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# The Use of Homochiral 2-Methylene-4,5-diaryl-1,3-dioxolanes as Recyclable Acetic Ester Enolate Equivalents: Asymmetric Synthesis of Terpenoids

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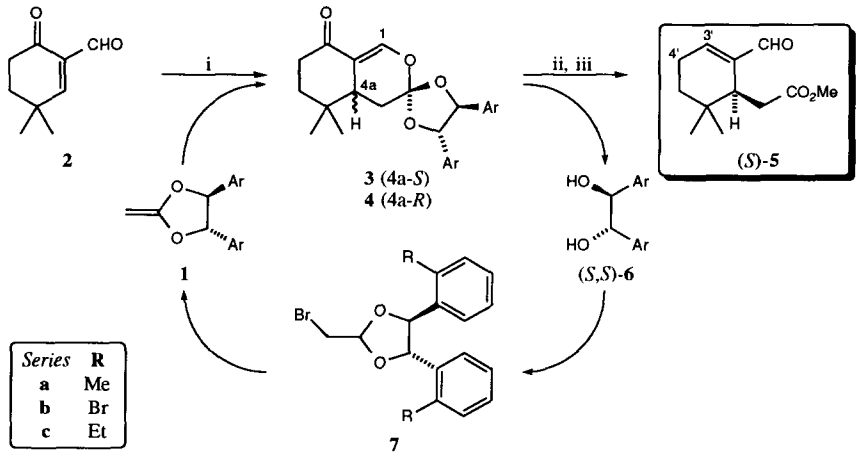
**Abstract:** The α-cyclocitral derivatives **5** and **10** are accessible in homochiral form *via* an auxiliary-based sequence using the heterodiene cycloaddition of a 2-methylene-4,5-diaryl-1,3-dioxolane **1** to 2-formyl-4,4-dimethyl-2-cyclohexen-1-one **2** as the key step.


The conjugate addition of an acetic ester enolate to an α,β-unsaturated carbonyl function is a useful synthetic manoeuvre, and we recently described an auxiliary-based variant of this process utilising as the key step the diastereoselective heterodiene cycloaddition of a formyl-activated enone to a $C_2$-symmetric ketene acetal derived from a homochiral 1,2-diarylethane-1,2-diol.[1] The major cycloadduct can be isolated and transformed into the conjugate addition product with simultaneous release of the auxiliary diol, which can be recycled. Herein we describe the application of such a sequence (Scheme 1) to the preparation of some functionalised α-cyclocitral derivatives, which we required in connection with the synthesis of various terpenoids.




**SCHEME 1** *Reagents:* i, see Table 1; ii, L-Selectride®, THF, then $H_2O$ (77%); iii, NaOMe, MeOH (68%).

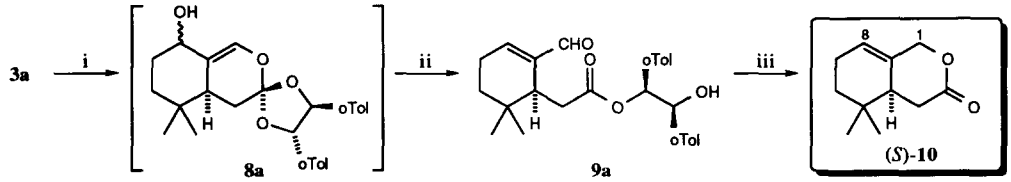
The *bis*(*o*-tolyl) system **1a** was the most effective of three ketene acetals examined (Table 1[2]), the diol **6a** being available in both enantiomeric forms[1] and giving crystalline intermediates throughout the sequence. Thus, stirring a tetrahydrofuran (THF) solution of the dioxolane **1a**[1] and an equivalent of the aldehyde **2**[3] for 3–4 days at room temperature, followed by evaporation and flash chromatography, gave the mixed cycloadducts **3a** and **4a** in >85% yield; crystallisation from ether gave a single diastereoisomer **3a**. The ketene acetals **1b** and **1c** were more selective than **1a**, but they were less easily prepared and crystallisation of their adducts was not efficient.

| Entry | Ketene acetal | Scale mmol | Reaction Temp. °C | Time h | Total yield 3 + 4 (%) | Major product | Ratio 3 : 4 | Isolated yield of 3 (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | **1a** | 7 | 20 | 96 | 86 | **3a** | 3.3 : 1 | 55 |
| 2 | **1a** | 27 | 20 | 65 | 89 | **3a** | 3.4 : 1 | 57 |
| 3 | **1a** | 7 | –28 | 96 | 44 | **3a** | 4.5 : 1 | 24 |
| 4 | **1b** | 0.4 | 20 | 96 | 70 | **3b** | 4.6 : 1 | 9 |
| 5 | *ent*-**1c** | 0.03 | 0 | 72 | 42 | *ent*-**3c** | 5.5 : 1 † | – |

† Ratio refers to *ent*-**3c** : *ent*-**4c**; the major product was not isolated in this case.

TABLE 1.[2] CYCLOADDITIONS OF KETENE ACETALS 1 TO THE ALDEHYDE 2

Reduction of the cycloadduct **3a** gave an epimeric mixture of alcohols **8a**, which readily rearranged to the ester **9a** (Scheme 2). The latter was converted into the ester–aldehyde **5** or the lactone **10** *via* transesterification or reduction respectively, with concomitant release of the auxiliary diol (*S,S*)-**6a** (recovery 70–95%) with an optical purity better than 98% [as indicated by 300 MHz $^1$H NMR analysis in the presence of Pr(hfc)$_3$[1]].




SCHEME 2 (oTol = 2-MeC$_6$H$_4$) *Reagents:* i, L-Selectride®, THF (70%); ii, p-TsOH, $CH_2Cl_2$ (75%); iii, NaBH(OAc)$_3$, PhMe, 80 °C, 40 min, then aq. HCl, 20 °C, 2 d (80%).

The development and application of the above and analogous sequences will be described in due course. We thank the EPSRC for financial support (Postdoctoral Fellowship grant no. GR/G13822), and are grateful to Ruth Howard and Mike Stuckey for their assistance with mass and NMR spectroscopy respectively.

## REFERENCES AND NOTES

1. Wallace, T.W.; Wardell, I.; Li, K.-D.; Leeming, P.; Redhouse, A.D.; Challand, S.R. *J. Chem. Soc., Perkin Trans. I* **1995**, 2293.
2. Yields refer to isolated material with spectra and analytical data consistent with the structures depicted. The stereochemical assignment for **3** is based on the mechanistic model proposed in ref. 1. The **3**:**4** ratios were estimated by $^1$H-n.m.r. spectroscopy. Characteristic data (all $\delta_H$ at 300 MHz, $CDCl_3$): **3a**, m.p. 167–169 °C (ether), $[\alpha]_D^{20}$ +132° (*c* 1.0, acetone), δ 5.57 (1 H, d, *J* 9.1 Hz, 4'- or 5'-H), 5.26 (1 H, d, *J* 9.1 Hz, 5'- or 4'-H), 1.76, 1.65 (each 3 H, s, ArMe), 1.11, 0.93 (each 3 H, s, 5-Me); **4a**, δ 5.39 (1 H, d, *J* 9.1 Hz, 4'- or 5'-H); **3b**, m.p. 209–210 °C (chloroform - petroleum), $[\alpha]_D^{20}$ –9° (*c* 0.34, acetone), δ 7.63 (1 H, d, *J* 2.5 Hz, 1-H); **4b**, δ 7.54 (1 H, d, *J* 2.5 Hz, 1-H); **3c** + **4c**, δ 7.66 (0.83 H, d, *J* 2.4 Hz, 1-H of **3c**), 7.57 (0.17 H, d, *J* 2.3 Hz, 1-H of **4c**); (*S*)-**5a**, oil, $[\alpha]_D^{20}$ –69° (*c* 0.61, acetone); δ 9.40 (1 H, s, C*H*O), 6.79 (1 H, t, *J* 3.5 Hz, 3'-H), 3.64 (3 H, s, OMe); (*S,S,S*)-**9a**, m.p. 74–77 °C, $[\alpha]_D^{20}$ +76° (*c* 0.5, acetone), δ 9.40 (1 H, s, C*H*O), 5.95 (1 H, d, *J* 9 Hz, ArC*H*OCO), 5.27 (1 H, d, *J* 9 Hz, ArC*H*OH), 1.78, 1.73 (each 3 H, s, ArMe), 0.90, 0.87 (each 3 H, s, 6'-Me); (*S*)-**10a**, oil, $[\alpha]_D^{21}$ –46° (*c* 0.5, acetone), δ 5.69 (1 H, br s, 8-H), 4.70 (1 H, dd, *J* 1, 13 Hz, 1-H), 4.59 (1 H, dd, *J* 1, 13 Hz, 1-H), 2.66 (1 H, dd, *J* 10.5, 19.5 Hz, 4-H), 0.96, 0.77 (each 3 H, s, 5-Me).
3. Liotta, D.; Barnum, C.; Puleo, R.; Zima, G.; Bayer, C.; Kezar, H.S. *J. Org. Chem.* **1981**, *46*, 2920.

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