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A STRATEGY TO 3-ACYL-4-METHYL FURANS. SYNTHESIS OF (±)-EVODONE

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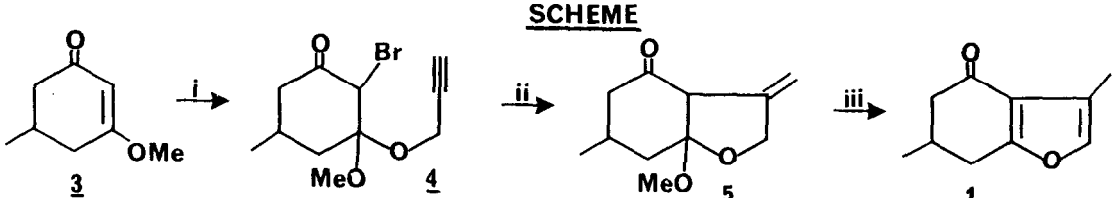
Abstract: Synthesis of Evodone 1 via the radical cyclisation of the bromoacetal 4 to methylene tetrahydrofuran 5 is described.

Evodone (1), a furanomonoterpene isolated from Evonia hortensis Forst., contains 3-acyl-4-methyl furan unit,[1,2] a structural moiety frequently encountered in terpenoids. In this communication, we now describe the synthesis of 1 starting from 5-methyl cyclohexane-1,3-dione (2)[3] based on radical cyclisation reaction.[4] This in turn provides a general methodology to 3-acyl-4-methyl furans from 1,3-dicarbonyl compounds.

The synthetic sequence is depicted in the Scheme 1. Enol ether 3, obtained by treatment of 2 with diazomethane or trimethyl orthoformate in presence of toluene-p-sulfonic acid (PTSA), was brominated with N-bromo succinimide (NBS) in propargyl alcohol-methylene chloride medium at ice temperature to furnish the key radical precursor 4 in ~60% yield. The radical cyclisation of 4 was carried out by refluxing a 0.02 M solution in benzene with 1.2 equiv. of tributyltinhydride[5] in presence of a catalytic amount of azobisisobutyronitrile (AIBN) to generate the 4-methylene tetrahydrofuran 5, which is too labile to purify. Compound 5 was directly aromatised, using a catalytic amount of PTSA in benzene at room temperature for 15 min, to Evodone 1 (45% from 4), which exhibited spectral data identical to those reported in the literature.[2]

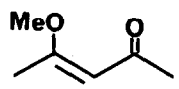
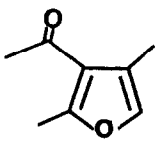
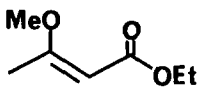
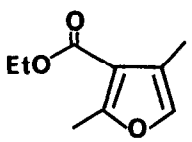
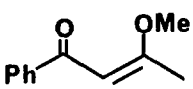
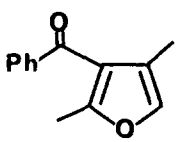
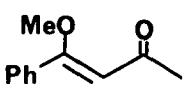
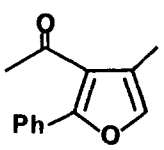
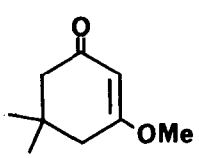
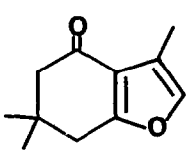
This methodology has been extended to several 1,3-dicarbonyl compounds, both acyclic and cyclic to generate various 3-acyl-4-methyl furans. The results are summarised in table 1.[6] It is interesting to note entries c and d in the table, where mixtures of isomeric furans were formed in the aromatisation step, probably via ring opening and reclosure of intermediates 5c and 5d under acidic conditions.

SCHEME



i. NBS (1.2 eq), $HC{\equiv}C\text{-}CH_2OH$, CH_2Cl_2, 10^oC, 2h; ii. $^nBu_3SnH$(1.2eq), AIBN (cat.), Benzene, 80^oC, 1.5h iii. PTSA (cat.), benzene, 15min.

Table 1: 3-Acyl-4-methyl furans from enol ethers (3).[a]

entry	enol ether(3)	Furan(1)	Yields of 4	Yields of 1
a			85	69
b			84	47
c			85	35[b]
d			87	62[c]
e			60	46

a.Reactions were carried out typically on one mmole scale and yields (not optimised) refer to isolated and chromatographically pure products.
b. contains 4:1 mixture of 1c and 1d. c. Contains 1:1 mixture of 1c and 1d.

References and notes:

1. A.J. Birch and R.W. Richards, Aust. J. Chem., 9, 241 (1956) and references cited therein.
2. P.A. Jacobi, D.G. Walker and I.M.A. Odeh, J. Org. Chem., 46, 2065 (1981) M. Miyashita, T. Kumazawa and A. Yoshikoshi, J. Org. Chem., 45, 2945 (1980) and references cited therein.
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6. Spectral data for 4a(5:2 mixture ofdiastereomers): IR (neat), 1720 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$), δ 4.6&4.54 (1H,s), 4.2&4.18 (2H,d,J=2Hz), 3.3& 3.2 (3H,s), 2.45&2.48 (1H,t,J=2Hz), 2.4&2.36 (3H,s), 1.54&1.55 (3H,s); for 5a: IR (neat),1705, 900, 860 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$), δ 5.1 (2H,brs), 4.6 & 4.4 (2H,ABq,J=13Hz), 3.55 (1H,s), 3.23 (3H,s), 2.18 (3H, s), 1.39 (3H,s); for 1a: IR (neat), 1670 cm^{-1}, ^1H NMR (270 MHz, $CDCl_3$), δ 7.03 (1H,s), 2.55 (3H,s), 2.43 (3H,s), 2.17 (3H,s).

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