Pergamon

Tetrahedron, Vol. 53, No. 6, pp. 2241-2252, 1997
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0040-4020/97 $17.00 + 0.00

PII: S0040-4020(96)01126-X

Novel Michael-Wittig Reactions of Methyl 3-oxo-4-(triphenylarsoranylidene)butanoate and Substituted 2*H*-Pyran-5-carboxylates; The Synthesis of Highly Functionalised 2-Cyclohexenonedicarboxylates.

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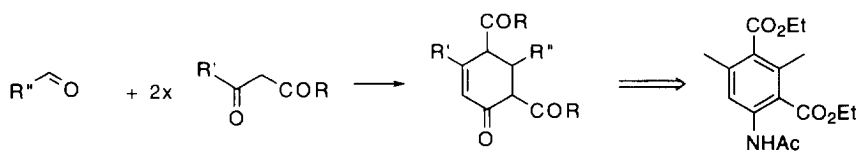
Abstract: Novel Michael-Wittig condensations of methyl 3-oxo-4-(triphenylarsoranylidene)-butanoate **6** and substituted 2,2-dimethyl-2*H*-pyran-5-carboxylates **5a** to **5e** gave substituted 4-alkyl-6-oxo-4-cyclohexene-1,3-dicarboxylates **8a** to **8e** in a mixture of three keto diastereomers and two enol diastereomers. Apart from substituted 4-alkyl-6-oxo-4-cyclohexene-1,3-dicarboxylates **8f** to **8g**, less hindered substituted 2-methyl-2*H*-pyran-5-carboxylates **5f** and **5g** gave the substituted tetrahydrobenzofurans **9f** and **9g**. 4-Halomethyl-6-oxo-4-cyclohexene-1,3-dicarboxylates **8** were mostly in the enol diastereomeric form. A plausible mechanism is given for the unique formation for these products. © 1997, Elsevier Science Ltd. All rights reserved.

INTRODUCTION

New annulation techniques in organic chemistry are important. It is well known that substituted cyclohexenones are essential intermediates in organic synthesis.[1] Diethyl 2,4-dimethyl-6-oxo-2-cyclohexene-1,3-dicarboxylates **3** (R = OEt, R' = R" = Me) are precursors for the preparation of certain anti-hypertensives like diethyl 6-acetamido-2,4-dimethylisophtalate **4**, and have been patented as such (Scheme 1).[2,3]

Scheme 1



1 **2** **3** **4**

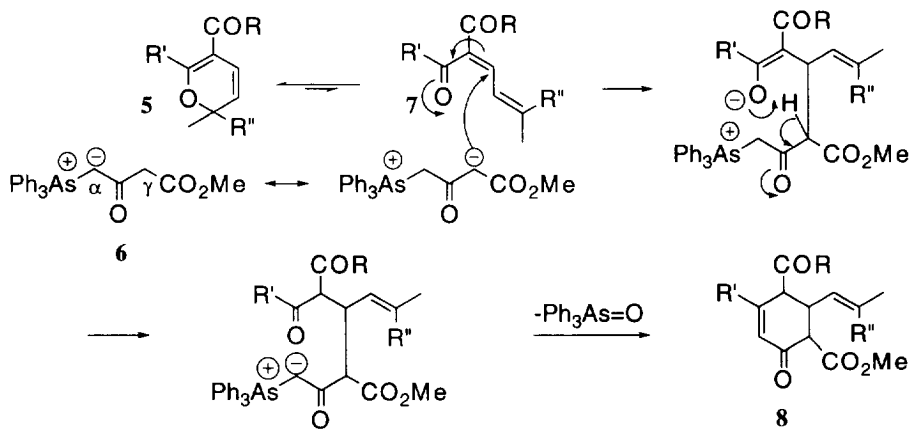
Reliable syntheses of 6-oxo-2-cyclohexene-1,3-dicarboxylates **3** are not very common. A simple 6-oxo-2-cyclohexene-1,3-dicarboxylate **3** (R = OEt, R' = Me, R" = H) can be prepared from formaldehyde **1** (R" = H) and two equivalents of ethyl 3-oxobutanoate **2** (R' = Me, R = OEt) (Scheme 1).[4] Some time ago a series of 6-oxo-2-cyclohexene-1,3-dicarboxylates **3** (R = OEt, R' = Me, R" = 4-$NO_2C_6H_4O$, $PhCH_2O$, PhO, $PhCO_2$) has been prepared.[5] The yield of 4,6-diacetyl-5-ethyl-3-methyl-2-cyclohexenone **3** (R = R' = Me, R" = Et), prepared from propanal **1** (R" = Et) and 2,4-pentadione **2** (R = R' = Me) under base catalysed conditions, has not been reported.[6] None of these methods provide a general synthesis for highly substituted 6-oxo-2-cyclohexene-1,3-dicarboxylates **3**. In a previous study we have found that ethyl 3-oxo-4-(triphenyl-

phosphoranylidene)butanoate **2** (R = OEt, R' = Ph_3P=CH) reacted with 3-methyl-2-butenal **1** [R" = $(CH_3)_2C$=CH] to form the conjugated 6-oxo-2-cyclohexene-1,3-dicarboxylate **3** [R = OEt, R' = $(CH_3)_2C$=CHCH=CH, R" = $(CH_3)_2C$=CH] in a rather low yield.[7,8] The last mentioned condensation is unique, and is in fact a Michael-Wittig condensation of the ketoform of the conjugated 2*H*-pyran-5-carboxylate **5** [R = $(CH_3)_2C$=CHCH=CH, R' = OEt, R" = Me] and the γ-ylide of ethyl 3-oxo-4-(triphenylphosphoranylidene)-butanoate **2** (R = OEt, R' = Ph_3P=CH) (Scheme 2).[7,8] In this paper we report the investigation of the unique Michael-Wittig condensations of methyl 3-oxo-4-(triphenylarsoranylidene)-butanoate **6** and substituted 2*H*-pyran-5-carboxylates **5**.

RESULTS

Methyl 3-oxo-4-(triphenylarsoranylidene)butanoate **6** was prepared *in situ* by adding K*t*-OBu to a fine suspension of (3-methoxycarbonyl-2-oxopropyl)triphenylarsonium bromide[9] in THF. The pale yellow ylide **6**[10] reacted within two hours at room temperature with methyl 2,2,6-trimethyl-2*H*-pyran-5-carboxylate **5a** (R = OMe, R' = R" = Me) and after workup and chromatography gave dimethyl 4-methyl-2-(2-methyl-1-propenyl)-6-oxo-4-cyclohexene-1,3-dicarboxylate **8a** (R = OMe, R' = R" = Me). The mechanism of this reaction can be rationalized as follows; 2*H*-Pyran-5-carboxylate **5a** (R = OMe, R' = R" = Me)[11,12] has the ability to undergo reversible electrocyclic ring opening to the conjugated ketodiene **7a** (R = OMe, R' = R" = Me).[13,14] Michael-attack of the γ-ylide form of **6**[15] on **7a** followed by an intramolecular Wittig condensation furnishes **8a** (Scheme 2).[16] Likewise, 2*H*-pyrans **5c** - **5e** reacted with **6** to form 6-oxo-4-cyclohexene-1,3-dicarboxylates **8b** - **8e** (Table 1).

Scheme 2. The Mechanism of the Michael-Wittig Condensation of 2*H*-Pyran-5-carboxylates 5 and Methyl 3-oxo-4-(triphenylarsoranylidene)butanoate 6

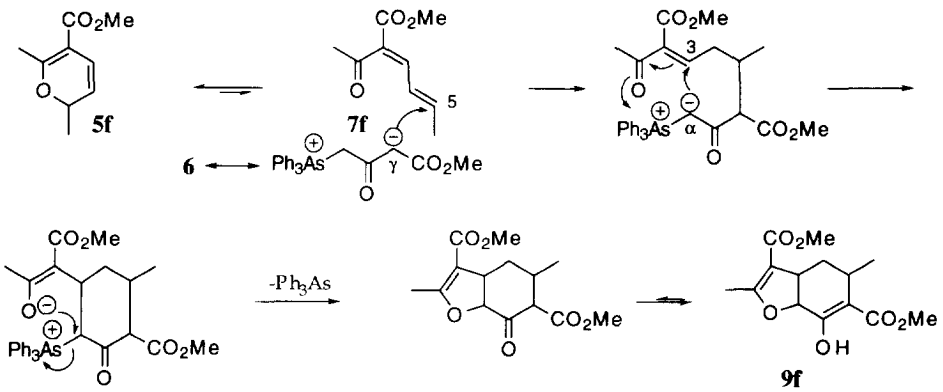


The possibility of a Wittig-Michael mechanism seems unlikely; no detectable acyclic Wittig intermediate was isolated. Direct nucleophilic attack of **6** on **5** did not seem to have taken place and no five- or larger than 6 membered products could be found in noticeable quantities. Perhaps surprisingly, we did not isolate cyclopropane derivatives in any identifiable amounts.[17] However, some triphenylarsine (Ph_3As) was

liberated during the reaction. Triphenylarsine was also isolated when **6** was left for 24 h. at 40 °C. We have not analysed the polar residual triphenylarsine oxide and unreacted arsonium ylide **6** fraction.[16c, 16d]

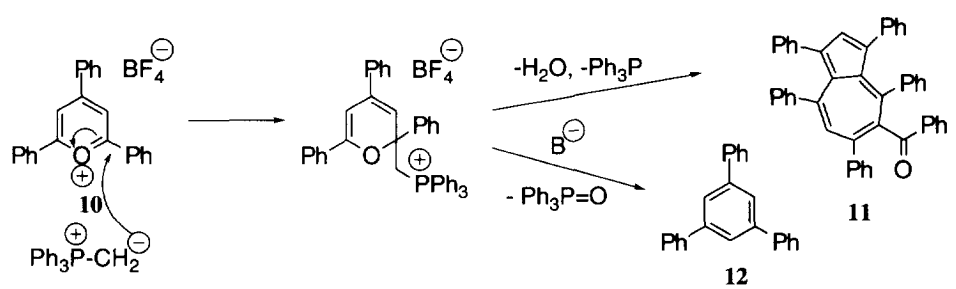
2H-pyrans **5f** and **5g** reacted with **6** and gave, apart from the expected 6-oxo-4-cyclohexene-1,3-dicarboxylates **8f** and **8g** respectively, a further unique product, the tetrahydrobenzofurans **9f** and **9g** in a low yield of the diastereomeric mixture. These products **9f**, **9g** are *trans*-fused and in $CDCl_3$ only in the enol form (Table 1). A plausible mechanism is given in Scheme 3. A C_γ-C_5 Michael addition of **6** and **7f** gives after transylidation a new arsonium ylide. This is followed by an intramolecular C_α-C_3 attack to give tetrahydrobenzofuran **9f** and triphenylarsine (CAUTION; chromatography of the crude reaction mixture using 100% petroleum ether on silica gel gives triphenylarsine).

Scheme 3. The Mechanism for the Formation of Tetrahydrobenzofuran 9f



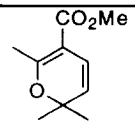
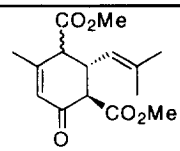
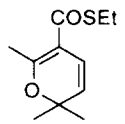
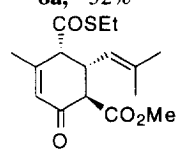
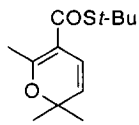
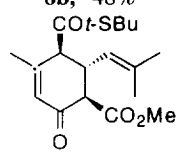
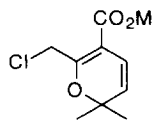
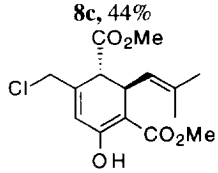
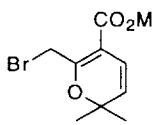
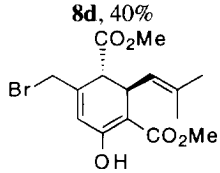
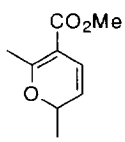
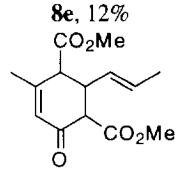
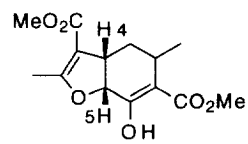
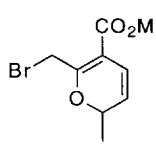
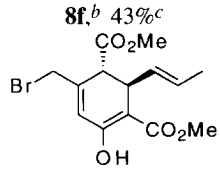
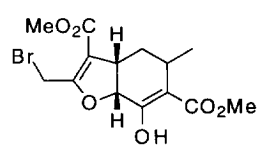
Apart from our previous work,[7,8] few Wittig condensation reactions of ylides with 2*H*-pyrans are known.[18,19] For example, the formation of an azulene **11** from pyrylium salt **10** and methylphosphoranylidene seems to involve a 2*H*-pyran intermediate (Scheme 4).[18,19,20] Performing the condensation in little acetonitrile produced the benzene derivative **12**.[19] When the reaction was allowed to react in larger volumes of acetonitrile and dichloromethane a novel azulene **11** was produced.[18]

Scheme 4. Some Previous 2*H*-Pyran - Phosphonium Ylide Reactions[18,19]



We investigated whether we could induce assymetric preference for one of the three diastereomers of ketodiester **8a** by using *S*-limonene as a co-solvent together with THF (1:1) and comparing the result with that

Table 1

Entry	2*H*-Pyran **5**[a]	Reaction conditions Time, Temp	Products and Yield: Ph_3As	Unreacted **5**	Cyclohexenone **8**	Tetrahydrobenzofuran **9**
a	 **5a**	3.5 h, rt	16%	25%	 **8a**,[b] 52%[c]	-
b	 **5b**	3.5 h, rt	21%	5%	 **8b**,[b] 48%	-
c	 **5c**	12h, 40 °C	33%	~10%	 **8c**, 44%	-
d	 **5d**	12 h, 40 °C	21%	0%	 **8d**, 40%	-
e	 **5e**	6h, rt	12%	30%	 **8e**, 12%	-
f	 **5f**	72h, -21 °C	13%	0%	 **8f**,[b] 43%[c]	 **9f**,[b] 20%
g	 **5g**	5h, rt	28%	9%	 **8g**, 12%	 **9g**,[b] 6%

[a] Details for the preparation of these 2*H*-pyrans are available on request. Also see ref. 11 and 12.

[b] Heteronuclear (^{13}C-^{1}H) and homonuclear (^{1}H-^{1}H) shift correlations were used to assign unambiguously the chemical shift and coupling constants reported. For **8b** and **9f** NOESY was also used; for **9f** NOE 2D spectrometry was consistent with the *cis*-configuration of protons H-4 and H-5 (see experimental section).

[c] **8a** and **8f** were obtained in 24% and 31% respectively using the corresponding phosphonium ylide.[8]

obtained using *R*-Limonene (Table 2). However, the ratio-difference of the three keto diastereomers is most probably due to a change in the polarity of the solvent. Although the ylide **6** will attack, for example, **7a** from a prefered, less-hindered, position (Scheme 5), chromatography on silica gel seems to enhance enolisation which will naturally equilibrate with two new ketodiesters of **8a**. In fact, it was found that of the possible four ketodiesters of **8a** only three are found together with the expected two enoldiesters. The ratio of 56:26:18 for the three ketodiesters of **8a** (Table 2) was obtained from the relative intensities of the ketocarbonyl ^{13}C-NMR peaks. This ratio was further verified with the two vinyl protons in the ^{1}H-NMR. In the beginning, freshly chromatographed (silica gel) **8a** gave a total enolisation ($CDCl_3$) of ~21%. The ratio of the three ketodiesters **8a** changed within 24 hours ($CDCl_3$) to 61:28:11, due to a drop in enolisation. The thermodynamically more stable main isomer was slowly further enriched. After seven days the ratio had changed to 61:30:9. After two weeks almost no enoldiester of **8a** was left ($CDCl_3$). It seems that one of the enoldiesters of **8a** shifts faster out of enolisation than the other.

Scheme 5

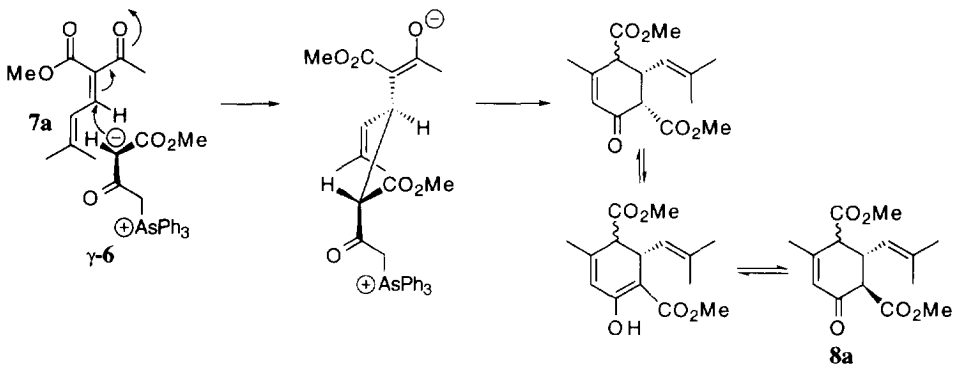


Table 2.

Entry	conditions	ketoform ratio 1	2	3	enolisation
1	THF (old sample)	71	21	8	no enol
2	R-Limonene : THF (1:1)	57	24	18	enolised
3	,, after 24 hours	59	24	17	less enolised
4	S-Limonene : THF (1:1)	56	26	18	21% enolised
5	,, after 24 hours	61	28	11	less enolised
6	,, after 7 days	61	30	9	no enol
7	,, after 5 months	69	28	3	no enol

The assignment of the chemical shifts for different protons in the ring system was established by ^{1}H-NMR and confirmed by 2-D COSY and (^{1}H-^{13}C)-HETCOR correlation experiments. We were not able to assign the correct stereochemistry for **8a**, as one of the protons was hidden under the methoxy protons, while

another proton was partially obscured by protons of other keto- and enoldiesters of **8a**. However **8b** showed all three aliphatic protons of the ring system, and it was therefore possible to assign the correct stereochemistry and the preferred conformation showed two substituents in the equatorial positions.[21,22] The stereochemistry of **8c** was less clear due to overlap of two other ketoforms, but the main isomer showed two large vicinal coupling constants (two different doublets), again the preferred conformation showed all three substituents in the equatorial position. From the analyses of the NMR spectra, compounds **8d**, **8e** and **8g** were shown to be strongly enolised (>50%); this complicated the NMR analyses of the minor ketodiesters of these compounds. All three aliphatic protons of the cyclohexenone ring of the three ketodiesters **8f** were in one multiplet and no stereochemical assignment could be made. In fact, the HETCOR of **8f** actually showed the correct vicinity of the three protons of the main ketodiester of **8f**. We were able to assign the correct stereochemistry of bicyclic *cis*-fused sytem of the main isomer for compounds **9f** and **9g**, Both compounds exhibited large vicinal coupling constants (J = 9.2 and 10.4 Hz respectively).

CONCLUSION

The investigation of Michael-Wittig condensations of **6** with 2*H*-pyran-5-carboxylates **5**, has shown that for these type of Michael-Wittig condensations the arsonium ylide **6** is a superior reagent[8] to phosphonium analogue **2** (R = OEt, R' = Ph_3P=CH).[23]

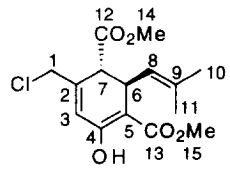
EXPERIMENTAL SECTION

^{1}H-NMR and ^{13}C-NMR were recorded on a Varian Gemini-200 spectrometer at 200 MHz and 50.3 MHz respectively in $CDCl_3$ with TMS as an internal standard for ^{1}H-NMR. High resolution electron ionization (EI) mass spectra and chemical ionization spectra (CI) using ammonia, were obtained from a Kratos Concept ISQ instrument. Infrared spectra were obtained on a Hitachi 270-30 FTIR spectrophotometer (film, NaCl plates). Ultraviolet absorbance was measured as solutions in 96% EtOH on a Shimadzu UV-150 spectrophotometer. Microanalyses were performed using a Carlo Erba, CHNS-O EA 1108 Elemental Analyser. Column chromatography was performed using Merck Si-60 (40-63mm) silica gel. (3-Methoxycarbonyl-2-oxopropyl)triphenylarsonium bromide was prepared by heating neat methyl 4-bromo-3-oxobutanoate with triphenylarsine in a melt.[9]

Typical Procedure for the Michael-Wittig Condensation of 2*H*-pyran-5-carboxylate 5 and Methyl 3-oxo-4-(triphenyl-arsoranylidene)butanoate 6.

K*t*-OBu (0.32 g, 2.85 mmol) was added all at once to a fine suspension (3-methoxycarbonyl-2-oxopropyl)triphenylarsonium bromide (1.50 g, 3.00 mmol) in anhyd. THF (10 mL) at 0 °C. A bright yellow colour appeared immediately but slowly faded after 10 min. at 0 °C. The solution of the ylide **6** was treated with methyl 6-chloromethyl-2,2-dimethyl-2*H*-pyran-5-carboxylate **5d** (0.55 g, 2.54 mmol) in THF (2 mL) at 0 °C and stirred under argon for 12 hours at 40 °C. The reaction mixture was treated with ether:petroleum ether (1:1) (50 mL) and the solution filtered over silica gel. The filtrate was concentrated and the residue

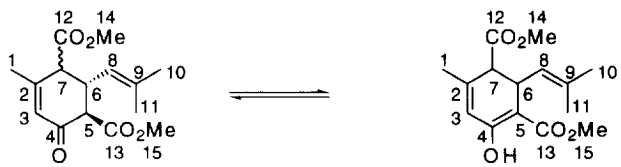
chromatographed on silica gel. Elution with petroleum ether gave triphenylarsine (194 mg, 21%) and further elution with ether:petroleum ether (1:9) gave dimethyl 6-chloromethyl-4-hydroxy-2-(2-methyl-1-propenyl) 3,5-cyclohexadiene-1,3-dicarboxylate **8d** (316 mg, 40%).



HRMS (CI) calcd for $C_{15}H_{20}ClO_5$ ($MH^{+\cdot}$) m/z 315.0999, found 315.0992. MS; 332 (MNH_4^+, 50), 315 ($M^{+\cdot}$, 20), 298 (100), 281 (50). ν_{max} (film) 2954 (m), 1738 (s), 1666 (s), 1634 (m), 1601 (m), 1443 (s), 1356 (m), 1288 (s), 1224 (s), 1076 (m) cm^{-1}. λ_{max} = 206 (sh), 230, 320 (ε = 6500, 7700, 3600). ^1H NMR: δ = 1.6 (3H, s, CH_3-11), 1.7 (3H, s, CH_3-10), 3.2-3.3 (1H, m, CH-6), 3.6-3.8 (1H, m, CH-7), 3.698 and 3.764 (2x3H, 2s, CH-14 and CH-15), 4.265 (2H, s, CH_2-1), 5.068 (1H, dm, J = 10.1 Hz, CH-8), 6.213 (1H, sm, CH-3), 12.0 (OH, s). ^{13}C NMR: δ = 17.84 (CH_3-11), 25.57 (CH_3-10), 33.09 (CH-6), 46.64 (CH-7), 46.84 (CH_2-1), 51.49 and 52.38 (2xCH_3-14, -15), 97.96 (C-5), 123.31, 123.49 (C-3, C-8), 132.49 (C-9) 140.56 (C-2), 163.40 (C-4), 170.91 (C-12; C-13).

Anal. Calcd for $C_{15}H_{19}ClO_5$: C, 57.24; H, 6.08. Found: C, 57.11; H, 5.87.

For: dimethyl 4-methyl-2-(2-methyl-1-propenyl)-6-oxo-4-cyclohexene-1,3-dicarboxylate **8a**[8]



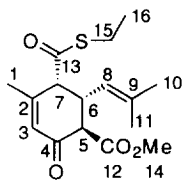
HRMS (EI) calcd for $C_{15}H_{20}O_5$ *m/z* 280.1311, Found: 280.1315. MS; 280 ($M^{+\cdot}$, 10), 265 (10), 248 (20), 233 (15), 221 (70), 189 (100), 161 (50), 112 (80). ν_{max} (film) 2953 (m), 2916 (m), 1743 (s), 1673 (s), 1634 (m), 1437 (m), 1265 (m), 1247 (m), 1152 (m) cm^{-1}. λ_{max} = 233, 316 (ε = 10100, 1440). ^1H NMR (major keto isomer, 70%): δ = 1.635 (3H, d, J = 1.2 Hz, CH_3-11), 1.681 (3H, d, J = 1.2 Hz, CH_3-10), 1.951 (3H, d, J = 1.1 Hz, CH_3-1), 3.197 (1H, d, J = 12.4 Hz, CH-7), 3.220 (1H, dm, J = 10.3 Hz, CH-5), 3.75-3.70 (1H, m, CH-6), 3.705 and 3.715 (6H, 2s, CH-14, CH-15), 4.954 (1H, dm, J = 10.1, 1.3 Hz, CH-8), 6.021 (1H, sm, J = 0.9 Hz, CH-3); (minor keto-isomer, 30%): δ = 1.640 (3H, s, CH_3-11), 1.683 (3H, d, J = 1.2 Hz, CH_3-10), 2.019 (3H, d, J = 1.2 Hz, CH_3-1), 3.197 (1H, d, J = 12.4 Hz, CH-7), 3.220 (1H, dm, J = 10.3 Hz, CH-5), 3.75-3.70 (1H, m, CH-6), 3.705 and 3.715 (6H, 2s, CH-14, CH-15), 4.954 (1H, dm, J = 10.1, 1.3 Hz, CH-8), 6.021 (1H, sm, J = 0.9 Hz, CH-3). ^{13}C NMR: δ = 17.27 (CH_3-11), 21.38 (CH_3-1), 25.25 (CH_3-10), 40.03 (CH-6), 51.33 and 51.59 (CH_3-14, CH_3-15), 52.46 (CH-7), 57.91 (CH-5), 121.66 (CH-8), 126.61 (CH-3), 136.85 (C-9) 156.77 (C-2), 168.95 (C-13), 171.01 (C-12), 191.94 (C-4).

^1H NMR (enol-isomer): δ = major 1.761 (3H, d, J=1.2 Hz, CH_3-11), 1.707 (3H, s-, CH_3-10), 1.954, [*minor*; *2.031*] (3H, s, CH_3-1), 3.8-3.2 2H, m, CH-6, CH-7), 3.705 and 3.715 (6H, 2s, CH-14, CH-15), 5.070 (1H, dm, J=10.2 Hz, CH-8), 5.933 (1H, sm, CH-3) 11.891, [*minor12.053*] (1H, OH); ^{13}C NMR (major enol

isomer, 68%): δ = 17.68 (CH_3-11), 20.33 (CH_3-1), 25.48 (CH_3-10), 23.70 (CH-6), 33.23 (CH-7), 51.33 and 51.59 (CH_3-14, CH_3-15), 95.21 (C-5), 120.61 (CH-8), 124.36 (CH-3), 132.02 (C-2), 144.02 (C-9), 164.97 (C-4), 171.47, 172.02 (C-12, C-13); (minor enol isomer, 32%): δ = 17.37 (CH_3-11), 21.19 (CH_3-1), 25.42 (CH_3-10), 22.89 (CH-6), 35.98 (CH-7), 51.33 and 51.59 (CH_3-14, CH_3-15), 99.09 (C-5), 120.77 (CH-8), 124.97 (CH-3), 131.90 (C-2), 137.56 (C-9), 167.01 (C-4), 171.47, 172.02 (C-12, C-13).

Anal. Calcd. for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.30; H, 6.99.

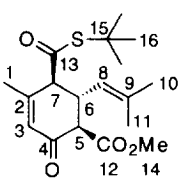
For: S-ethyl, methyl 4-methyl-2-(2-methyl-1-propenyl)-6-oxo-4-cyclohexene-1,3-dicarboxylate **8b**



HRMS (EI) calcd for $C_{16}H_{22}O_4S$ *m/z* 310.1239, found 310.1239. MS; 310 ($M^{+\cdot}$, 5), 249 (20), 221 (70), 189 (100), 161 (40), 109 (85). ν_{max} (film) 2970 (m), 2932 (m), 2875 (w), 1746 (s), 1675 (s), 1634 (m), 1601 (m), 1442 (m), 1350 (m), 1258 (s), 1154 (m), 833 (m), 733 (m) cm^{-1}. λ_{max} = 207 (sh), 236 (ε = 6600, 13800). ^1H NMR: δ = 1.272 (3H, t, *J* = 7.4 Hz, CH_3-16), 1.685 (3H, d, *J* = 1.4 Hz, CH_3-10), 1.705 (3H, d, *J* = 1.2 Hz, CH_3-11), 2.018 (3H, d, *J* = 1.2 Hz, CH_3-1), 2.908 and 2.933 (2H, 2xq, *J* = 7.4 Hz, CH_2-15), 3.422 (1H, d, *J* = 5.0 Hz, CH-7), 3.568 (1H, ddd, *J* = 12.7, 9.8, and 5.0 Hz, CH-6), 3.695 (3H, s, CH_3-14), 3.893 (1H, d, *J* = 12.7 Hz, CH-5), 4.940 (1H, dm, *J* = 9.8 Hz, CH-8), 6.035 (CH, sm, CH-3). ^{13}C NMR: δ= 14.46 (CH_3-16), 18.01 (CH_3-10), 23.39 (CH_3-1), 24.20 (CH_2-15), 25.78 (CH_3-11), 39.83 (CH-6), 52.04 (CH_3-14), 55.35 (CH-5), 58.94 (CH-7), 120.95 (CH-8), 127.54 (CH-3), 137.15 (C-9) 156.36 (C-2), 170.35 (C-12), 193.57 (C-13), 196.59 (C-4).

Anal. Calcd for $C_{16}H_{22}O_4S$: C, 61.91; H, 7.14; S, 10.33. Found: C, 61.85; H, 7.32; S, 10.62.

For: S-*t*-Butyl, methyl 4-methyl-2-(2-methyl-1-propenyl)-6-oxo-4-cyclohexene-1,3-dicarboxylate **8c**



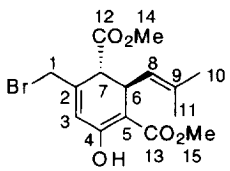
61 : 28 : 11

HRMS (EI) calcd for $C_{18}H_{26}O_4S$ *m/z* 338.1552, found 338.1566. MS; 338 ($M^{+\cdot}$, 25), 310 (30), 281 (10), 249 (10), 222 (25), 189 (50), 163 (25), 109 (40), 57 (100). ν_{max} (film) 2965 (m), 2915 (m), 1747 (s), 1673 (s), 1633 (m), 1602 (w), 1438 (m), 1364 (m), 1281 (m), 1258 (m), 1155 (m), 733 (m) cm^{-1}. λ_{max} = 237, 315 (sh) (ε = 15200, 600). ^1H NMR (major keto-isomer): δ = 1.453 (9H, s, 3xCH_3-16), 1.596 (3H, d, *J* = 1.3 Hz, CH_3-11), 1.682 (3H, s, CH_3-10), 1.993 (3H, d, *J* = 1.3Hz, CH_3-1), 3.219 (1H, d, *J* = 12.7 Hz, CH-7), 3.304 (1H, d, *J* = 13.7 Hz, CH-5), 3.6-3.4 (1H, m, CH-6), 3.686 (3H, s, CH-14), 4.969 (1H, dm, *J* = 12.2, 1.3 Hz, CH-8), 5.988 (CH, sm, *J* = 1.3 Hz, CH-3). Minor keto-isomer: δ = 1.474 (9H, s, 3xCH_3-16), 1.719 (3H, d, *J* = 1.3 Hz,

CH_3-11), 1.775 (3H, d, J = 1.3 Hz, CH_3-10), 2.016 (3H, d, J = 1.3Hz, CH_3-1), 3.892 (1H, d, J = 12.7 Hz, CH-5), 3.7-3.3 (2H, m, CH-6, CH-7), 3.724 (3H, s, CH-14), 4.969 (1H, dm, J = 12.2, 1.3 Hz, CH-8), 5.988 (CH, sm, J = 1.3 Hz, CH-3). ^{13}C NMR (major keto-isomer): δ = 17.79 (CH_3-11), 21.54 (CH_3-1), 25.50 (CH_3-10), 29.15 (3xCH_3-16), 40.58 (CH-6), 48.62 (C-15), 51.72 (CH_3-14), 58.66 (CH-5), 60.08 (CH-7), 121.87 (CH-8), 127.62 (CH-3), 136.92 (C-9) 157.88 (C-2), 169.19 (C-12), 192.25 (C-13), 198.79 (C-4). Minor keto-isomer: δ = 17.79 (CH_3-11), 21.54 (CH_3-1), 25.56 (CH_3-10), 29.46 (3xCH_3-16), 39.68 (CH-6), 49.16 (C-15), 51.12 (CH_3-14), 58.92 (CH-5), 60.47 (CH-7), 121.07 (CH-8), 127.16 (CH-3), 136.68 (C-9) 156.35 (C-2), 170.26 (C-12), 193.34 (C-13), 197.03 (C-4).

Anal. Calcd for $C_{18}H_{26}O_4S$: C, 63.88; H, 7.74; S, 9.47. Found: C, 63.85; H, 7.74; S, 9.59.

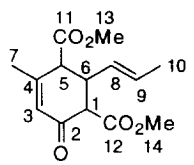
For: dimethyl 6-bromomethyl-4-hydroxy-2-(2-methyl-1-propenyl)-3,5-cyclohexadiene-1,3-dicarboxylate **8e**



HRMS (CI) calcd for $C_{15}H_{19}BrO_5$ ($MH^{+\cdot}$) m/z 359.0494, found 359.0461 MS; 359 ($MH^{+\cdot}$, 10). λ_{max} = 207, 231, 325 (ε = 9600, 9980, 3800). ν_{max} (film) cm^{-1}. ^{1}H NMR: δ = 1.674 (3H, d, J = 1.1 Hz, CH_3-11) [isomer: 1.646 (d, J = 1.1 Hz)], 1.773 (3H, d, J = 1.3 Hz, CH_3-10) [isomer: 1.739 (d, J = 1.0 Hz), 3.234 (1H, d, J = 1.4 Hz, CH-7), 3.7-3.6 (1H, m, CH-6), 3.700 and 3.772 (6H, 2s, CH_3-14, CH_3-15), 4.282 (1H, d, J = 9.8 Hz, CH_2-1a), 4.437 (1H, d, J = 9.8 Hz, CH_2-1b), 5.076 (1H, dm, J = 10.1, 1.3 Hz, CH-8), 6.204 (1H, sm, CH-3), 11.781 (1H, s, OH) [isomer: 12.088 (1H, s, OH)]. ^{13}C NMR: δ = 18.02 (CH_3-11), 25.68 (CH_3-10), 33.13 [33.66] (CH-6), 35.48 [36.78] (CH_2-7), 47.03 (CH-5), 51.62 and 52.49 (CH_3-14, CH_3-15), 98.19 [98.97] (C-1), 123.85 (CH-3), 123.98, (CH-8), 132.91 (C-2), 140.61 (C-9), 163.44, [166.95] (C-4), 171.08 and 172.02 (C-12, C-13).

Anal. Calcd. for $C_{15}H_{19}BrO_5$: C, 50.16; H, 5.33. Found: C, 50.29; H, 5.31.

For: dimethyl 4-methyl-2-(1-propenyl)-6-oxo-4-cyclohexene-1,3-dicarboxylate **8f**[8]

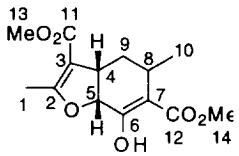


HRMS (EI) calcd for $C_{14}H_{18}BrO_5$ m/z 266.1154, found 266.1154. MS; 266 ($M^{+\cdot}$, 10), 234 (35), 207 (60), 175 (100), 147 (45), 135 (30), 121 (35), 112 (70). ν_{max} (film) 2953 (m), 1740 (s), 1674 (s), 1634 (m), 1437 (m), 1226 (s), 1156 (m) cm^{-1}. λ_{max} = 231, 312 (ε = 9600, 2400). ^{1}H NMR (major keto isomer, 70%): δ = 1.631 (3H, dd, J = 6.5, 1.5 Hz, CH_3-10), 1.953 (3H, s, CH_3-1), 3.4 - 3.2 (1H, m, CH-6), 3.36-3.31 (2H, m, CH-1, CH-5), 3.712 and 3.737 (6H, 2s, CH-13, CH-14), 5.4-5.2 (1H, m, CH-8), 5.620 (1H, ddm, J = 15.1, 6.4 Hz, CH-9), 5.994 (1H, sm, CH-3). ^{13}C NMR: δ = 17.49 (CH_3-10), 21.67 (CH_3-7), 44.17 (CH-6), 51.63 and

51.79 (CH_3-13, CH_3-14), 52.44 (CH-7), 57.73 (CH-1), 126.78 (CH-3), 126.83 (CH-8), 127.83 (CH-9), 156.63 (C-4), 169.03 (C-12), 171.02 (C-11), 191.92 (C-2).

Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.00; H, 7.15.

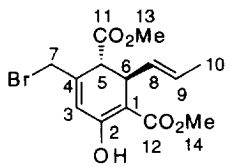
For: dimethyl 7-hydroxy-2,5-dimethyl-4a,4,5,7a-tetrahydrobenzofuran-3,6-dicarboxylate **9f**



HRMS (EI) calcd for $C_{14}H_{18}O_6$ m/z 282.1103, found 282.1095. MS; 282 ($M^{+\cdot}$, 20), 251 (20), 222 (20), 190 (30), 168 (50), 153 (100), 135 (70). ν_{max} (film) 2954 (m), 1702 (s), 1654 (s), 1438 (s), 1381 (m), 1357 (m), 1295 (s), 1216 (vs), 1084 (m) cm^{-1}. λ_{max} = 206 (sh), 251, 265 (sh) (ε = 3900, 13300, 11400). ^1H NMR: δ = 1.096 (3H, d, J = 7.0 Hz, CH_3-10), 1.358 (1H, ddd, J = 13.1, 12.9, 4.7 Hz, CH-9), 2.028 (1H, ddd, J = 13.1, 5.0, 2.4 Hz, CH-9), 2.245 (3H, s, CH_3-1), 2.860 (1H, qdd, J = 7.0, 4.7, 2.4 Hz, CH-8), 3.402 (1H, ddd, J = 12.9, 9.2, 5.0 Hz, CH-4), 3.739 and 3.828 (6H, 2s, CH_3-13, CH_3-14), 4.811 (1H, d, J = 9.2 Hz, CH-5), 12.119 (OH, 1H). ^{13}C NMR: δ = 14.19 (CH_3-1), 19.51 (CH_3-10), 26.87 (CH-8), 32.72 (CH_2-9), 37.15 (CH-4), 50.84 and 51.89 (CH_3-13, CH_3-14), 77.53 (CH-5), 107.38 (C-3), 107.84 (C-7), 163.36 (C-2), 165.86 (C-6), 167.72 (C-11), 172.16 (C-12).

Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.75; H, 6.78.

For: dimethyl 6-bromomethyl-4-hydroxy-2-(1-propenyl)-3,5-cyclohexadiene-1,3-dicarboxylate **8g**

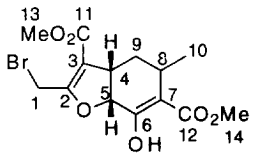


67-72% (isomer 28-33%)

HRMS (CI) calcd for $C_{14}H_{18}BrO_5$ ($MH^{+\cdot}$) m/z 345.0338, found 345.0336. MS; 345 ($MH^{+\cdot}$, 55), 283 (30), 267 (100), 251 (50), 235 (30), 207 (40), 175 (30). ν_{max} (film) 2954 (m), 1738 (s), 1662 (s), 1600 (m), 1442 (s), 1356 (m), 1224 (s), 1076 (m) cm^{-1}. λ_{max} = 208 (sh), 235, 324 (ε = 7100, 7600. 5000). ^1H NMR: δ = 1.636 (3H, d, J = 6.2 Hz, CH_3-10), 3.324 (1H, d, J = 1.3 Hz, CH-5), 3.691 and 3.782 (6H, 2s, CH_3-13, CH_3-14), 3.9 - 3.8 (1H, m, CH-6), 4.147 (1H, d, J = 10.5 Hz, CH_2-1a), 4.237 (1H, d, J = 10.5 Hz, CH_2-1b), [isomer: 4.060 (2H, s, CH_2-1)] 5.350 (1H, dm, J = 15.0 Hz, CH-8), 5.555 (1H, dqd J = 15.0, 6.2, 1.0 Hz, CH-9), 6.181 (1H, sm, CH-3), 11.866 (1H, s, OH) [isomer: 12.102 (1H, d, J = 0.8 Hz, OH)]. ^{13}C NMR: δ = 17.68 (CH_3-10), 35.42 (CH-6), 36.83 (CH_2-7), 46.63 (CH-5), 51.76 and 52.54 (CH_3-13, CH_3-14), 97.14 (C-1), 123.85 (CH-3), 126.19 (CH-9), 129.75 (CH-8), 140.61 (C-4), 163.84 (C-2), 170.99 and 171.94 (C-11, C-12).

Anal. Calcd for $C_{14}H_{17}BrO_5$: C, 48.71; H, 4.96. Found: C, 48.73; H, 4.99.

For: dimethyl 2-bromomethyl-7-hydroxy-5-methyl-4a,4,5,7a-tetrahydrobenzofuran-3,6-dicarboxylate **9g**



HRMS (CI) calcd for $C_{14}H_{18}BrO_6$ ($MH^{+\cdot}$) *m/z* 361.0287, found 361.0290. MS; 361 ($MH^{+\cdot}$, 55), 329 (20), 281 (100), 249 (45), 221 (40). n_{max} (film) 2955 (m), 1731 (s), 1704 (s), 1660 (s), 1651 (s), 1440 (s), 1357 (m), 1327 (m), 1295 (s), 1216 (s), 1123 (m), 1075 (m), 960 (m), 914 (m), 733 (m) cm^{-1}. λ_{max} = 207, 254, 320 (sh) (ε = 9700, 13000, 2070). ^1H NMR: δ = ^1H NMR: δ = 1.105 (3H, d, *J* = 6.9 Hz, CH_3-10), 1.856 (1H, ddd, *J* = 14.2, 5.6, 5.4 Hz, CH-9), 1.931 (1H, ddd, *J* = 14.2, 5.4, 5.4 Hz, CH-9), 2.681 (1H, qd, *J* = 6.9, 5.4 Hz, CH-8), 3.541 (1H, ddd, *J* = 10.4, 5.6, 5.4 Hz, CH-4), 3.800 and 3.822 (6H, 2s, CH_3-13, CH_3-14), 4.353 (2H, sm, CH_2-1), 5.094 (1H, d, *J* = 10.4 Hz, CH-5), 11.976 (OH, 1H). ^{13}C NMR: δ = 20.96 (CH_3-10), 21.69 (CH_3-1), 26.70 (CH-8), 30.81 (CH_2-9), 40.08 (CH-4), 51.40 and 51.88 (CH_3-13, CH_3-14), 79.21 (CH-5), 107.76 (C-3), 109.81 (C-7), 163.04 (C-2), 163.20 (C-6), 164.59 (C-11), 172.30 (C-12).

Anal. Calcd for $C_{14}H_{17}BrO_6$: C, 46.56; H, 4.74. Found: C, 46.79; H, 4.58.

ACKNOWLEDGMENTS

The author thanks Dr Graham Rowbottom for elemental analyses, Dr. Noel Davies for mass spectral analyses and Dr. Evan Peacock for NOE 2D spectrometry. We acknowledged financial assistance from the Australian Research Council.

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(*Received in UK* 4 *November* 1996; *revised* 2 *December* 1996; *accepted* 5 *December* 1996)