

## Reactivity of 2-Methylene-1,3-dicarbonyl Compounds. Inverse Electron-Demand Diels–Alder Reactions with Alkyl Vinyl Ethers

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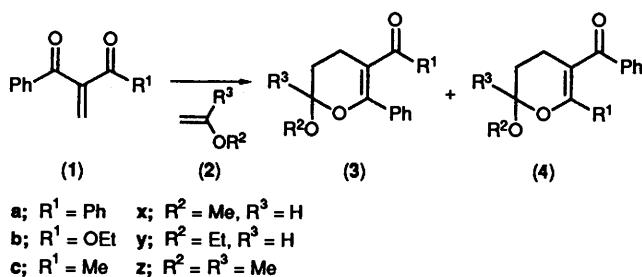
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Highly regioselective hetero-Diels–Alder reactions were achieved by reaction of 2-methylene-1,3-dicarbonyl compounds **1** with alkyl vinyl ethers **2**. This regioselectivity of the cycloadditions was consistent with the results that could be predicted by considering the frontier orbital of **1**.

The cycloaddition reactions of  $\alpha,\beta$ -unsaturated carbonyl compounds as heterodienes are well known and a useful method to prepare dihydropyran derivatives.<sup>1</sup> In general, this hetero-Diels–Alder reaction requires very severe experimental conditions with acyclic or cyclic  $\alpha,\beta$ -unsaturated carbonyl compounds. The introduction of electron-withdrawing groups at the  $\alpha$ -position of the  $\alpha,\beta$ -unsaturated carbonyl compounds would be expected to lower the LUMO energy level,<sup>2</sup> and therefore increase the reactivity of such a heterodiene in the inverse electron-demand Diels–Alder reaction.<sup>3</sup> Although many examples of this have been reported, most reports have been related to cyclic compounds containing at least one carbonyl group in the ring.<sup>4</sup> On the other hand, few examples have been reported with respect to acyclic analogues,<sup>5</sup> and all of these have  $\beta$ -substituents, with the exception of methyl  $\alpha$ -cyanoacrylate.<sup>5c</sup> Because of the instability of 1,1-dicarbonyl ethene,<sup>6</sup> it was used as a reaction intermediate in normal electron-demand Diels–Alder reaction.<sup>7</sup> Recently we reported the synthesis of 1,1-dicarbonyl ethene **1** of which at least one carbonyl group was benzoyl.<sup>8</sup> When the two carbonyl groups on ethene are different this affords an interesting problem: *i.e.* which carbonyl group would serve as the heterodiene. We wish to report the highly regioselective hetero-Diels–Alder reaction of 1,1-dicarbonyl ethene **1** with alkyl vinyl ethers **2**.

### Results

Treatment of 1,1-dicarbonyl ethene **1** with two equivalent of alkyl vinyl ethers **2** in benzene gave 3,4-dihydro-2*H*-pyrans [**3** and/or **4**]. The reaction was exothermic, and so it was necessary to cool the reaction vessel when the solution of alkyl vinyl ether in benzene was added to the solution of dicarbonyl ethene. At ambient temperature a single cycloaddition product was obtained. The reaction product of **1** has the structure **3** or **4** (Scheme 1) and the anomeric protons at C-2 appeared at *ca.*



Scheme 1.

$\delta$  5.0–5.4 in the <sup>1</sup>H NMR spectrum. The small coupling constant ( $J < 3$  Hz) shows that these protons occupy equatorial positions. The adducts with ethyl vinyl ether **2**, when examined

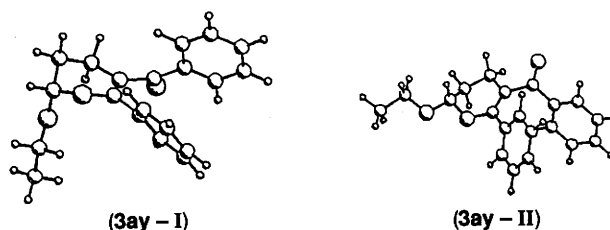


Fig. 1

by <sup>1</sup>H NMR spectroscopy, showed the methylene protons of the ethoxy group at C-2 as a pair of double quartets. As this pattern of **3ay**† in [<sup>2</sup>H<sub>6</sub>]DMSO was not changed at various measuring temperatures (25, 80 and 120 °C), it is not due to restricted rotation around the C–O bond but due to the chiral centre<sup>9</sup> (C-2 position in dihydropyran ring). Molecular mechanics calculations were carried out on the two possible conformers **3ay-I** and **3ay-II** of **3ay** (Fig. 1). The energy-minimized structures of the isomers **3ay-I** and **3ay-II** have strain energies of 43.72 and 46.38 kcal mol<sup>-1</sup> respectively.‡ The dihedral angles ( $\psi$ ) and the calculated coupling constants ( $J$ ) between the anomeric proton and the vicinal axial–equatorial pair of methylene protons are  $\psi_{ee}$  60°,  $J$  2.81 Hz,  $\psi_{ea}$  57°  $J$  3.12 Hz in the more stable conformer **3ay-I** in which the ethoxy group is axial. The observed coupling constants ( $J$  3.5 and 2.5 Hz) correspond with the calculated values.

The structure of the adduct of 1-ethoxycarbonyl-1-benzoyl ethene **1b** with ethyl vinyl ether **2y** was determined by the <sup>1</sup>H NMR spectrum of the lithium aluminium hydride (LAH) reduction product **5**. The singlet due to the methylene proton of the hydroxymethyl group appeared at  $\delta$  4.05. In addition the signals of aromatic protons of the adduct were changed into a broad singlet, which indicated no carbonyl group attached to the benzene ring. From these results, it is clear that the benzoyl carbonyl oxygen is the reactive site.

Finally, the structure of the adduct of 1-acetyl-1-benzoyl ethene **1c** with ethyl vinyl ether **2y** was determined as follows. In the <sup>1</sup>H NMR spectrum of the isomeric alcohol **6**, LAH reduction product of **3cy**, the singlet due to the benzylic proton appears at  $\delta$  5.64. The methyl proton at C-6 position is a split triplet ( $J < 2$  Hz)<sup>10</sup> due to homoallylic coupling with the methylene protons at C-4. The alcohol **4** was so unstable that an attempt to purify **6** by silica gel chromatography gave the keto-aldehyde **7**, produced *via* hydrolysis of acetal and dehydration

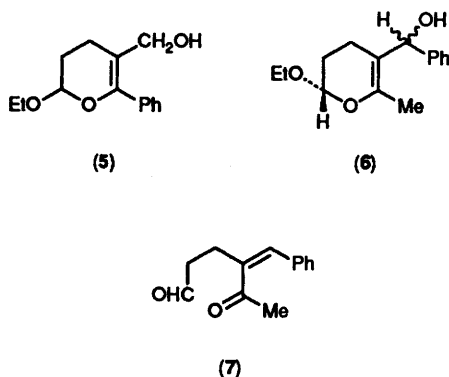
† Although there is no distinction between **3** and **4** in this case, we used **3** as the hetero-Diels–Alder reaction product of 1,1-dibenzoyl ethene with alkyl vinyl ether.

‡ 1 cal = 4.184 J.

**Table 1.** Reaction of 2-methylene-1,3-dicarbonyl compounds with alkyl vinyl ethers.

Run	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Reaction conditions <sup>a</sup>	Yields (%) of adducts	Ratio <sup>b</sup> of 3:4
1	Ph	Me	H	A	98	
2	OEt	Me	H	A	98	100:0
3	OEt	Me	H	B	94	<i>c</i>
4	Me	Me	H	A	96	0:100
5	Me	Me	H	B	95	<i>c</i>
6	Ph	Et	H	A	98	
7	OEt	Et	H	A	99	100:0
8	OEt	Et	H	B	97	<i>c</i>
9	Me	Et	H	A	97	0:100
10	Me	Et	H	B	92	17:83
11	Ph	Me	Me	A	97	
12	OEt	Me	Me	A	98	100:0
13	OEt	Me	Me	B	98	<i>c</i>
14	Me	Me	Me	A	98	0:100
15	Me	Me	Me	B	95	29:71

<sup>a</sup> A; Method A, B; Method B (see Experimental). <sup>b</sup> Ratios refer to pure isolated compounds. <sup>c</sup> Regioisomers were not isolated. Ratios were determined from <sup>1</sup>H NMR spectroscopy.



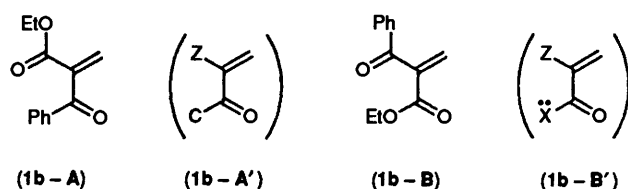
of benzyl alcohol. These suggest that regioselective cyclization took place at the acetyl carbonyl oxygen of two carbonyl groups in **1c**. Furthermore the splitting pattern of aromatic proton was not changed in the <sup>1</sup>H NMR spectra of both the starting material and the adduct: *i.e.* carbonyl group attached to benzene ring still remains in the adduct.

When the reaction was carried out at 40 °C two possible regioisomers were yielded. The ratio of the minor components were below 10% in the case of the adducts of 1-benzoyl-1-ethoxycarbonyl ethene **1b** with each alkyl vinyl ethers (Table 1; runs 3, 8 and 13). However, in the case of 1-benzoyl-1-acetylene **1c** considerable amounts of the minor components were observed [17% with ethyl vinyl ether **2y**; run 10, 29% with methyl isopropenyl ether **2z**; run 15]. From these results the reactivity in the hetero-Diels-Alder reaction of 1,1-dicarbonyl substituted ethenes is the order of acetyl > benzoyl > ester. Schmidt and Maier reported<sup>5b</sup> that regioselective cyclization at acetyl carbonyl group was observed in the hetero-Diels-Alder reaction of methyl 2-methoxyethenylacetoacetate with alkyl vinyl ethers **2**.

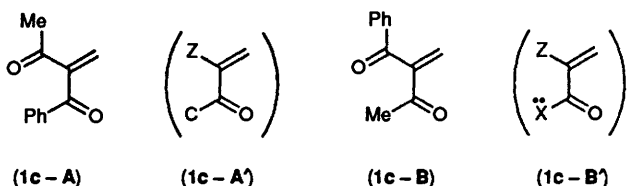
## Discussion

Of the many theories available, the frontier molecular orbital (FMO) approach has been the most successful in the prediction of the regioselectivity in the Diels-Alder reaction. The following sequence is applied: (a) the principle stabilization of the

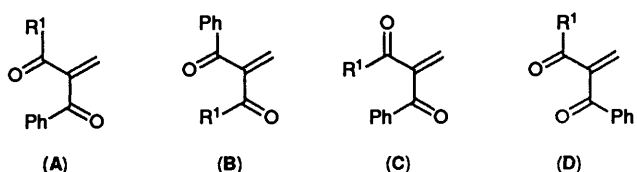
transition state arises from the HOMO-LUMO interaction which is closest in energy; (b) the large primary orbital coefficient of the diene will bond preferentially with the large primary orbital coefficient of the dienophile. We applied the theoretical results from a normal electron-demand Diels-Alder reaction to our compounds. Initially we predicted qualitatively the regiochemistry of the hetero-Diels-Alder reaction as follows. First, it is expected that the LUMO of the heterodiene and the HOMO of the dienophile are closer in energy as well as a general inverse electron-demand Diels-Alder reaction, for  $\alpha,\beta$ -unsaturated carbonyl compound with electron-withdrawing group should lower the LUMO energy level. Conformer **1b-A** was regarded as **1b-A'** because it contained an electron-withdrawing group, ethoxycarbonyl (substituent Z), and a phenyl group (substituent C). Similarly, conformer **1b-B** was regarded as **1b-B'**. Provided the



contribution of each electron-withdrawing group to the heterodiene is the same, the other substituent will determine the LUMO energy level. In principle, both C (extra conjugation) and Z (electron-withdrawing) substituents lower the LUMO energy, whereas X (electron-donation) substituent raises the energy. Therefore, as the LUMO energy level of **1b-A'** is lower than that of **1b-B'** the cycloaddition should take place between the LUMO of the **1b-A** and the HOMO of alkyl vinyl ether, and this prediction was consistent with the experimental result. In the case of **1c**, the possible two conformers, **1c-A** and **1c-B**, were regarded as **1c-A'** and **1c-B'**, respectively. From these two

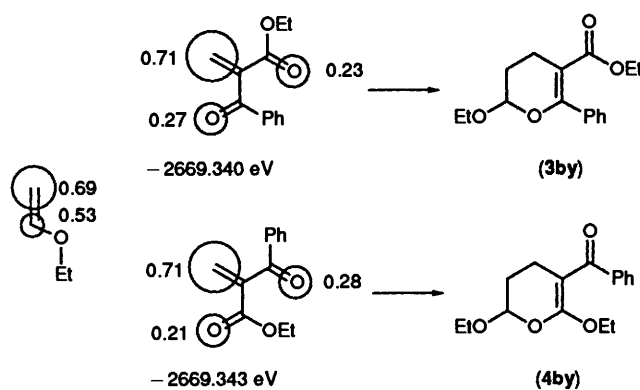


conformers the LUMO energy level of **1c-A'** is lower than that of **1c-B'** and the Diels-Alder adduct should be **3**. However this prediction was not consistent with the experimental result; this error might be caused by the over-simplification in assuming that all electron-withdrawing groups have the same contribution to the diene. To resolve this problem we have carried out MO calculations. Among four possible conformers A-D of **1**, the conformer D, in which two carbonyl groups and *exo*-methylene are in an *s-trans* relationship, is not important because this cannot lead to the specific transition state structure of the hetero-Diels-Alder reaction. MNDO calculations reveal



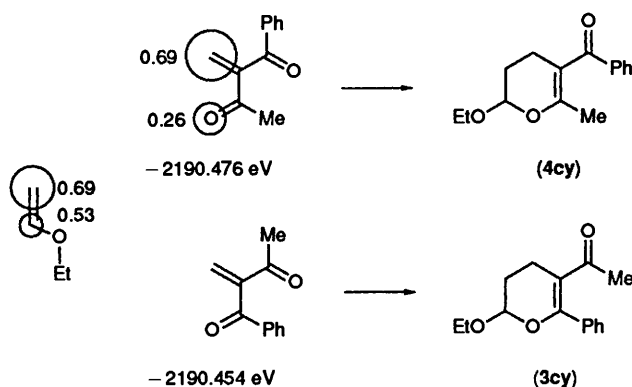
that in each conformer A-C the most stable form is one in which the benzene ring plane is vertical to the ene-dione plane in both compounds **1b** and **1c**, presumably because of the steric

hindrance between the aromatic hydrogen and the carbonyl oxygen (in **A**), vinyl hydrogen (in **B**), or  $R^1$  group (in **C**). The total energy of the conformer **C** is much higher than that of **A** or **B** in each case. The total energy levels of **1b-A** and **1b-B** are almost similar in the case of 1-benzoyl-1-ethoxycarbonylethene **1b**, whereas, in 1-benzoyl-1-acetylene **1c**, that of **1c-B** is lower than **1c-A**. According to the Hammond principle<sup>11</sup> the geometry of the transition state in the exothermic reaction should resemble that of the starting material. Among many conformers existing the most stable one is that which contributes more to the transition state than the other conformers.<sup>12</sup> Thus the hetero-Diels-Alder reaction of **1b** with alkyl vinyl ethers may proceed through the interaction between both **1b-A** and **1b-B** to give **3by** and **4by** with low regioselectivity as long as the total energies are compared (Scheme 2). However, on comparing the coefficients of reactive



Scheme 2.

sites, the largest coefficient is found to be that of *exo*-methylene and the coefficient of benzoyl carbonyl oxygen is larger than that of ester carbonyl oxygen in both conformers. The bonds should be formed in order of the magnitude of the modulus of coefficient; the hetero-Diels-Alder reaction of **1b** with alkyl vinyl ether occur at *exo*-methylene and benzoyl carbonyl oxygen. In the case of 1-benzoyl-1-acetylene **1c** the LUMO energy level of **1c-B** is lower than that of **1c-A**. So the cyclization with ethyl vinyl ether must occur at *exo*-methylene and acetyl carbonyl oxygen to give **3cy**, *i.e.* following the order of the coefficients (Scheme 3).



Scheme 3.

## Experimental

M.p.s were measured on a Yanako micro-m.p. apparatus and are uncorrected. Extracts were dried over anhydrous magnesium sulphate. IR spectra of solids (KBr) and liquids (film) were recorded on a JASCO-IR-810 spectrophotometer.

Mass spectra were taken on a Shimadzu LKB-9000 mass spectrometer, and high-resolution mass spectra with a JEOL JMS-01SG or a JEOL JMS-DX300 instruments. NMR spectra were obtained with JEOL PS-100 and JEOL JMN-GX 270 spectrometers (in  $CDCl_3$  with tetramethylsilane as internal reference). Molecular mechanics and molecular orbital calculations were carried out with IBM PC/2 using MMX and MNDO programs.

*Reaction of 2-methylene-1,3-dicarbonyl compounds with alkyl vinyl ether. Method A.*—A 0.1M solution of alkyl vinyl ether in benzene (2 ml) was added to a solution of 2-methylene-1,3-dicarbonyl compounds (1.0 mmol) in benzene (3 ml) in ice-cooled bath. The reaction mixture was stirred for 3 h at ambient temperature and evaporated off at reduced pressure. The resulting residue was subjected to column chromatography or centrifuged chromatography or medium pressure chromatography to yield one of the two possible regioisomeric dihydropyrans.

(a) With methyl vinyl ether **2a**.

1,1-Dibenzoylethene **1a** gave 5-benzoyl-2-methoxy-6-phenyl-3,4-dihydro-2H-pyran **3ax**, m.p. 89–91 °C (from *n*-hexane) (Found: C, 77.6; H, 6.3%;  $M^+$ , 294.1212.  $C_{19}H_{18}O_3$  requires C, 77.53; H, 6.16%.  $M$ , 294.1253);  $m/z$  (%) 294 ( $M^+$ , 19), 276 (19), 149 (13), 105 (base peak) and 77 (34);  $\nu_{max}$  1625 and 1595  $cm^{-1}$ ;  $\delta_H$  1.9–2.1 (2 H, m, 3-H), 2.4–2.7 (2 H, m, 4-H), 3.67 (3 H, s,  $OCH_3$ ), 5.19 (1 H, dd,  $J$  3.0, 3.0 Hz, 2-H), 6.9–7.3 (8 H, m, ArH) and 7.50 (2 H, dd,  $J$  7.0, 2.0 Hz, 2', 6'-ArH).

1-Benzoyl-1-ethoxycarbonylethene **1b** gave 5-ethoxycarbonyl-2-methoxy-6-phenyl-3,4-dihydro-2H-pyran **3bx**; b.p. 135 °C (3 mmHg) (Found: C, 68.6; H, 6.9%;  $M^+$ , 262.1192.  $C_{15}H_{18}O_4$  requires C, 68.68; H, 6.92%;  $M$ , 262.1203);  $m/z$  262 ( $M^+$ ), 244, 217, 105 (base peak) and 77;  $\nu_{max}$  1692, 1634 and 1598  $cm^{-1}$ ;  $\delta_H(CCl_4)$  0.87 (3 H, t,  $J$  7.0 Hz,  $COOCH_2CH_3$ ), 1.8–2.0 (2 H, m, 3-H), 2.3–2.5 (2 H, m, 4-H), 3.52 (3 H, s,  $OCH_3$ ), 3.83 (2 H, q,  $J$  7.0 Hz,  $COOCH_2CH_3$ ), 5.03 (1 H, dd,  $J$  3.0, 3.0 Hz, 2-H) and 7.2–7.5 (5 H, m, ArH).

1-Benzoyl-1-acetylene **1c** gave 5-benzoyl-2-methoxy-6-methyl-3,4-dihydro-2H-pyran **4cx**, b.p. 100–105 °C (1 mmHg) (Found: C, 72.1; H, 6.9.  $C_{14}H_{16}O_3$  requires C, 72.39; H, 6.94%);  $m/z$  232 ( $M^+$ ), 214, 105 (base peak) and 77;  $\nu_{max}$  1618 and 1593  $cm^{-1}$ ;  $\delta_H$  1.79 (3 H, t,  $J$  2.0 Hz,  $CH_3$ ), 1.8–2.0 (2 H, m, 3-H), 2.3–2.5 (2 H, m, 4-H), 3.54 (3 H, s,  $OCH_3$ ), 5.03 (1 H, dd,  $J$  3.0, 3.0 Hz, 2-H), 7.3–7.5 (3 H, m, ArH) and 7.70 (2 H, dd,  $J$  7.0, 2.0 Hz).

(b) With ethyl vinyl ether **2b**.

1,1-Dibenzoylethene **1a** gave 5-benzoyl-2-ethoxy-6-phenyl-3,4-dihydro-2H-pyran **3ay**, m.p. 98–99 °C (from *n*-hexane) (Found: C, 77.7; H, 6.4%;  $M^+$ , 308.1378.  $C_{20}H_{20}O_3$  requires C, 77.90; H, 6.54%;  $M$ , 308.1410);  $m/z$  (%) 308 ( $M^+$ , 42), 290 (42), 105 (base peak) and 77 (53);  $\nu_{max}$  1623 and 1595  $cm^{-1}$ ;  $\delta_H$  1.35 (3 H, t,  $J$  7.0 Hz,  $OCH_2CH_3$ ), 1.9–2.1 (2 H, m, 3-H), 2.4–2.7 (2 H, m, 4-H), 4.00 (2 H, ddq,  $J$  9.5, 7.0 Hz,  $OCH_2CH_3$ ), 5.36 (1 H, dd,  $J$  3.5, 2.5 Hz), 6.9–7.3 (8 H, m, ArH) and 7.51 (2 H, ddd,  $J$  7.9, 2.8, 1.5 Hz, 2', 6'-ArH).

1-Benzoyl-1-ethoxycarbonylethene **1b** gave 2-ethoxy-5-ethoxycarbonyl-6-phenyl-3,4-dihydro-2H-pyran **3by**, b.p. 140 °C (3 mmHg) (Found: C, 69.3; H, 7.4%;  $M^+$ , 276.1302.  $C_{16}H_{20}O_4$  requires C, 69.54; H, 7.30%;  $M$ , 276.1360);  $m/z$  276 ( $M^+$ ), 231, 105 (base peak) and 77;  $\delta_H$  0.88 (3 H, t,  $J$  7.0 Hz,  $CO_2CH_2CH_3$ ), 1.25 (3 H, t,  $J$  7.0 Hz,  $OCH_2CH_3$ ), 1.7–2.0 (2 H, m, 3-H), 2.4–2.5 (2 H, m, 4-H), 3.80 (2 H, ddq,  $J$  9.5, 7.0, 7.0 Hz,  $OCH_2CH_3$ ), 3.83 (2 H, q,  $J$  7.0 Hz,  $CO_2CH_2CH_3$ ), 5.20 (1 H, dd,  $J$  3.7, 2.5 Hz, 2-H) and 7.2–7.4 (5 H, m, ArH).

1-Benzoyl-1-acetylene **1c** gave 5-benzoyl-2-ethoxy-6-methyl-3,4-dihydro-2H-pyran **4cy**, b.p. 105–110 °C (1 mmHg) (Found: C, 72.9; H, 7.45.  $C_{15}H_{18}O_3$  requires C, 73.14; H, 7.34%);  $m/z$  (%) 246 ( $M^+$ , 2), 228 (27), 105 (base peak) and 77 (53);  $\nu_{max}$  1622 and 1597  $cm^{-1}$ ;  $\delta_H$  1.28 (3 H, t,  $J$  7.0 Hz,  $OCH_2CH_3$ ), 1.78

(3 H, t,  $J$  1.5 Hz,  $\text{CH}_3$ ), 1.8–2.0 (2 H, m, 3-H), 2.35–2.55 (2 H, m, 4-H), 3.80 (2 H, ddq,  $J$  9.7, 7.0, 7.0 Hz,  $\text{OCH}_2\text{CH}_3$ ), 5.14 (1 H, dd,  $J$  3.2, 2.8 Hz), 7.35–7.5 (3 H, m, ArH), and 7.70 (2 H, dd,  $J$  7.0, 2.0 Hz, aromatic 2', 6'-ArH).

(c) *With methyl isopropenyl ether 2c.*

1,1-Dibenzylethene **1a** gave 5-benzoyl-2-methoxy-2-methyl-6-phenyl-3,4-dihydro-2H-pyran **3cz**, b.p. 150–160 °C (1 mmHg) (Found: C, 77.8; H, 6.6%;  $M^+$ , 308.1410.  $\text{C}_{20}\text{H}_{20}\text{O}_3$  requires C, 77.90; H, 6.54%;  $M$ , 308.1410);  $m/z$  (%) 308 ( $M^+$ , 42), 276 (53), 149 (19), 105 (base peak), 77 (38), 72 (91) and 51 (83);  $\nu_{\text{max}}$  1617 and 1595  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  1.61 (3 H, s,  $\text{CH}_3$ ), 1.7–2.2 (2 H, m, 3-H), 2.5–2.7 (2 H, m, 4-H), 3.56 (3 H, s,  $\text{OCH}_3$ ), 7.0–7.3 (8 H, m, ArH), 7.55 (2 H, dd,  $J$  7.5, 1.5 Hz, 2', 6'-H).

1-Benzoyl-1-ethoxycarbonyl-1-ethoxy-2-methyl-6-phenyl-3,4-dihydro-2H-pyran **3bz**, b.p. 140 °C (1 mmHg) (Found: C, 69.7; H, 7.3%;  $M^+$ , 276.1357.  $\text{C}_{16}\text{H}_{20}\text{O}_4$  requires C, 69.54; H, 7.30%;  $M$ , 276.1360);  $m/z$  (%) ( $M^+$ , 44), 105 (55), 77 (19), 72 (base peak);  $\nu_{\text{max}}$  1690, 1628 and 1597  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  0.92 (3 H, t,  $J$  7.3 Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.52 (3 H, s,  $\text{CH}_3$ ), 1.65–2.2 (2 H, m, 3-H), 2.45–2.6 (2 H, m, 4-H), 3.41 (3 H, s,  $\text{OCH}_3$ ), 3.96 (2 H, q,  $J$  7.3 Hz,  $\text{OCH}_2\text{CH}_3$ ) and 7.34 (5 H, br s, ArH).

1-Acetyl-1-benzylethene **1c** gave 5-benzoyl-2-methoxy-2,6-dimethyl-3,4-dihydro-2H-pyran **4cz**, b.p. 105–110 °C (1 mmHg) (Found: C, 72.9; H, 7.5.  $\text{C}_{15}\text{H}_{18}\text{O}_3$  requires C, 73.14; H, 7.37%)  $m/z$  246 ( $M^+$ , 7), 228 (10), 214 (39), 105 (75), 77 (40) and 72 (base peak);  $\nu_{\text{max}}$  1663, 1618 and 1580  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  1.50 (3 H, s, Me), 1.79 (3 H, t,  $J$  1.5 Hz, Me), 1.90–1.99 (2 H, m, 3-H), 2.35–2.41 (2 H, m, 4-H), 3.37 (3 H, s,  $\text{OCH}_3$ ), 7.35–7.50 (3 H, m, ArH) and 7.70 (2 H, dd,  $J$  7.0, 2.0 Hz, 2', 6'-ArH).

*Method B.*—A solution of alkyl vinyl ether (0.1M) in benzene (2 ml) was added dropwise to a solution of 2-methylene-1,3-dicarbonyl compound (1.0 mmol) in benzene (3 ml) at 40 °C. The reaction mixture was stirred for 2 h at this temperature. The solvent was evaporated off under reduced pressure and the resulting residue was subjected to centrifuged chromatography or medium pressure chromatography to yield two regioisomeric dihydropyrans.

(a) *With ethyl vinyl ether 2b.*

1-Benzoyl-1-acetylene **1c** gave a mixture of 5-benzoyl-2-ethoxy-6-methyl-3,4-dihydro-2H-pyran **4cy** and 5-acetyl-2-ethoxy-6-phenyl-3,4-dihydro-2H-pyran **3cy**, b.p. 105–110 °C (1 mmHg);  $m/z$  (%) 246 ( $M^+$ , 7), 228 (24), 105 (base peak), 77 (46), 72 (41) and 43 (70);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 1620 and 1595  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  1.28 (3 H, t,  $J$  7.0 Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.72 (3 H, s,  $\text{COCH}_3$ ), 1.9–2.0 (2 H, m, 3-H), 2.4–2.6 (2 H, m, 4-H), 3.86 (2 H, ddq,  $J$  9.7, 7.0, 7.0 Hz,  $\text{OCH}_2\text{CH}_3$ ), 5.24 (1 H, dd,  $J$  3.0, 3.0 Hz, 2-H) and 7.40 (5 H, br s, ArH).

(b) *With methyl isopropenyl ether 2c.*

1-Benzoyl-1-acetylene **1c** gave a mixture of compounds **4cz** and **3cz**, b.p. 110 °C (1 mmHg);  $m/z$  (%) 246 ( $M^+$ , 7), 228 (7), 214 (33), 105 (34), 77 (23), 72 (base peak) and 43 (57);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 1621 and 1595  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  1.53 (3 H, s,  $\text{CH}_3$ ), 1.71 (3 H, s,  $\text{COCH}_3$ ), 1.8–2.1 (2 H, m, 3-H), 2.35–2.6 (2 H, m, 4-H), 3.43 (3 H, s,  $\text{OCH}_3$ ) and 7.40 (5 H, br s, ArH).

$\text{LiAlH}_4$  reduction of 2-ethoxy-5-ethoxycarbonyl-6-phenyl-3,4-dihydro-2H-pyran **3by**.—A solution of compound **3by** (100 mg) in ether (5 ml) was added to a solution of  $\text{LiAlH}_4$  (1.29M), in ether (5 ml), in an ice bath. The reaction mixture was stirred for 30 min below 5 °C. The excess  $\text{LiAlH}_4$  was decomposed with water-saturated ether, and the precipitate was filtered off through Celite. The filtrate was dried, evaporated to give 2-ethoxy-5-hydroxymethyl-6-phenyl-3,4-dihydro-2H-pyran **5**. (Found:  $M^+$ , 234.1251.  $\text{C}_{14}\text{H}_{18}\text{O}_3$  requires  $M$ , 234.1255);  $m/z$

(%) 234 ( $M^+$ , 32), 217 (26), 188 (55), 170 (31), 160 (33), 145 (34) and 105 (base peak);  $\nu_{\text{max}}$  3450 and 1660  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  1.26 (3 H, t,  $J$  7.0 Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.9–2.0 (2 H, m, 3-H), 2.2–2.4 (2 H, m, 4-H), 3.84 (2 H, ddq,  $J$  9.5, 7.0, 7.0 Hz,  $\text{OCH}_2\text{CH}_3$ ), 4.05 (2 H, d,  $J$  1.8 Hz,  $\text{CH}_2\text{OH}$ ), 5.15 (1 H, dd,  $J$  3.7, 2.5 Hz, 2-H) and 7.3–7.45 (5 H, m, ArH).

$\text{LiAlH}_4$  reduction of 5-benzoyl-2-ethoxy-6-methyl-3,4-dihydro-2H-pyran **4cy**.—A solution of compound **4cy** (150 mg) in ether (10 ml) was added to a solution of  $\text{LiAlH}_4$  (1.29M) in ether (8 ml) at ambient temperature. The reaction mixture was stirred for 1 h at the same temperature. The excess  $\text{LiAlH}_4$  was decomposed with  $\text{AcOEt}$ , then water-saturated ether, and the precipitate was filtered off through Celite. The filtrate was dried and evaporated to give a mixture of 2-ethoxy-5-(1-hydroxyphenylmethyl)-6-methyl-3,4-dihydro-2H-pyran **6** (140 mg). (Found:  $M^+$ , 248.1424.  $\text{C}_{15}\text{H}_{20}\text{O}_3$  requires  $M$ , 248.1411);  $m/z$  (%) 248 ( $M^+$ , 7), 202 (30), 184 (31), 174 (31), 173 (33), 159 (77), 141 (30), 131 (52), 129 (56), 117 (72), 115 (base peak), 105 (57), 91 (86) and 77 (61);  $\nu_{\text{max}}$  3400 and 1670  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  1.20 (t,  $J$  7.2 Hz,  $\text{CH}_2\text{CH}_3$ ), 1.23 (t,  $J$  7.2 Hz,  $\text{CH}_2\text{CH}_3$ ), 1.96 (t,  $J$  1.7 Hz,  $=\text{CCH}_3$ ), 1.97 (t,  $J$  1.7 Hz,  $=\text{CCH}_3$ ), 3.57 (m,  $\text{CH}_2\text{CH}_3$ ), 3.85 (m,  $\text{CH}_2\text{CH}_3$ ), 4.90 (dd,  $J$  2.7, 2.2 Hz, 2-H), 4.97 (dd,  $J$  2.8, 2.2 Hz, 2-H), 5.64 [s,  $\text{CH}(\text{OH})$ ] and 7.3–7.6 (m, Ar-H). This compound was subjected to column chromatography to afford 4-benzylidene-5-oxohexanal **7**. (Found:  $M^+$ , 202.1011.  $\text{C}_{13}\text{H}_{14}\text{O}_2$  requires  $M$ , 202.0993);  $m/z$  (%) 202 ( $M^+$ , 41), 184 (61), 183 (84), 174 (38), 166 (30), 159 (base peak), 141 (48), 131 (61), 117 (73), 115 (99), 91 (81) and 77 (44);  $\nu_{\text{max}}$  3050, 2730, 1720 and 1660  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  2.46 (3 H, s,  $\text{CH}_3$ ), 2.59 (2 H, dt,  $J$  7.3, 1.4 Hz, 2-H), 2.83 (2 H, t,  $J$  7.3 Hz, 3-H), 7.3–7.5 (5 H, m, Ar-H), 7.58 (1 H, s,  $=\text{CH}$ ), 9.74 (1 H, t,  $J$  1.4 Hz, CHO).

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