Facile Syntheses of *gem*-Difluoroalkenes from Chlorodifluoromethylketones

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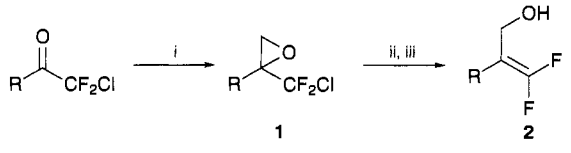
Chlorodifluoromethyl ketones reacted with diazomethane to afford epoxides in high yield; upon treatment with butyllithium, the epoxides underwent efficient ring opening to afford 3,3-difluoro-2-alkyl-alken-1-ols, suitable substrates for sigmatropic rearrangement leading to compounds containing a CF_2 group in mid-chain.

Consistent with our general interest in the chemistry of functionalised difluoroalkenes,[1] we have developed a new method for the preparaton of geminally dialkylated difluoroalkenes. We,[1] and others,[2] have shown that difluoroenol derivatives can be made from trifluoroethanol by dehydrofluorination–metallation sequences. However, few general approaches to geminal or 1,1-difluoro-2,2-dialkylalkenes have appeared in the literature. Ishihara and coworkers[3] transformed aryl chlorodifluoromethyl ketones to *gem*-dialkyl difluoroalkenes *via* the corresponding difluoroenol phosphates. These underwent an addition–elimination reaction with Gilman reagents, thus introducing an alkyl substituent. An alternative ylide-based approach starting from dibromodifluoromethane was described by Burton and coworkers.[4] However, applications to functionalised systems are limited and low yields of products are often obtained.[5]

Recently, the dechlorinative ring opening of chlorodifluoromethyl epoxides was shown to lead to the formation of difluoroallylic alcohols in high yield.[6] We anticipated that a modification of the published route would lead to the less accessible title compounds. Readily available chlorodifluoromethyl ketones[7] reacted efficiently with diazomethane in diethyl ether at ambient temperature (Scheme 1),[8] allowing the isolation of a range of epoxides **1** (Table 1), setting the stage for the ring opening reaction. We found that the reagent of choice



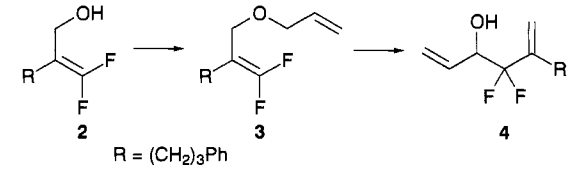
1 2

Scheme 1 *Reagents and conditions*: i, CH_2N_2, diethyl ether, 25 °C; ii, 1.1 equiv. BuLi, THF, −78 °C, 5 min; iii, NH_4Cl, MeOH, −78 °C

Table 1

R		Yield[a] **1** (%)	Yield[a] **2** (%)
a	$Ph(CH_2)_3$	90	80
b	$Ph(CH_2)_2$	88	82
c	$PhCH_2$	85	75
d	Ph	65[b]	70
e	$Me(CH_2)_6$	80	80
f	cyclohexyl$(CH_2)_2$	85	78

[a] Yields refer to chromatographically pure compounds. [b] The ketone reacted very slowly with diazomethane. Three sequential treatments were required to obtain the quoted yield.



2 3 4

R = $(CH_2)_3Ph$

Scheme 2 *Reagents and conditions*: i, allyl bromide, 50% $NaOH_{(aq)}$, Bu_4NHSO_4 (cat.), 25 °C, 18 h; ii, 2.0 equiv. LDA, THF, −78 °C, 2 h then −30 °C, 18 h

for initiating the ring opening reaction was butyllithium (1.1 equiv.).† The allylic alcohol products **2** are attractive because of their potential for further transformation by way of sigmatropic rearrangement.[9] For example, **2a** [R=$(CH_2)_3Ph$] was converted to allyl ether **3** (60%, unoptimised) which underwent [2,3]-Wittig rearrangement[10] following treatment with LDA (Scheme 2) resulting in the formation of **4** in high (81%) yield.

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Footnote

† In a typical procedure, butyllithium (0.45 ml of a 2.45 mol dm^{-3} solution in hexanes) was added to a cold (−78 °C) solution of epoxide **1a** (0.25 g, 1 mmol) in anhydrous THF (15 ml). The orange solution was stirred for 5 min then quenched with saturated methanolic ammonium chloride solution at −78 °C. The reaction mixture was poured into saturated ammonium chloride solution (25 ml) and extracted with diethyl ether (3 × 70 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo* to afford a pale yellow oil. Flash chromatography (silica gel, 5% *v/v* diethyl ether in pentane) afforded alcohol **2a** (0.19 g, 90%), ν_{max} (film) 1720 cm^{-1} (C=C); δ_H ($CDCl_3$, 200 MHz) 7.40–7.20 (5 H, m, Ar–H), 4.15 (2 H, s, CH_2OH), 2.70 [2 H, t, J = 7.8 Hz, $CH_2(CH_2)_2$], 2.50 (1 H, s, OH), 2.20–2.06 (2 H, m, CH_2Ph) and 1.90–1.75 (2 H, m, $CH_2CH_2CH_2$); δ_C ($CDCl_3$, 200 MHz) 154.5 (t, $^1J_{CF}$ 286.2 Hz), 142.1, 128.6, 126.2, 90.1 (t, $^2J_{CF}$ 14.7 Hz), 57.5 (t, $^3J_{CF}$ 5.0 Hz), 35.6, 29.4 ($^1J_{CF}$ 2.3 Hz) and 24.5; δ_F ($CDCl_3$, 400 MHz) −91.05 (d, $^2J_{FF}$ 47 Hz) and −92.05 (d, $^2J_{FF}$ 47 Hz).

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