERVALENT IODINE OXIDATION OF 1,3,5-TRI-SUBSTITUTED PYRAZOLINES : A FACILE SYNTHESIS OF 1,3,5-TRISUBSTITUTED PYRAZOLES

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Abstract : 1,3,5-Trisubstituted pyrazolines (**1a-i**) undergo facile oxidation to the corresponding pyrazoles (**2a-i**) in the presence of iodobenzene diacetate.

Hypervalent iodine reagents are versatile reagents in organic synthesis[1]. We have recently shown that iodobenzene diacetate (IBD) is an excellent reagent for the synthesis of a wide variety of heterocyclic compounds[2]. We wish to report that this reagent can be successfully utilized for the conversion of pyrazolines to pyrazoles.

Treatment of one equivalent of 1,3,5-trisubstituted pyrazolines (**1a-e**), which were obtained by the reaction of the corresponding

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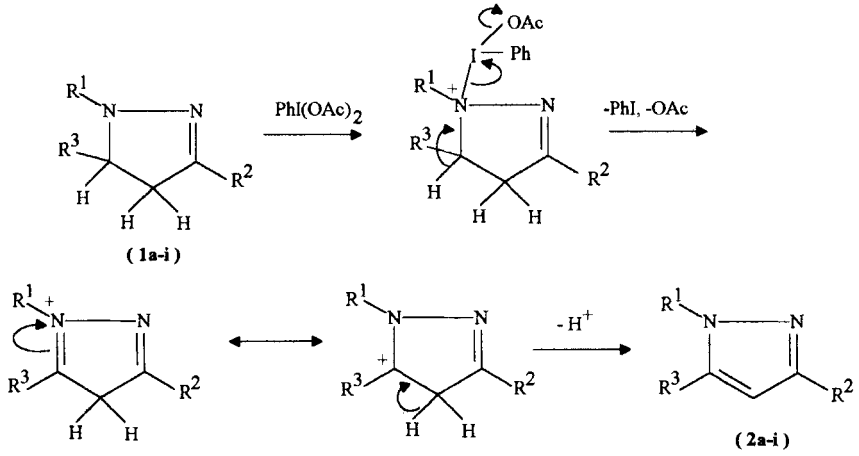
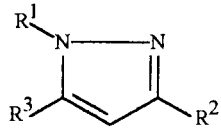
chalcones with appropriate hydrazines, with 1.5 equivalent of IBD in dichloromethane at room temperature provided 1,3,5-tri-substituted pyrazoles (**2a-e**) in good yields.

However, oxidation of pyrazolines having heterocyclic moieties (**1f-i**) did not succeed with IBD even on refluxing and stirring in dichloromethane for prolonged time. On refluxing these pyrazolines (**1f-i**) in acetic acid, however, the corresponding pyrazoles could be obtained in good yields. A plausible mechanistic pathway for this reaction is outlined in the Scheme.



The hypervalent iodine method for the conversion of **1a-i** to **2a-i** has distinct advantages over earlier methods[3-8] : (i) the reaction is general; (ii) the experimental procedure is simple; (iii) no side products are formed, which is often the case with existing methods and (iv) IBD is relatively less toxic than the commonly

Physical data of 1,3,5-trisubstituted pyrazoles (2a-i)



(2a-i)

2a-i	R^1	R^2	R^3	m.p. (Lit. m.p.) (°C)	Yield† (%)
a	C_6H_5	C_6H_5	C_6H_5	138-39 (140[11])	65
b	C_6H_5	4-BrC_6H_4	C_6H_5	156-57 (159[11])	62
c	C_6H_5	C_6H_5	4-ClC_6H_4	107-08(115[12])	70
d	C_6H_5	C_6H_5	4-$CH_3OC_6H_4$	77-78(79-80[13])	60
e	C_6H_5	C_6H_5	4-$NO_2C_6H_4$	143(142[12])	65
f	C_6H_5	4-ClC_6H_4	2-Thienyl	127-28	58
g	C_6H_5	4-$CH_3C_6H_4$	2-Furyl	93-94	55
h	2-Benzo-thiazolyl	C_6H_5	4-ClC_6H_4	172	52
i	2-(4-Methyl-quinolyl)	C_6H_5	4-ClC_6H_4	134-35	55

† Yield of the isolated products **2** with respect to the quantity of dihydropyrazoline **1** used.

used reagents such as bromine[3], lead tetraacetate[7] and manganese dioxide[10].

Experimental

Melting points were determined in open capillaries and are uncorrected. ^{1}H NMR spectra were recorded on Perkin-Elmer R-32 (90 MHz) instrument using TMS as an internal standard. Chalcones[9] and dihydropyrazolines[10] were prepared according to literature procedures.

Conversion of 1,3,5-trisubstituted pyrazolines (1a-e) to 1,3,5-trisubstituted pyrazoles (2a-e)

General Procedure

To a stirred solution of a **1a-e** (1mmol) in dichloromethane (40ml) was added IBD (1.5mmol) at room temperature. The reaction mixture was stirred for 5 hrs. Excess of dichloromethane was distilled off on a steam bath and the residual mass was crystallized from an appropriate solvent.

Conversion of 1,3,5-trisubstituted pyrazolines (1f-i) to 1,3,5-trisubstituted pyrazoles (2f-i)

General Procedure

To a solution of **2f-i** (1mmol) in acetic acid (40ml) was added IBD (1.5mmol) and the reaction mixture was refluxed for 4 hrs. Excess of acetic acid was distilled off under reduced pressure and the residual mass was extracted with chloroform (3×20ml). The

organic phase was dried (Na_2SO_4) and the solvent evaporated. The residual mass thus obtained was percolated over a column of silica-gel using pet-ether : ethyl acetate (19:1) as an eluent. The physical data of compounds thus synthesized are listed in the Table. The characterization and spectral data of the new compounds (**2f-i**) are given as under :

2f : ^{1}H NMR($CDCl_3$) : δ 6.59 (s, 1H, C_4-H), 7.13-7.41 (m, 10H, Ar-H), 7.67-7.85 (dd, 2H, Ar-H). Found N, 8.10 $C_{19}H_{13}ClN_2S$ requires 8.33.

2g, ^{1}H NMR($CDCl_3$) : δ 2.37 (s, 3H, C_4''-CH_3), 5.96 (dd, 1H, C_3'''-H), 6.32 (dd, 1H, C_4'''-H), 6.94 (s, 1H, C_4-H), 7.22 (dd, 2H, C_3''-H & C_5''-H), 7.39-7.49 (m, 6H, C_3'-H, C_4'-H, C_5'-H, C_2''-H, C_6''-H & C_5'''-H), 7.78 (dd, 2H, C_2'-H & C_6'-H). Found N, 9.10 $C_{20}H_{16}N_2O$ requires 9.33.

2h, ^{1}H NMR($CDCl_3$) : δ 6.80 (s, 1H, C_4-H), 7.31-7.57 (m, 9H, Ar-H), 7.68 (dd, 1H, C_6'-H), 7.79 (dd, 1H, C_5'-H), 7.95-8.03 (dd, 2H, C_4'-H & C_7'-H). Found N, 10.40 $C_{22}H_{14}ClN_3S$ requires 10.79.

2i, ^{1}H NMR($CDCl_3$) : δ 2.73 (s, 3H, C_4-CH_3), 6.81 (s, 1H, C_4-H), 7.27-7.61 (m, 10H, Ar-H), 7.85-7.97 (m, 4H, Ar-H). Found N, 10.63 $C_{25}H_{18}ClN_3$ requires 10.57.

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