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HYPERVALENT IODINE OXIDATION OF 2-METHYL-4-QUINOLONES USING [HYDROXY(TOSYLOXY)IODO]BENZENE : SYNTHESIS OF 2-METHYL-3-IODO-4-PHENOXYQUINOLINES VIA NOVEL MONOCARBONYL IODONIUM YLIDES

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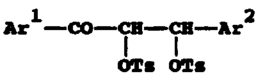
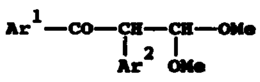
Abstract: Hypervalent iodine oxidation of 2-methyl-4-quinolones using [hydroxy(tosyloxy)iodo]benzene afforded 2-methyl-3-iodo-4-phenoxyquinolines with the intermediacy of isolable α-phenyliodonio tosylates and novel monocarbonyl iodonium ylides.

The application of [hydroxy(tosyloxy)iodo]benzene (HTIB) in organic synthesis has received considerable attention in recent years[1]. Reaction of α,β-unsaturated carbonyl compounds with HTIB in dichloromethane has been shown to provide *vic*-ditosylates 1[2], whereas in methanol as solvent the oxidation proceeds through rearrangement process with the formation of products 2 containing a dimethylacetal function[3]. These observations coupled with our on-going interest in utilizing the iodine (III) reagents[4] prompted us to investigate the reaction of 2-methyl-4-quinolones 3 with HTIB. A preliminary account of this study is presented in this communication.



$\mathrm{Ar^1{-}CO{-}\underset{OTs}{CH}{-}\underset{OTs}{CH}{-}Ar^2}$

1



$\mathrm{Ar^1{-}CO{-}\underset{Ar^2}{CH}{-}\underset{OMe}{CH}{-}OMe}$

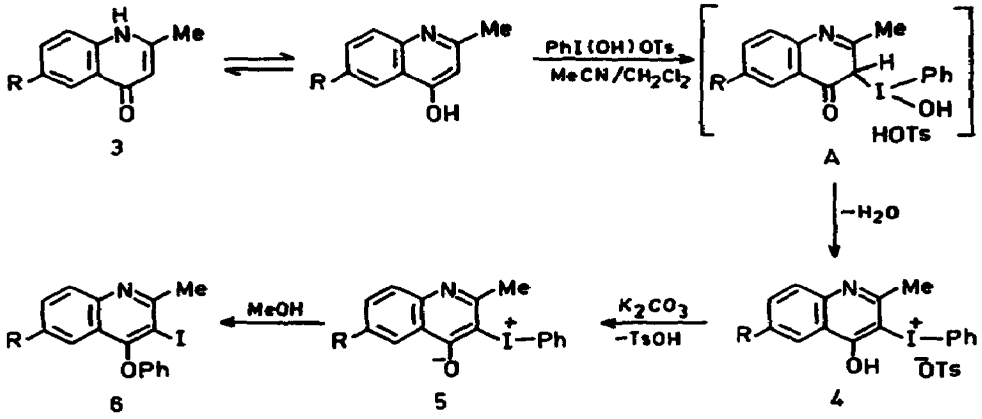
2

Thus treatment of 3a with HTIB in acetonitrile/dichloromethane at room temperature afforded a crystalline solid, identified as α-phenyliodonio tosylate 4a. The tosylate 4a on basification with aqueous potassium carbonate, resulted in the formation of stable novel monocarbonyl ylide 5a, which on refluxing in methanol underwent intramolecular rearrangement thereby yielding 2-methyl-3-iodo-4-phenoxyquinoline 6a. The above reaction sequence was found to be of general applicability as differently substituted quinolones 3b-d were transformed to 4b-d, 5b-d and 6b-d in good yields (Scheme 1).

The plausible pathways for the transformations 3→4→5→6 may be rationalised in the following manner. The conversion 3→4 occurs simply by electrophilic attack of iodine (III) reagent, PhI(OH)OTs at C(3) of 3 with the concomitant dehydroxylation at iodine from resultant intermediate A. This is then followed by the formation of novel iodonium ylides 5 from 4 under the influence of base accompanied by removal of p-toluenesulphonic acid. Finally, production of 6 from 5 may be explained by the migration of phenyl group bound to iodine to the adjacent oxygen in a formal [1,4] sigmatropic transformation.

It is important to mention that iodonium ylides of type 5 belong to monocarbonyl system, which are not well established in the literature, probably because of their instability[5]. However, in the present case, the formation of stable ylides may be accounted for due to increase in resonance stabilization provided by C(2)=N. It may also be noted that the rearrangement process analogous to 5→6 has been observed earlier in iodonium ylides prepared from phenols bearing strongly electron-withdrawing substituent, or cyclic and acyclic β-dicabonyl compounds[6].

The noteworthy features which account for the significance of present investigation are : (i) The synthesis of iodoethers of type 6, which have further synthetic use and otherwise difficult to obtain, has been accomplished involving simple experimentation starting from easily available quinolones 3. (ii) Ready access of 6 from the present approach may provide a convenient procedure for the synthesis of new 2-methyl analogues of reversible inhibitor of gastric (H^+/K^+) ATPase, i.e., 3-butyryl-4-[(2-methylphenyl)amino]-8-methoxyquinoline, which is currently undergoing clinical trials[7]. It also serves as an excellent precursor for obtaining benzofuroquinoline by photolysis in one step[8] than involving multisteps as reported earlier[9]. Interestingly, these benzofuroquinolines (analogues of furoquinoline alkaloids) are claimed as mutagens, carcinogens and antitumour substances[9]. (iii) Monocarbonyl ylides 5 having quinoline moiety, obtainted from this study are novel compounds. (iv) The intermediates 4 and 5 may be useful precursors for synthesizing various interesting products by nucleophilic displacements. Further investigations dealing with the scope of this study, properties and applications of the products 6 are under progress. The results relevant to this studies will be reported in our full paper.



a; R=H, b; R=Me, c; R=OMe, d; R=Cl

Scheme 1

Table 1. Compounds 4-6 Prepared According to Scheme-1.

Compounds[10]	m.p. (°C)	Yield[a] (%)	Compounds[10]	m.p. (°C)	Yield[a] (%)
4a	184-185	85	5c	85-86	85
4b	161-162	82	5d	153-155	92
4c	175-176	80	6a	159-161	72
4d	178-179	90	6b	145-146	72
5a	138-140	88	6c	129-131	70
5b	128-129	89	6d	154-155	75

[a] yields are based on isolated crystalline products : 4, 5, 6 with respect to 3, 4, 5 used.

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References and Notes

1. Moriarty, R.M.; Vaid, R.K.; Koser, G.F. *Synlett.*, **1990**, 365-383.
2. Rebrovic, L.; Koser, G.F. *J.Org.Chem.*, **1984**, 49, 2462-2472.
3. Moriarty, R.M.; Khosrowshahi, J.S.; Prakash, O. *Tetrahedron Lett.*, **1985**, 26, 2961-2964.
4. (a) Prakash, O.; Tanwar, M.P.; Goyal, S.; Pahuja, S. *Tetrahedron Lett.* **1992**, 33, 6519-6522; (b) Prakash, O.; Rani, N.; Goyal, S. *J.Chem.Soc.,Perkin Trans. I,* **1992**, 707-709; (c) Kumar, D.; Prakash, O.; Singh, S.P. *J.Chem.Res.(S),* **1993**, 244-245; (d) Moriarty, R.M.;Prakash, O.; Vaid, R.K.; Zhao, L. *J.Am.Chem. Soc.,* **1989**, 111, 6443-6444.
5. Only monocarbonyl ylide of type $CF_3CON{=}I{-}Ph$ is known in literature : (a) Mansuy, D.; Mahy, J.; Dureault, A.; Bedi, G.; Battioni, P. *J.Chem.Soc.,Chem.Commun.*, **1984**, 1161-1163.; (b) Lazbin, I.M.; Koser, G.F. *J.Org Chem.*, **1987**, 52, 476-477.
6. Koser, G.F. *Hypervalent Halogen Compounds* in *The Chemistry of Functional Groups* Supplement D; Patai, S.; Rappoport, Z., Eds.; Wiley, Chichester, **1983**, pp. 774-806.
7. Ife, R.J.; Brown, T.H.; Keeling, D.J.; Leach, C.A.; Meason, M.L.; Parsons, M.E.; Reavill, D.R.; Theobald, C.J.; Wiggall, K.J. *J.Med.Chem.*, **1992**, 35, 3413-3422.
8. We have obtained 6-methylbenzofuro[3,2-c]quinoline m.p. 134-135°C (lit.[9] m.p. 132-133°C) by the photolysis of **6a** in benzene using 450 watt UV lamp.
9. (a) Yamaguchi, S.; Tsuzuki, K.; Kinoshita, M.; Oh-hira, Y.; Kawase, Y. *J.Heterocyclic Chem.*, **1989**, 26, 281-284; (b) Kawase, Y.; Yamaguchi, S.; Maeda, O.; Hayashi, A.; Hayashi, I.; Tabata, K.; Kondo, M. *J.Heterocyclic Chem.*, **1979**, 16, 487-491.
10. (a) All the compounds were characterised by their elemental analysis, IR and ^{1}H NMR spectra ; (b) HRMS data : **6a**, $M^{\dot{+}}$ m/z 360.9962(74), 234.0915(100); **6b**, $M^{\dot{+}}$ m/z 375.0124(73),248.1087 (100); **6c**, $M^{\dot{+}}$ m/z 391.0046(100), 264.1070(34); **6d**, $M^{\dot{+}}$ m/z 394.9550/396.9567(85/29), 268.0429/270.0432(100/33).

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