Pergamon

Tetrahedron Letters 39 (1998) 1839–1842

TETRAHEDRON
LETTERS

Applications of Free and Resin-bound Novel (Trifluoromethyl)dioxiranes

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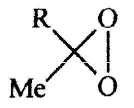
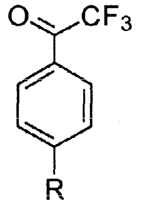
Received 12 November 1997; revised 22 December 1997; accepted 9 January 1998

Abstract: Recyclable resin-bound and other trifluoromethyl aryl ketones are efficient catalysts for oxone® mediated epoxidations.

Dioxiranes are important powerful and environmentally safe oxidants which may be generated *in situ*[1] or isolated in solution, in some cases, notably dimethyldioxirane (1) and methyl(trifluoromethyl)dioxirane (2).[2,3,4]



(1) R= Me
(2) R= CF_3



(3) R= H (5) R= CO_2CH_3
(4) R= CO_2H (8) R= COCl

Methyl(trifluoromethyl)dioxirane (2) is a more powerful oxidant and is available in more concentrated solutions than dimethyldioxirane[4] and may also be effectively generated from Oxone® ($2KHSO_5$. $KHSO_4$. K_2SO_4) *in situ* using acetonitrile/water as the medium.[1f] However, in the conventional biphasic system (methylene chloride/water) hydrophilicity is reported to be important and 1,1,1-trifluoroacetone is not a very effective catalyst for Oxone®-mediated reactions.[1e] Furthermore, 1,1,1-trifluoroacetone is relatively expensive and not readily recyclable owing to its volatility. In continuation of our own interest in this area[5] and to explore further the reactivity of fluoroketones as oxidation catalysts, we report here the use of trifluoromethyl aryl ketones (3-7) as effective and recyclable catalysts. In particular, we have been able to prepare re-usable solid phase catalysts by attaching 4-(trifluoroacetyl)benzoic acid to suitably functionalised resins. A recent report[6] of the preparation of a polystyrene-bound methyldioxirane prompts us to report these findings.

We have investigated trifluoroacetophenone (3),[7] 4-(trifluoroacetyl)benzoic acid (4),[8] methyl 4-(trifluoroacetyl)benzoate (5),[9] and the resin-bound esters (6) and (7) as catalysts in Oxone®-mediated epoxidations. We found that the methyl ester (5) was best prepared by heating the acid with MeOH/PTSA rather than by the reported[9] reaction with diazomethane. The resin-bound ester (6) was prepared by reaction

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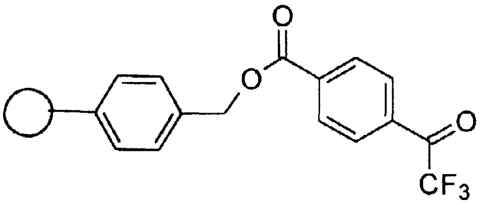
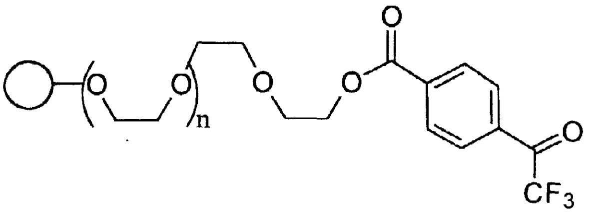
PII: S0040-4039(98)00101-4

of the hydroxy methyl resin[10] with the acid chloride (8) prepared from the acid (4) by reaction with oxalyl chloride/DMF. The alternative resin (7) was prepared by reaction of TentaGel S-Br[10] with the acid (4) under Merrifield conditions.[11] The attachments of the 4-(trifluoroacetyl)benzoyl group to the resins were confirmed through IR spectra and by isolation of the acid from the resin by treatment of the resin with trifluoroacetic acid in ethyl acetate.

(6)



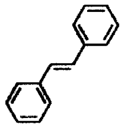
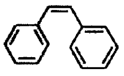
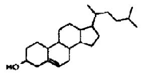
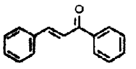
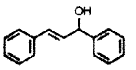
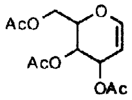
(7)



The evaluation of the trifluoromethyl aryl ketones (3-7) as catalysts was carried out either in acetonitrile/water and/or methylene chloride/water/phase transfer catalyst (Table 1). Solvent ratios and sodium bicarbonate concentrations were similiar to those employed by Yang and co-workers.[1f] In general, acceptable or high conversions were observed and in two examples no significant difference was noted between reactions at 0°C and room temperature. Although as observed, *trans*-chalcone would be expected to be relatively unreactive, this result contrasts with that of earlier work using (2).[1f] 4-(Trifluoroacetyl)benzoic acid (4) proved to be less effective in general in methylene chloride/water presumably owing, in part, to its relatively high solubility in the aqueous phase. Similiar solubility effects have been reported by Denmark.[1e] Some of the epoxidation activity of (4) may arise from the presence of the carboxylic acid which may be converted to the peracid with Oxone®. In fact, as indicated in the Table, 4-chlorobenzoic acid did show some activity with *trans*-stilbene in acetonitrile/water.

It did not seem likely to us that a polymer-bound trifluoromethyl dioxirane would be sufficiently stable to be stored and treatment of the resin bound esters (6) and (7) with Oxone® in tetrahydrofuran/water/sodium hydrogen carbonate as reported[6] for 2-oxoalkyl resins did not provide an oxidatively active resin in either case. The resin-bound esters (6) and (7) were, however, re-usable many times as *in situ* catalysts and the 4-trifluoroacetyl)benzoic acid was readily isolated for re-use by simple base-extraction (recovery *ca* 60% not optimised).

Table 1: Oxidation of various alkenes by *in situ* generation of dioxiranes[a]

Substrates	Tentagel S-Br (7)[1b]	hydroxymethyl resin (6)[1c]	trifluoro-acetophenone (3)[d]	4-(trifluoroacetyl)-benzoic acid (4)[d]	methyl 4-(trifluoroacetyl)-benzoate (5)[d]
 *Trans*-Stilbene[g]	48hrs = 97%	17hrs = 41% 36hrs = 64%	24 hrs = 70%[1] 24 hrs = 32%[2] 24 hrs = 23%[2f]	24 hrs = 81%[1] 24 hrs = 11%[2] 24 hrs = 53%[2e] <u>4-chlorobenzoic acid</u>: 12 hrs = 20%[1]	24 hrs = 91%[1] 24 hrs = 98%[2]
 *Cis*-Stilbene[g]	48hrs = 61%	38hrs = 51%	24 hrs =100%[1] 12 hrs = 77%[2]	24 hrs = 100%[1] 48 hrs = 36%[2]	24 hrs = 97%[1] 24 hrs = 99%[2]
 Cholesterol[h]	48hrs = 76% 48hrs = 70%[f]	48hrs = 37%	24 hrs = 52%[1] 24 hrs = 76%[2]	24 hrs = 100%[1] 24 hrs = 69%[2]	24 hrs = 72%[1] 24 hrs = 100%[2]
 *Trans*-Chalcone[g]	48hrs = 13%	48hrs = 9%	24 hrs = 11%[1] 24 hrs = 11%[2]	24 hrs = 34%[1] 24 hrs = 21%[2]	24 hrs = 7%[1] 24 hrs = 8%[2]
 *Trans*-Chalcol[h]	48hrs=>90%		24hrs = 100%[1]	24hr = 100%[1]	24hrs = 100%[1]
 Tri-O-acetyl-glucal[h]	48hrs = 80%		24hrs = 100%[1]	24hr = 100%[1]	24hrs = 100%[1]
 Cyclohexene[g]			24 hrs = 38%[1] 12 hrs = 55%[2]	24 hrs = 5%[1] 12 hrs = 65%[2]	24 hrs = 0%[1] 12 hrs = 98%[2]

1) reactions were run in 10ml of a 1.5:1 acetonitrile/EDTA solution (4X10^{-4}M), 1eq of alkene, 15.5eq of NaHCO$_3$ and 5eq of Oxone® at room temperature; 2) As in (1) with a catalytic amount of tetrabutylammonium hydrogen sulphate and dichloromethane rather than acetonitrile; a) results are expressed as percentage composition of epoxide isolated in alkene/epoxide reaction mixtures: on average, blanks gave < 5% of epoxide; in the reactions of stilbenes in acetonitrile/water, blanks gave up to 10% epoxide; b) 2eq of resin based on reported maximum loading[10]; c) 6eq of resin based on reported maximum loading[10]; d) 5eq of ketone; e) 2eq of tetrabutylammonium hydrogen sulphate; f) reactions were run at 0°C; g) product compositions were obtained from GLC analysis of the crude reaction mixture; h) product compositions were obtained from NMR analysis of the crude reaction mixture.

Acknowledgements. We thank SmithKline Beecham and Loughborough University for Finanical support, the EPSRC for spectroscopic services and Dr. S.M. Allin for a sample of Tentagel S-Br.

References

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1. a) Curci, R. "Advances in Oxygenated Processes", Baumstark, A.L., Ed.; Greenwich, CT, 1990; Vol. 2, Chapter 1. pp. 1-5. b) Adam, W. *Topics in Current Chemistry*, **1993**, *164*, 45 c) Murray, R.W. *Chem. Rev.*, **1989**, *89*, 1187. For more recent examples see: d) Kurihara, M.; Ito, S.; Tsutsumi, N.; Miyata, N. *Tetrahedron Lett.*, **1994**, *35*, 1577. e) Denmark, S.E.; Forbes, D.C.; Hays, D.S.; DePue, J.S.; Wilde, R.G. *J.Org.Chem.*, **1995**, 60, 1391. f) Yang, D.; Wong, M.K.; Yip, Y.C. *J.Org.Chem.*, **1995**, *60*, 3887. g) Wang, Z.X.; Tu, Y.; Frohn, M.; Shi, Y. *J. Org. Chem.*, **1997**, *62*, 2328.
2. Murray, R.W.; Jeyaramann, R. *J.Org.Chem.*, **1985**, *50*, 2847.
3. Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J.Am.Chem.Soc.*, **1989**, *111*, 6749.
4. a) Mello, R.; Fiorentino, M.; Sciacovelli, O.; Curci, R. *J.Org.Chem.*, **1988**, *53*, 3890. b) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J.Am.Chem.Soc.*, **1989**, *111*, 6749. c) Mello, R.; Cassidei, L.; Fiorentino, M.; Fusco, C.; Curci, R. *Tetrahedron Lett.*, **1990**, *31*, 3067. d) Altamura, A.; Fusco, C.; D'Accolti, L.; Mello, R.; Prencipe, T.; Curci, R. *Tetrahedron Lett.*, **1991**, *32*, 5445.
5. Brown, D.S.; Marples, B.A.; Smith, P.; Walton, L. *Tetrahedron*, **1995**, *51*, 3587.
6. Shiney, A.; Rajan, P.K.; Sreekumar, K. *Polymer International*, **1996**, *41*, 377.
7. Trifluoroacetophenone has been reported as a catalyst in the oxidation of sulphides in the presence of bovine serum albumin (Colonna,S.; Gaggero, N.; Leone, M. *Tetrahedron Lett.*, **1991**, *47*, 8385.) and preliminary results have been reported in these laboratories for its use in epoxidation (Muxworthy, J.P. *Synthetic and Mechanistic Aspects of Dioxirane Chemistry*, Ph.D. Thesis, Loughborough University, 1992).
8. 4-(Trifluoroacetyl) benzoic acid was supplied by Lancaster and was also synthesised by the published procedure (Chen, L.S.; Chen, G.J.; Tamborski, C. *Journal of Organometallic Chemistry*, **1983**, *251*, 139).
9. Fujisawa, T.; Ichikawa, K.; Shimizu, M. *Tetrahedron: Asymmetry*, **1993**, *4*, 1237.
10. The hydroxymethyl resin [01-64-0110] was obtained from Novabiochem with a reported loading of 1.16mMols/g; isolation of the acid from the resin showed that the resin was in fact 33% substituted. The TentaGel S-Br resin [O-(2-Bromoethyl)polyethylene glycol polymer bound] is available from Fluka with a reported loading of ≈ 0.26 mmol Br/g; isolation of the acid from the resin showed that the resin was in fact 50% substituted.
11. Merrifield, R.B. *J.Am.Chem.Soc.* , **1963**, *83*, 2149.