SYNTHESIS OF ETHER ANALOGUES OF (±)-ACETOMYCIN‡

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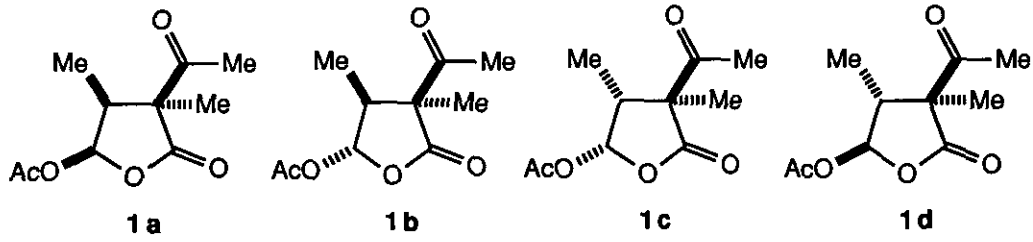
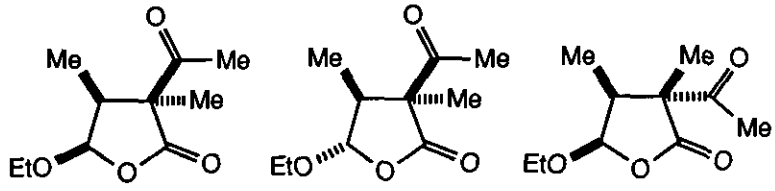
Abstract-Short syntheses of (±)-**2a-c**, ether analogues of acetomycin (**1a**) are described. The approach is based on a novel entry to furanones by rearrangement of *tert*-butyl 1-vinylcyclopropane-1-carboxylates. The cyclopropanes are stereoselectively formed by the rhodium(II) catalyzed decomposition of vinyldiazomethanes in the presence of vinyl ethers.

The furanone antibiotic (-)-acetomycin (**1a**), originally isolated in 1958,[1] has generated considerable interest[2] since it was discovered to have potent in vitro activity against HCT-8 human colon adenocarcinoma cells and L1210 murine leukemia cells.[3] Reasonable in vitro activity was also seen in the isomeric structures (**1b-d**). Similar in vivo activity was not observed for **1a**, which has been ascribed to the rapid hydrolysis of the acetoxy group by esterases.[3] Thus, the potential utility of acetomycin as an antitumour agent would depend on developing derivatives that are resistant to esterase inactivation. One approach has been to prepare more bulky ester derivatives of acetomycin.[2c] In this paper we describe a short preparation of (±)-**2a-c**, ether analogs of



1a **1b** **1c** **1d**



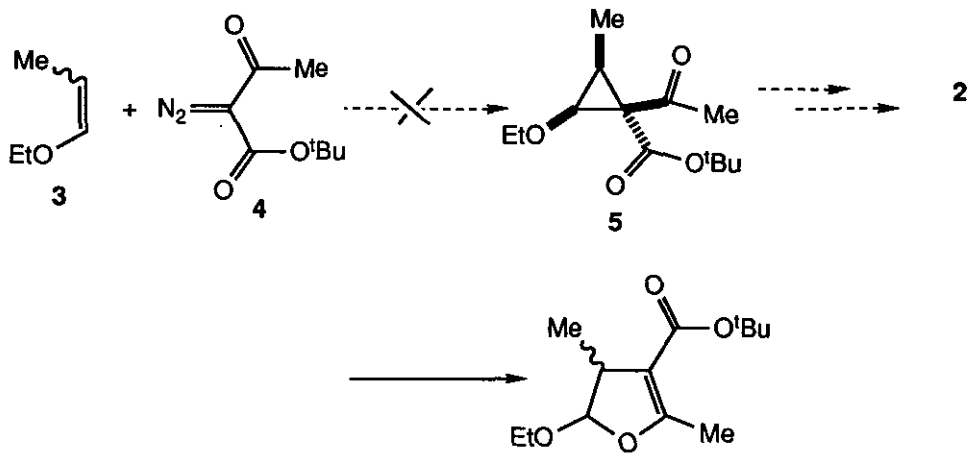
2a **2b** **2c**

‡Dedicated with warm regards to Professor E. C. Taylor on the occasion of his 70th birthday.

acetomycin. The synthetic scheme is based on a novel rearrangement of *tert*-butyl 1-vinylcyclopropane-1-carboxylates to furanones.[4]

At the onset of this work a four step synthesis of **2** was conceived starting from the readily available diazoacetoacetate (**4**) as illustrated in Scheme 1. In practice, however, rhodium(II) catalyzed decomposition of **4** in the presence of propenyl ethyl ether (**3**) failed to generate the desired cyclopropane (**5**). Even with pentane as solvent and rhodium(II) octanoate as catalyst, conditions which favor cyclopropanation over side reactions occurring through dipolar intermediates,[5] the only isolable products were the isomeric [3 + 2] cycloadducts (**6a,b**). Products such as **6a,b** are common in reactions of carbenoids derived from diazoacetoacetates, particularly when the alkenes used to trap the carbenoids are electron rich.[6] Hence, an alternative approach was required and it became of interest to determine whether a suitably functionalized vinyldiazomethane[7] could be used in place of the diazoacetoacetate.

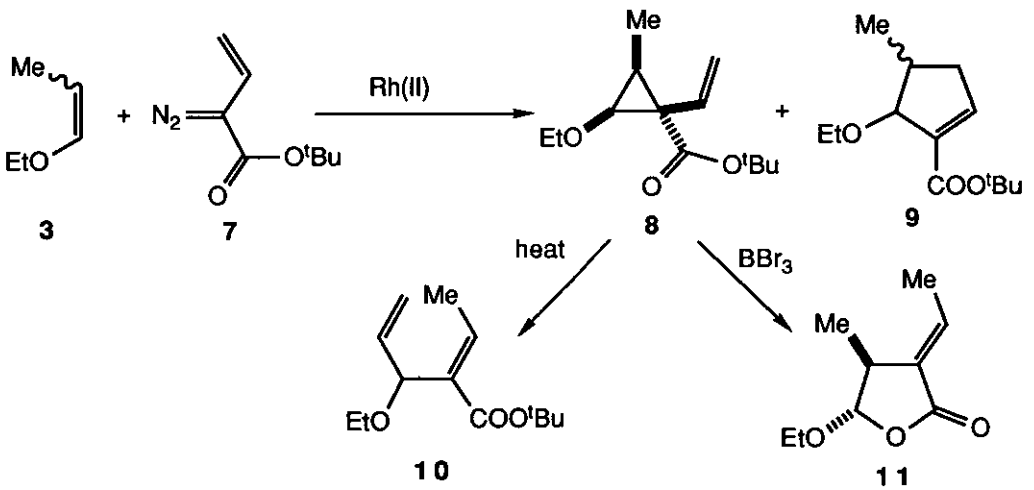
Scheme 1



Rhodium(II) pivalate catalyzed decomposition of the vinyldiazomethane (**7**)[5a] in the presence of **3** with pentane as solvent resulted in a promising result (Scheme 2). The major product was the *cis* cyclopropane (**8**) (37% yield), whereby cyclopropanation had occurred exclusively with the *cis*-vinyl ether and with the typically high stereoselectivity observed in vinylcarbenoid cyclopropanations.[8] This stereochemical assignment was readily determined by the characteristic coupling constants for the cyclopropyl protons and confirmed by NOE difference experiments.[8] The minor product was an isomeric mixture of the cyclopentene (**9**) (24% yield). Cyclopentene formation has been observed by us in earlier studies on vinylcarbenoids containing a single electron withdrawing group and is caused by initial reaction of the vinyl ether at the vinyl terminus of the vinylcarbenoid.[7] The next step would require rearrangement of **8**[9] to a furanone which would need to proceed with retention of stereochemistry for the ultimate formation of **2a**. The thermal conditions that had been successfully employed for

the rearrangement of simpler vinylcyclopropanes did not result in the formation of a furanone from **8** (Scheme 2). Instead, a retro-ene reaction of **8** occurred to form **10** in 73% yield.[9] Boron tribromide induced rearrangement of **8**, however, generated the furanone (**11**) in 47% yield, which was readily shown to be the *trans* isomer through NOE difference analysis. Further utilization of **11** for the synthesis of acetomycin analogs would require oxidation of the α,β-unsatutated ester in **11** to a β-keto ester but all attempts at achieving this transformation were unsuccessful.

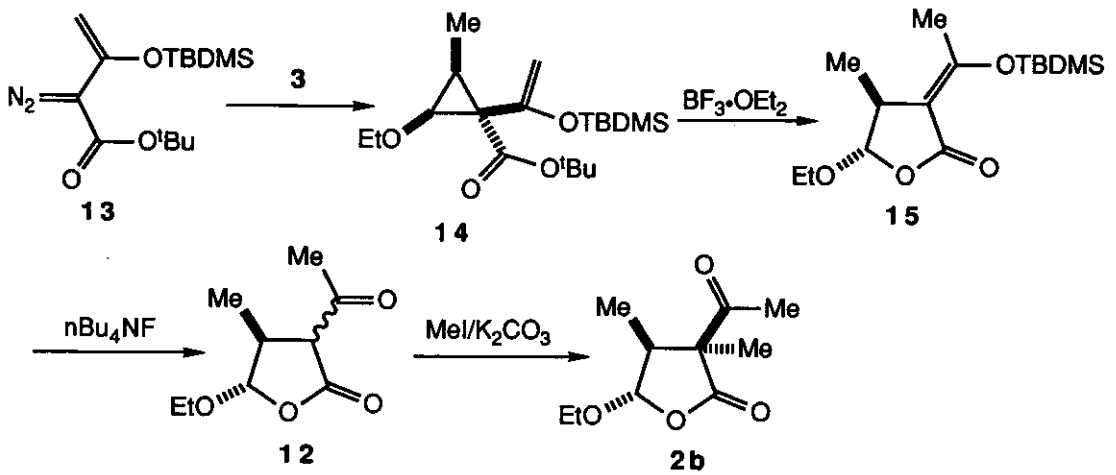
Scheme 2



A modified approach was then examined in which the vinylcarbenoid already contained an oxygen functionality and so only a hydrolysis would be required in the last step to generate the β-keto ester (**12**). Rhodium(II) octanoate catalyzed decomposition of the *tert*-butyldimethylsilyloxy derivative (**13**)[10] in the presence of **3** proceeded smoothly to generate the cyclopropane (**14**) in 82% yield. In this case no cyclopentene product related to **9** was observed which is consistent with the expectation that the silyloxy group would decrease the electrophilicity of the vinyl terminus. On treatment of **14** with BF_3-etherate rearrangement occurred to form the *trans*-furanone (**15**) (50% yield), in which the *tert*-butyldimethylsiloxy group remained intact. Deprotection of **15** with tetrabutylammonium fluoride gave the β-keto ester (**12**) (84% yield),[11] which was readily methylated on the opposite face to the C-4 methyl group using methyl iodide and potassium carbonate as base to generate the acetomycin analog (**2b**) (76% yield).[12]

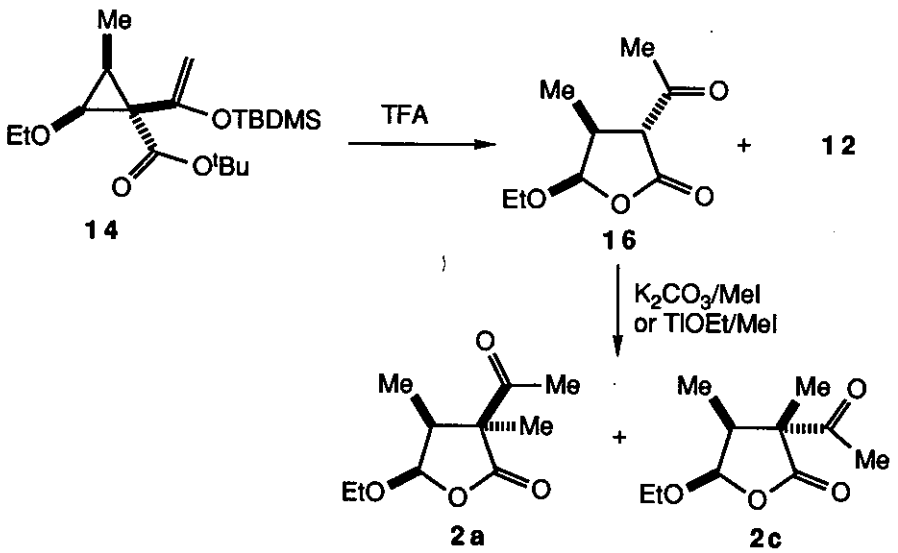
The BF_3-etherate or BBr_3 conditions for the vinylcyclopropane rearrangement readily formed the thermodynamically most stable *trans*-furanones. We have previously shown that Lewis acid catalyzed rearrangement of donor-acceptor substituted vinylcyclopropanes to cyclopentenes proceeds with retention of stereochemistry.[7] Therefore, it became of interest to determine if reaction conditions could be developed so that rearrangement of **14** would also proceed with retention of stereochemistry. After considerable experimentation, optimum conditions for the rearrangement of **14** to *cis* products were found to be TFA at -78 °C which resulted in

Scheme 3



the predominant formation of the *cis* isomer (**16**)[12] (2 : 1 *cis/trans* ratio, 40% isolated yield of **16**). The final step for the synthesis of **2a** would require introduction of a methyl group from what was expected to be the more accessible face of **16**. Treatment of **16**, however, with methyl iodide / K_2CO_3 resulted in the formation of **2c** as the major product (ratio **2a** : **2c** = 1 : 5) in which the methyl group had been introduced on the same side as the bulky substituents.[13] Modification of product ratios was possible and even though **2c** was always the dominant product, reasonable amounts of **2a** could be formed by using thallous ethoxide[14] as base (ratio **2a** : **2c** = 2 : 3).

Scheme 4



The short syntheses of three isomeric analogs of acetomycin further illustrate that the rearrangement of *tert*-butyl 1-vinylcyclopropane-1-carboxylates is a useful method for the synthesis of highly functionalized furanones. Also, oxygen functionalized vinyldiazomethanes can be advantageously used in place of diazoacetoacetates in cyclopropanation reactions. The biological evaluation of the ether analogues of acetomycin will be reported in due course.

ACKNOWLEDGEMENT

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EXPERIMENTAL SECTION

General. ^1H and ^{13}C nmr spectra were recorded at 200 and 50.3 MHz, respectively. CH_2Cl_2 was freshly distilled from CaH_2. Column chromatography was carried out on silica gel 60 (230-400 mesh).

1,1-Dimethylethyl 2,4-Dimethyl-5-ethoxy-4,5-dihydro-3-furancarboxylate (6a,b). A solution of **4** (1.84 g, 10 mmol) in pentane (50 ml) was added dropwise over 15 min to a stirred mixture of rhodium(II) octanoate (0.0778 g, 0.1 mmol) and ethyl-1-propenyl ether (**3**) (4.32 g, 50 mmol, E / Z ratio =1 : 2.4) in pentane (50 ml), heated under reflux in an argon atmosphere. After heating for a further 20 min, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel using ether-petroleum ether (1 : 19) as eluant. Yield of *cis* isomer **6a** 0.60 g (25%): Ir (neat) 1680, 1640 cm^{-1}; ^1H nmr ($CDCl_3$) δ 5.43 (d, J = 7.6 Hz, 1 H), 3.85 (dq, J = 9.7, 7.1 Hz, 1 H), 3.56 (dq, J = 9.7, 7.1 Hz, 1 H), 3.12 (dqq, J = 7.6, 7.1, 1.5 Hz, 1 H), 2.14 (d, J = 1.5 Hz, 3 H); 1.47 (s, 9 H), 1.22 (t, J = 7.1 Hz, 3 H), 1.14 (d, J = 7.6 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 165.2, 164.7, 108.4, 107.1, 79.4, 65.3, 40.3, 28.4, 15.0, 14.3, 11.8. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.23; H, 9.16. An nmr spectrum of the crude reaction mixture indicated a mixture of **6a : 6b** in a ratio of 1 : 2.3, but the *trans* isomer (**6b**) decomposed on attempted chromatography on either silica gel or alumina.

1,1-Dimethylethyl 2α-Ethoxy-3α-methyl-1α-vinylcyclopropane-1β-carboxylate (8) and 1,1-Dimethylethyl 5-Ethoxy-4-methyl-1-cyclopentene-1-carboxylate (9). A solution of **7**[5a] (1.68 g, 10 mmol) in pentane (50 ml) was added dropwise over 30 min to a stirred mixture of rhodium(II) pivalate (0.056 g, 0.1 mmol) and **3** (4.32 g, 50 mmol, E / Z ratio =1 : 2.4) in pentane (50 ml), heated under reflux in an argon atmosphere. After heating for a further 30 min, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel using ether-petroleum ether (1 : 19) as eluant to give: **8** 0.83 g (37% yield): Ir (neat) 1700, 1630 cm^{-1}; ^1H nmr ($CDCl_3$) δ 5.66 (dd, J = 18.0, 11.0 Hz, 1 H), 5.48 (dd, J = 18.0, 2.9 Hz, 1 H), 5.31 (dd, J = 11.0, 2.9 Hz, 1 H), 3.65 (d, J = 7.1 Hz, 1 H), 3.56 (q, J = 7.0 Hz, 2 H), 1.86 (dq, J = 7.1, 6.6 Hz, 1 H), 1.42 (s, 9 H), 1.20 (t, J = 7.0 Hz, 3 H), 1.07 (d, J = 6.6 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 171.9, 128.8, 118.7, 80.4, 67.2, 66.6, 32.7, 28.1, 26.7, 14.8, 7.0. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.98; H, 9.78.

9 0.55 g (24% yield): Ir (neat) 1700, 1620 cm^{-1}; ^1H nmr ($CDCl_3$) δ 6.80 (dd, J = 2.5, 2.0 Hz, 1 H), 4.28 (dd, J = 6.0, 2.0 Hz, 1 H), 3.59 (q, J = 7.0 Hz, 2 H), 2.50 - 2.11 (m, 3 H), 1.44 (s, 9 H), 1.13 (t, J = 7.0 Hz, 3 H), 1.06 (d, J = 6.3 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 164.0, 146.3, 139.7, 83.2, 79.9, 66.7, 39.1, 37.8, 28.0, 15.5, 13.6. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.84; H, 9.78.

1,1-Dimethylethyl 3-Ethoxy-2-ethylidene-4-pentene-1-carboxylate (10). **8** (0.18 g, 0.70 mmol) was sealed under Ar in a heavy-walled Pyrex tube which had been previously treated with concd. NH_4OH. The sealed tube was placed in an oil bath at 230 °C for 15 min. The product was purified by column chromatography on silica gel using ether-petroleum ether (1 : 9) as eluant. Yield 0.13 g (73%): Ir (neat) 1695, 1640 cm^{-1}; ^1H nmr ($CDCl_3$) δ 6.86 (q, J = 7.3 Hz, 1 H), 6.02 (ddd, J = 17.2, 10.3, 6.3 Hz, 1 H), 5.20 (d, J = 17.2 Hz, 1 H), 5.08 (d, J = 10.3 Hz, 1 H), 4.87 (d, J = 6.3 Hz, 1 H), 3.41 (q, J = 7.0 Hz, 2 H), 1.90 (d, J = 7.3 Hz, 3 H), 1.45 (s, 9 H),1.17 (t, J = 7.0 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 166.2, 140.1, 137.2, 133.7, 115.3, 80.3, 77.0, 63.7, 28.1, 15.2, 14.3. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.72; H, 9.72.

5α-Ethoxy-3-ethylidene-4β-methyl-4,5-dihydro-2-furanone (11). A solution of **8** (0.72g, 3.2 mmol) in CH_2Cl_2 (20 ml) was added dropwise over 10 min to a stirred solution of BBr_3 (2 ml, 1 M in CH_2Cl_2, 2 mmol) in CH_2Cl_2 (40 ml) under Ar at -78 °C. The mixture was maintained at -78 °C for 1 h. After quenching with ethanol, water was added and the mixture was extracted twice with ether. The combined organic layers were washed with water and saturated NaCl solution, dried (Na_2SO_4) and concentrated. The product was purified by column chromatography on silica gel using ether-petroleum ether (1 : 9) as eluant to give **11** as a colorless oil. Yield 0.25 g (47%): Ir (neat) 1760, 1680 cm^{-1}; ^1H nmr ($CDCl_3$) δ 6.78 (qd, J = 7.3, 2.0 Hz, 1 H), 5.09 (s, 1 H), 3.85(dq, J = 9.5, 7.2 Hz, 1 H), 3.55 (dq, J = 9.5, 7.2 Hz, 1 H), 2.95 (qd, J = 7.4, 2.0 Hz, 1 H), 1.86 (dd, J = 7.3, 1.0 Hz, 3 H), 1.19 (t, J = 7.2 Hz, 3 H), 1.17 (d, J = 7.4 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 170.0, 136.8, 131.5, 107.1, 64.8, 38.9, 17.0, 15.1, 14.9. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.28; H, 8.22.

Dimethylethyl 2-Diazo-3-((1,1-dimethylethyl)dimethylsilyloxy)-3-butenoate (13). *tert*-Butyldimethylsilyl trifluoromethanesulfonate (3.22 g, 2.8 ml, 12 mmol) was added to a stirred solution of **4** (1.86 g, 10 mmol) and triethylamine (1.45 g, 2 ml, 12 mmol) in dry CH_2Cl_2 (20 ml) at 0 °C under argon and the mixture was stirred at 0 °C for 30 min. The solution was then diluted with petroleum ether (20 ml), washed with dilute $NaHCO_3$ solution and saturated NaCl solution, dried (Na_2SO_4) and concentracted to offer **13** as an orange oil in quantitative yield: Ir (neat) 2090, 1690, 1600 cm^{-1}; ^1H nmr ($CDCl_3$) δ 4.95 (d, J = 2.0 Hz, 1 H), 4.20 (d, J = 2.0 Hz, 1 H), 1.49 (s, 9 H), 0.90 (s, 9 H), 0.21 (s, 6 H).

1,1-Dimethylethyl 2α-Ethoxy-3α-methyl-1α-(1-((1,1-dimethylethyl)dimethylsilyloxy)vinyl)-cyclopropane-1β-carboxylate (14). A solution of **13** (5.96 g, 20 mmol) in pentane (100 ml) was added dropwise over 30 min to a stirred mixture of rhodium(II) octanoate (0.156 g, 0.2 mmol) and ethyl 1-propenyl ether (8.6 g, 100 mmol, E / Z =1 : 2.4) in pentane (100 ml), heated under reflux in an argon atmosphere. After heating for a further 20 min, the solvent was evaporated under reduced pressure. Purification by column chromatography on Al_2O_3 (neutral) using ether-petroleum ether (1 : 19) as eluant gave **14**. Yield 5.88 g (82%): Ir

(neat) 1700, 1620 cm^{-1}; ^1H nmr ($CDCl_3$) δ 4.24 (s, 1 H), 4.16 (s, 1 H), 3.65 (dq, *J* = 10.5, 7.0 Hz, 1 H), 3.58 (dq, *J* = 10.5, 7.0 Hz, 1 H), 3.47 (d, *J* = 7.3 Hz, 1 H), 1.70 (dq, *J* = 7.3, 6.6 Hz, 1 H), 1.59 (s, 9 H), 1.20 (t, *J* = 7.0 Hz, 3 H), 1.13 (d, *J* = 6.6 Hz, 3 H), 0.91 (s, 9 H), 0.21 (s, 3 H), 0.19 (s, 3 H); ^{13}C nmr ($CDCl_3$) δ 172.0, 150.4, 94.8, 80.2, 66.9, 66.4, 37.2, 28.0, 25.7, 24.4, 18.0, 15.0, 8.0, –4.8, –5.1. Anal. Calcd for $C_{19}H_{36}O_4Si$: C, 64.00; H, 10.18. Found: C, 64.18; H, 10.22.

5α-Ethoxy-4β-methyl-3-(1-((1,1-dimethylethyl)dimethylsilyloxy)ethylidene-4,5-dihydro-2-furanone (15) A solution of **14** (1.78 g, 5 mmol) in CH_2Cl_2 (25 ml) was added dropwise over 5 min to a stirred solution of $BF_3{\cdot}OEt_2$ (5.77 g, 5 ml) in CH_2Cl_2 (25 ml) under Ar at 0 °C. The mixture was maintained at 0 °C for 30 min. After quenching with ethanol, water was added and the mixture was extracted twice with ether. The combined organic layers were washed with water and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated. Purification by column chromatography on silica gel using ether-petroleum ether (2 : 8) as eluant gave **15** as a colorless oil. Yield 0.71 g (50%): Ir (neat) 1740, 1640 cm^{-1}; ^1H nmr ($CDCl_3$) δ 4.94 (s, 1 H), 3.85 (dq, *J* = 9.6, 7.0 Hz, 1 H), 3.54 (dq, *J* = 9.6, 7.0 Hz, 1 H), 2.98 (q, *J* = 7.0 Hz, 1 H), 2.35 (s, 3 H), 1.20 (t, *J* = 7.0 Hz, 3 H), 1.14 (d, *J* = 7.0 Hz, 3 H), 0.94 (s, 9 H), 0.24 (s, 6 H); ^{13}C nmr ($CDCl_3$) δ 163.9, 109.4, 105.8, 64.3, 39.8, 28.0, 25.5, 19.0, 18.0, 17.0, 14.9, -3.3, -3.4. Anal. Calcd for $C_{15}H_{28}O_4Si$: C, 59.96; H, 9.39. Found: C, 60.03; H, 9.42.

Dihydro-3-acetyl-5α-ethoxy-4β-methyl-2(3H)-furanone (12) Tetrabutyl ammonium fluoride (3 ml, 1.0 M in THF, 3 mmol) was added dropwise to a stirred solution of dihydrofuran **15** (0.60 g, 2 mmol) in THF (30 ml) at room temperature and the mixture was stirred for a further 45 min. The mixture was then poured into water and extracted with CH_2Cl_2 (2X). The combined extracts were washed with saturated NaCl solution, dried ($MgSO_4$) and concentrated. Purification by column chromatography on silica gel using ether/petroleum ether (2 : 8) as eluant gave **12**. Yield 0.31 g (84%): Ir (neat) 1760, 1710, 1650 cm^{-1}; ^1H nmr ($CDCl_3$) (major isomer) δ 5.08 (d, *J* = 4.9 Hz, 1 H), 3.84 (dq, *J* = 9.7, 7.0 Hz, 1 H), 3.61 (dq, *J* = 9.7, 7.0 Hz, 1 H), 3.23 (d, *J* = 8.0 Hz, 1 H), 2.86 (dqd, *J* = 8.0, 7.0, 4.9 Hz, 1 H), 2.39 (s, 3 H), 1.21 (t, *J* = 7.0 Hz, 3 H), 1.14 (d, *J* = 7.0 Hz, 3 H). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.13; H, 7.63.

Dihydro-3β-acetyl-5α-ethoxy-3α,4β-dimethyl-2(3H)-furanone (2b) Iodomethane (5.25 g, 2.3 ml, 37 mmol) was added dropwise over 3 min to a stirred solution of **12** (0.69 g, 3.7 mmol) and K_2CO_3 (6.1g, 37 mmol) in DMF (40 ml) at room temperature and the mixture was stirred for a further 1.5 h. The mixture was then poured into water and extracted with ether (3X). The combined extracts were washed with saturated $NaHCO_3$ solution and saturated NH_4Cl solution, dried($MgSO_4$) and concentrated. Purification by column chromatography on silica gel using ether-petroleum ether (1 : 19) as eluant gave **2b**. Yield 0.56 g (76%): Ir (neat) 1770, 1700 cm^{-1}; ^1H nmr ($CDCl_3$) δ 5.24 (d, *J* = 6.6 Hz, 1 H), 3.90 (dq, *J* = 9.5, 7.1 Hz, 1 H), 3.65 (dq, *J* = 9.5, 7.1 Hz, 1 H), 2.81 (s, 3 H), 2.14 (qd, *J* = 7.3, 6.6 Hz, 1 H), 1.50 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H), 1.03 (d, *J* = 7.3 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 205.5, 174.4, 107.8, 66.8, 61.3, 47.9, 28.8, 19.5, 14.9, 10.7. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.10; H, 8.11.

Dihydro-3α-acetyl-5β-ethoxy-4β-methyl-2(3H)-furanone (16). A solution of **14** (0.71g, 2 mmol) in CH_2Cl_2 (10 ml) was added dropwise over 3 min to a stirred solution of TFA (7.40 g, 5 ml, 65 mmol) in CH_2Cl_2 (10 ml) under Ar at -78 °C. After stirring at -78 °C for a further 30 min the mixture was gradually warmed to room temperature over 2 h. Ethanol (5 ml) and water (50 ml) were then added and the mixture was extracted with ether(2X). The combined organic layers were washed with saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated. The nmr spectrum of crude reaction mixture showed that the ratio of **12** : **16** = 1 : 2. Purification by column chromatography on silica gel using ether-petroleum ether (1 : 9) as eluant gave **12** (0.08 g, 22 %) and **16** (0.15 g, 40 %): Ir (neat) 1770, 1720, 1650 cm^{-1}; ^1H nmr ($CDCl_3$) δ 5.33 (d, J = 5.4 Hz, 1 H), 3.82 (dq, J = 9.6, 7.1 Hz, 1 H), 3.55 (dq, J = 9.6, 7.1 Hz, 1 H), 3.45 (d, J = 11.0 Hz, 1 H), 2.95 (dqd, J = 11.0, 6.8, 5.4 Hz, 1 H), 2.41 (s, 3 H), 1.19 (t, J = 7.1 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 200.5, 172.0, 103.9, 65.3, 58.0, 36.6, 30.3, 14.8, 12.1. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.96; H, 7.54.

Dihydro-3α-acetyl-5β-ethoxy-3β,4β-dimethyl-2(3H)-furanone (2c) and Dihydro-3α-acetyl-5β-ethoxy-3α,4β-dimethyl-2(3H)-furanone (2a). A solution of thallous ethoxide (2.49 g, 10 mmol) in ligroin (4 ml) was added in one portion to a stirred solution of **16** (1.86 g, 10 mmol) in a mixture of ligroin (4 ml) and toluene (4 ml). After stirring for a further 30 min the resulting solid was filtered and dried in vacuo. The solid was combined with freshly distilled methyl iodide (10 ml, 160 mmol) and then heated under reflux in Ar for 50 min. The mixture was then cooled to room temperature and the supernatant was passed through a pad of Florisil. The solid residue was washed with THF, and the THF washings were also passed through a Florisil column. Evaporation of the solvent gave 1.19 g (60%) of **2a** and **2c** in a ratio of 1 : 1.5. which were separable by hplc on silica gel using isopropanol-hexane (1 : 9) as eluant. Under the reaction conditions described for the preparation of **2b**, the ratio of **2a** to **2c** was 1 : 5. **2a**: white solid, mp. 48-51 °C; ir (CCl_4) 1780, 1710 cm^{-1}; ^1H nmr ($CDCl_3$) δ 5.39 (d, J = 5.2 Hz, 1H), 3.85 (dq, J = 9.5, 7.1 Hz, 1H), 3.64 (dq, J = 9.5, 7.1Hz, 1H), 2.40 (qd, J = 7.3, 5.2 Hz, 1 H), 2.29 (s, 3 H), 1.39 (s, 3 H), 1.24 (t, J = 7.1 Hz, 3 H), 1.03 (d, J = 7.3 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 204.0, 178.4, 103.3, 65.2, 57.4, 46.6, 29.1, 21.0, 14.8, 9.5. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.94; H, 8.07.

2c : colorless oil, ir (neat) 1775, 1710 cm^{-1}; ^1H nmr ($CDCl_3$) δ 5.37 (d, J = 6.4 Hz, 1 H), 3.83 (dq, J = 9.7, 7.0 Hz, 1 H), 3.54 (dq, J = 9.7, 7.0 Hz, 1 H), 3.00 (qd, J = 7.1, 6.4 Hz, 1 H), 2.31 (s, 3 H), 1.47 (s, 3 H), 1.20 (t, J = 7.0 Hz, 3 H), 0.96 (d, J = 7.1 Hz, 3 H); ^{13}C nmr ($CDCl_3$) δ 204.0, 176.7, 104.0, 65.6, 58.1, 39.0, 25.8, 16.9, 14.8, 8.3. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.10; H, 8.07.

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