Indian Journal of Chemistry
Vol. 37B, June 1998, pp. 583 - 584

Note

Hypervalent iodine mediated synthesis of 3-substituted-*s*-triazolo [3,4-*a*]phthalazines

Om Prakash*, Hitesh Batra, Viyay Sharma & Shiv P Singh*

Department of Chemistry, Kurukshetra University, Kurukshetra 136 119, India.

Received 3 September 1997; accepted (revised) 22 December 1997

Phthalazine hydrazones **1a-g** on oxidation with iodobenene diacetate (IBD) in dichloromethane yield exclusively the 3-substituted-*s*-triazolo[3,4-*a*]phthalazines **2a-g**.

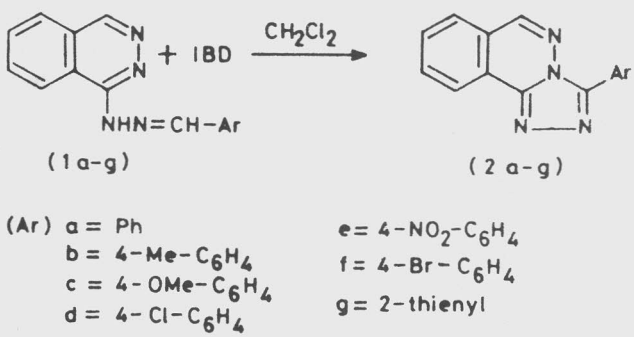
Hypervalent iodine reagents have drawn attention to the versatile synthesis of heterocycles[1]. We have recently shown that iodobenzene diacetate (IBD) is an excellent reagent for the synthesis of many useful bridgehead heterocyclic compounds[2].

The tricyclic heterocycles have an added significance, as many of them are potent antibacterials[3a,b] and antihypertensive agents[4]. Moreover, these compounds **2** are useful synthons for the synthesis of 3-phenyl[1,2,4]triazolo[1,4-*c*]quinazolin-5(6*H*)-one, a potent benzodiazepine receptor antagonist[5]. Herein we report the IBD mediated synthesis of 3-substituted-*s*-triazolo[3,4-*a*]phthalazines **2a-g**.

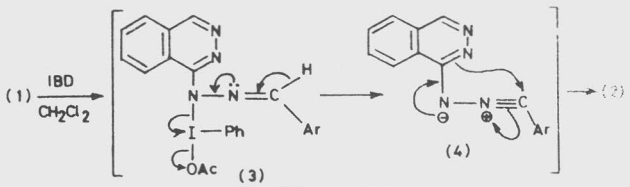
Stirring of phthalazine hydrazone **1a** with IBD in dichloromethane for 3-5 min. at room temperature resulted in the formation of a single product which was identified as 3-phenyl-*s*-triazolo[3,4-*a*]phthalazine **2a** on the basis of its m.p. 212-15° (lit.[5], m.p. 210-15°).

The generality of this facile transformation was established by treating other phthalazine hydrazones **1b-g** with IBD in dichloromethane under similar reaction conditions to get the corresponding triazolophthalazine derivatives **2b-g** in good yields (cf. Experimental and Scheme I).

The probable mechanism for the transformation of **1** to **2** is outlined in Scheme II, which is analogous to the oxidation of arenecarbaldehyde hydrazone with lead tetraacetate[6] and intramolecular cyclization of 2-benzothiazolyl hydrazone[2a].



Scheme I



Scheme II

Finally, this study provides a facile, quick and superior method for the synthesis of **2**, which is particularly advantageous over the reported procedures involving the use of toxic reagents such as lead tetraacetate and acid chloride[5].

Experimental Section

M.ps were taken in open capillaries and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1000 PC FTIR, and ^{1}HMR were taken on a Brucker 300 MHz instrument, using TMS as internal standard. All the phthalazine hydrazones **1a-g** were prepared according to the literature procedure[5,7]. The compound **1f** is not described in the literature and was identified by its spectral and analytical data.

1f: Yield 82%, m.p. 232-35°; ^{1}H NMR ($CDCl_3$); δ: 7.53-8.39 (m, 7H, phthalazine C_5-H, C_6-H, C_7-H and Ar-H), 8.81 (s, 1H, –N=CH–), 9.50-9.73 (m 2H, phthalazine C_4-H and C_8-H), 14.47 (brs, 1H, NH, exchangeable with D_2O); Anal. Found: C 54.38, H 3.02, N 17.06. Calcd for $C_{15}H_{11}BrN_4$: C 55.04, H 3.36, N 17.12%.

3-Substituted-*s*-triazolo[3,4-*a*]phthalaznes 2a-g: General procedure. To a stirred solution of **1a**

(5 mmoles) in 20 mL of dichloromethane at room temperature, IBD (5 mmoles) was added during 5 min. The excess solvent was evaporated *in vacuo* and the residue recrystallized from ethanol to get pure **2a**. In a similar manner **2b-g** were prepared.

The compounds **2a-d** were identified by comparing their properties with those that are reported in the literature[4,5]. The other products **2e-g** were characterised by their spectral and analytical data.

2a: Yield 82%, m.p. 214° (lit,[4,5], m.p. 210-12° and 214°).

2b: Yield 69%, m.p. 213° (lit,[4], m.p. 213°).

2c: Yield 64%, m.p. 203-6°, (lit.[4], m.p. 203-5°).

2d: Yield 80%, m.p. 229° (lit.[4,5], m.p. 230° and 224-25°).

2e: Yield 88%, m.p. 302°; ^{1}H NMR ($CDCl_3$); δ 7.67-8.47 (m, 7H, phthalazine C_7-H, C_8-H, C_9-H and Ar-H), 8.78-8.89 (m, 2H, phthalazine C_6-H and C_{10}-H); Anal. Found: C 61.32, H 2.92, N, 23.88. Calcd for $C_{15}H_9N_5O_2$: C 61.85, H 3.09, N 24.05%.

2f: Yield 78%, m.p. 226-28°; ^{1}H NMR ($CDCl_3$): δ 7.57-8.36 (m, 7H, phthalazine C_7-H, C_8H, C_9-H and Ar-H), 8.68-9.00 (m, 2H, phthalazine C_6-H and C_{10}-H); MS: m/z 324/326 (M^+); Anal. Found C 55.12, H 2.21, N 17. 21. Calcd for $C_{15}H_9BrN_4$: C 55.38, H 2.76, N 17.23%.

2g: Yield 58%, m.p. 202°; ^{1}H NMR ($CDCl_3$): δ 7.28-8.42 (m, 7H, phthalazine C_7-H, C_8-H, C_9-H and Ar-H), 8.90-9.03 (m, 2H, phthalazine C_6-H and C_{10}-H); Anal. Found: C, 61.42, H 3.12, N 22.02. Calcd for $C_{13}H_8N_4S$: C 61.90, H 3.17, N 22.22%.

Acknowledgement

We are grateful to Ranbaxy Research Laboratories Ltd and CSIR, New Delhi for financial assistance and RSIC, Chandigarh for providing us spectral facilities.

References

1 (a) Moriarity R M & Prakash O, *Adv Het Chem*, 69, **1998**, 1.
(b) Prakash O, *Aldrichimica Acta*, 28, **1995**, 63.
(c) Prakash O & Singh S P, *Aldrichimica Acta*, 27, **1994**, 15.
(d) Prakash O, Saini N & Sharma P K, *Synlett* (Account), 38, **1994**, 409
(e) Prakash O, Saini N & Sharma P K, *Heterocycles*, 38, **1994**, 221.
(f) Prakash O, Rani N & Goyal S, *J Chem Soc, Perkin Trans 1*, **1992**, 707.
(g) Prakash O & Goyal S, *Synthesis*, **1991**, 629.

2 (a) Singh S P, Prakash O & Kumar D, *J Chem Research (S)*, **1993**, 244.
(b) Prakash O, Singh S P, Saini R K & Kumar D, *Synthetic Commun*, 25, **1995**, 3363.

3 (a) Gvozkjakova A, Habsudova J & Kufcakova K, *Stid Zorg Chem (Amsterdam)*, 35, **1988**, 297; *Chem Abstr*, 110, **1989**, 114741n.
(b) Despande D S, *Acta Cienc India (Soer) chem*, 6, **1980**, 80; *Chem Abstr*, **1981**, 65568b.

4 Faid Allah H A & Raafat Soliman, *J Het Chem*, 24, **1987**, 667.

5 Francis J E, Cash W D, Barbaz B S, Bermard P S, Lovell R A, Mazzemga G C, Friedmann R C, Hyun J L, Braunwalder A F, Loo P S & Bennett D A, *J Med Chem*, 34, **1991**, 281.

6 Gladstone W A F, Aylward J B & Norman R O C, *J Chem Soc C*, **1969**, 2587.

7 Kathawala F G, *US Pat* 3850932, Nov 26, 1974; *Chem Abstr*, 82, **1975**, 140175d.