Rapid Side-chain Chlorination of Heterocyclic Compounds using Focused Microwave Irradiation†

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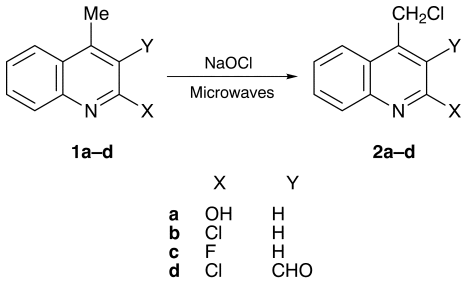
Rapid chlorination of side-chain Me groups of substituted quinolines and 2-mercapto-5-methyl 1,3,4-oxadiazole/thiadiazole is reported using sodium hypochlorite under microwave irradiation.

Presently there is considerable interest in the rapid synthesis of a variety of heterocyclic compounds under microwave irradiation in domestic microwave ovens[1] owing to substantial reduction in reaction times. Halogenoarenes are useful intermediate for industrial as well as laboratory purposes.[2] In continuation of our earlier work on microwave reactions[3–6] we report herein sodium hypochlorite as a selective and cheap reagent for chlorination of side-chain Me groups of 2-hydroxy-4-methyl-2-chloro-4-methyl- and 2-fluoro-4-methyl-quinoline, 2-chloro-4-methylquinoline-3-carbaldehyde and 2-mercapto-5-methyl-1,3,4-oxadiazole/thiadiazole.

2-Hydroxy-4-methylquinoline was prepared[7] by the cyclisation of acetoacetanilide using sulfuric acid; this on treatment with PCl_5–$POCl_3$ afforded 2-chloro-4-methylquinoline which on reaction with potassium fluoride in acetonitrile as a solvent gave 2-fluoro-4-methylquinoline. 2-Chloro-4-methylquinoline-3-carbaldehyde and 2-mercapto-5-methyl-1,3,4-oxadiazole/thiadiazole were prepared according to literature methods.[8,9]

The chlorination of side-chain Me groups of substituted quinolines and 2-mercapto-5-methyl-1,3,4-oxadiazole/thiadiazole has been carried out using microwave irradiation (Scheme 1). The reaction involves free radical monohalogenation[10] without affecting other substituents. All the synthesized compounds except **2b**[11] are new and are characterised by physical and spectral data. ^{1}H NMR of compounds **1e**,**f** showed a signal at δ 13.25 due to SH which was exchangeable with D_2O indicating that the compounds are not dehydrodimerised at sulfur. Quinoline **1a** and its chlorination product **2a** exist in the hydroxy tautomeric form and a peak at δ 5.00 confirms the presence of OH. The domestic multimode microwave oven confines the microwaves to the reaction vessel only and excess microwaves are absorbed by a dummy load,[12] hence leading to focused microwaves.



Scheme 1

Experimental

Physical data for the new compounds are listed in Table 1. Mps (uncorrected) were recorded on an electrothermal apparatus. IR (KBr) were recorded on a Model 599 Perkin-Elmer spectrophotometer and ^{1}H NMR were recorded on a Hitachi R-600 FT spectrophotometer using $SiMe_4$ as internal standard. Mass spectra were recorded on a JEOL-JMS-DX 303 mass spectrophotometer. Spectral data for the new compounds are listed in Table 2. The purities of the compounds were checked on silica coated A1 plates (Merck).

General procedure for the chlorination of side-chain methyl groups of various substituted quinolines and 2-mercapto-5-methyl-1,3,4-oxadiazole/thiadiazole.—To a solution of 5–8 ml sodium hypochlorite (0.03 mol) in a 100 ml conical flask were added appropriate substituted quinolines or 2-mercapto-5-methyl-1,3,4-oxadiazole/thiadiazole (0.01 mol). The reaction mixture was placed under focused microwaves in an unmodified domestic microwave oven at 2450 MHz. A dummy load of water was also introduced. TLC was run every 30 s to check the progress of the reaction. Once the reaction was complete the reaction mixture was poured into water. The solid obtained was filtered off, washed with water and dried to give the product.

Table 1 Physical data for the new compounds

Compound	Formula	% Yield (time/min)	Elemental analysis [Found (calc.) %] C	H	N	Mp
2a	$C_{10}H_8ClNO$	92 (2.0)	62.04 (62.01)	4.18 (4.13)	7.26 (7.23)	150
2b	$C_{10}H_7Cl_2N$	93 (2.5)	56.63 (56.60)	3.28 (3.30)	6.57 (6.60)	83
2c	$C_{10}H_7ClFN$	96 (2.3)	61.40 (61.38)	3.54 (3.58)	7.20 (7.16)	60
2d	$C_{11}H_7Cl_2NO$	90 (2.5)	54.80 (55.00)	2.93 (2.91)	5.81 (5.83)	120
2e	$C_3H_3ClN_2SO$	95 (1.3)	23.94 (23.92)	2.00 (1.99)	18.57 (18.60)	230
2f	$C_3H_3ClN_2S_2$	89 (1.5)	21.60 (21.62)	1.76 (1.80)	16.80 (16.81)	220

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Table 2 Spectral data for the new compounds

Compound	IR (ν_{max}/cm^{-1})	^{1}H NMR (δ)
2a	790 (C–Cl), 3400 (OH)	2.95 (s, 2 H, 4-CH_2Cl), 5.00 (br, 1 H, OH), 7.00–7.90 (m, 5 H, Ar-H)
2b	795 (C–Cl)	2.96 (s, 2 H, 4-CH_2Cl), 7.12–8.0 (m, 5 H, Ar-H)
2c	790 (C–Cl)	2.96 (s, 2 H, 4-CH_2Cl), 7.10–8.02 (m, 5 H, Ar-H)
2d	795 (C–Cl), 1680 (CO str.)	3.08 (s, 2 H, 4-CH_2Cl), 7.25–8.35 (m, 4 H, Ar-H), 10.35 (s, 1 H, CHO)
2e	795 (C–Cl), 1520 (C=N)	2.96 (s, 2 H, 5-CH_2Cl), 13.2 (s, 1 H, 2-SH)
2f	790 (C–Cl), 1530 (C=N)	2.94 (s, 2 H, 5-CH_2Cl), 13.2 (s, 1 H, 2-SH)

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References

1 S. Caddick, *Tetrahedron*, 1995, **51**, 10403.
2 *Speciality Chemicals*, ed. B. Pearson, Elsevier Applied Science, London, 1991, pp. 15–93.
3 M. Kidwai and P. Kumar, *J. Chem. Res.* (*S*), 1996, 254.
4 M. Kidwai, P. Kumar and S. Kohli, *J. Chem. Res.* (*S*), 1997, 24.
5 M. Kidwai, S. Kohli and P. Kumar, *J. Chem. Res.* (*S*), 1998, 52.
6 M. Kidwai, K. R. Bhushan, P. Kumar and R. Kumar, *Monatsh. Chem.*, 1997, **128**, 1291.
7 M. Kidwai, *Chem. Educ.*, 1993, **4**, 55.
8 O. Meth-Cohn, B. Narine and B. Tarnowski, *J. Chem. Soc., Perkin Trans 1*, 1981, 1520.
9 M. Kidwai, R. Kumar and Y. Goel, *Main Group Met. Chem.*, 1997, **20**, 367.
10 S. Futamura and Z. M. Zong, *Bull. Chem. Soc. Jpn.*, 1992, **65**, 345.
11 K. Otsubo, S. Morita, M. Uchida, K. Yamasaki, T. Kanbe and T. Shimizu, *Chem. Pharm. Bull.*, 1991, **39**, 2906.
12 M. Kidwai, P. Kumar, Y. Goel and K. Kumar, *Indian J. Chem. Sect. B*, 1997, **36**, 175.