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Antimony-Based "Forcing Knoevenagel" Methodology for the Conversion of Ketones into Alkylidenemalonates

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Abstract: The Knoevenagel condensation between ketones and malonate esters is often unattainable using conventional methodology. Antimony-based alternatives, arising from the studies of Zhang and co-workers, have been assessed in the context of "cholaphane" synthesis. New conditions have been established which allow the conversion of highly functionalised steroidal ketones into alkylidenemalonates by treatment with dibromomalonate esters and tributylstibine.

Introduction

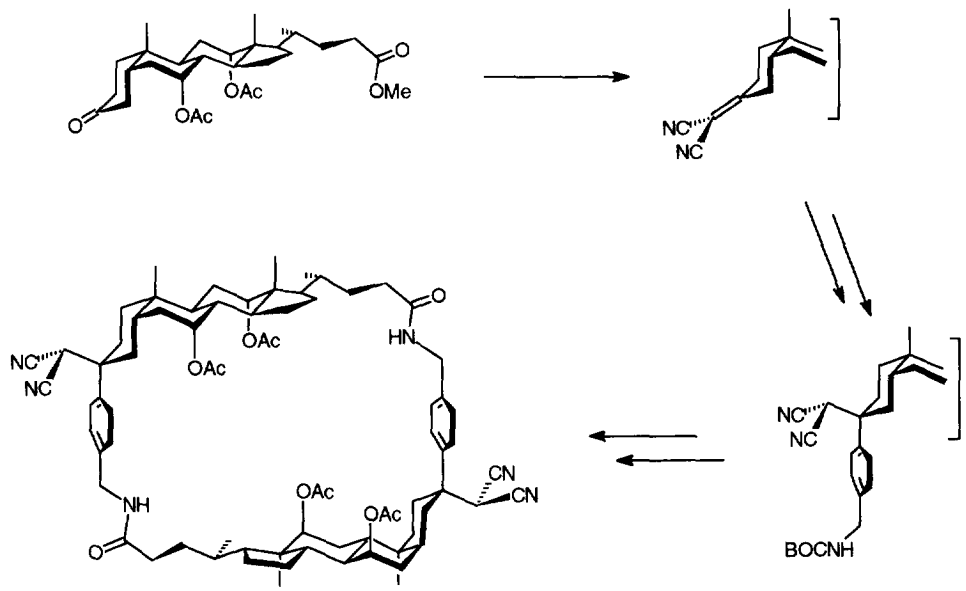
The classical Knoevenagel condensation (eq. 1) is a long-standing, mild and straightforward method for carbon-carbon bond formation.[1] However, while it is quite general and broad in scope when applied to aldehyde substrates, it is much less versatile if the electrophilic component **1** is a ketone. Indeed, for R^1, R^2 = alkyl or aryl, the only reagents **2** which will reliably perform the conversion under standard conditions of mild protic acid/base catalysis appear to be malononitrile (E^1, E^2 = CN) and cyanoacetate esters (E^1 = CN, E^2 = CO_2R).

1 **2** (1)

R^1, R^2 = alkyl, aryl, H E^1, E^2 = CN, COR, CO_2R, SO_2R etc.

This limitation came to the fore during our programme on the synthesis of "cholaphanes", synthetic macrocyclic receptors derived from the inexpensive steroid cholic acid.[2] As exemplified in Scheme 1,[3] we developed a strategy for assembling these macrocycles based on (a) Knoevenagel condensation of a 3-keto derivative of the steroid, (b) stereoselective addition of a *p*-substituted arylcuprate, and (c) elaboration of the adduct into an amino-acid, followed by cyclodimerisation. An important advantage of this protocol was the

appearance in the product of a pair of externally-directed substituents derived from the Knoevenagel "reagent" (e.g. the $CH(CN)_2$ groups in cholaphane **3**). In principle, these positions could be used to control the solubilities of the macrocycles without affecting the properties of the central framework, provided suitable functionality could be introduced in a controlled fashion. However, this potential proved difficult to realise with the limited range of groups available through the traditional Knoevenagel condensation,[4] and the restricted scope of this methodology emerged as a serious barrier to our progress.



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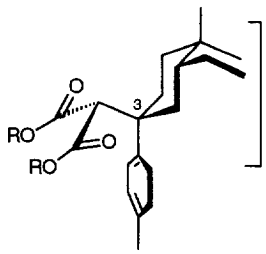
Scheme 1

One of the major aims in our programme was the attachment of flexible alkyl chains to the exteriors of the macrocycles, to promote solubility in organic solvents in opposition to the polar functional groups and preorganised central frameworks.[5] In principle, an efficient means to this end was to perform the Knoevenagel condensation with a dialkyl malonate, leading to the partial structure **4** at steroidal C3 in the final product. Unfortunately, our attempts to condense diethyl malonate with ketones **5** and **6** were completely unsuccessful, whether we used conventional methodology (AcOH, NH_4OAc, C_6H_6)[6,4] or the more vigorous conditions of Lehnert ($TiCl_4$, pyridine, THF).[7]

We therefore sought an alternative, more potent malonylidenation procedure, driven by a chemical change more favourable than simple elimination of water. A starting point was provided by the work of Zhang *et al.*,[8] who had accomplished the alkylidenation of carbonyl compounds using combinations of organo-antimony[9,10] or -tellurium[11] compounds with bromo- or diazo-malonate esters. While these authors had focussed mainly on aldehyde substrates, a unique feature of the methods was their success with a few simple ketones. It seemed that the extension of this methodology to a broader range of ketones could be useful in the



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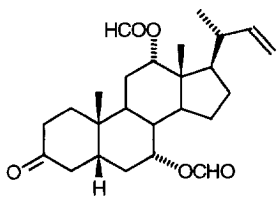

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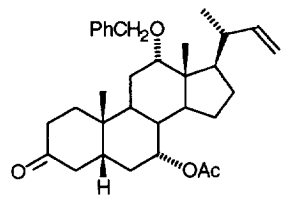

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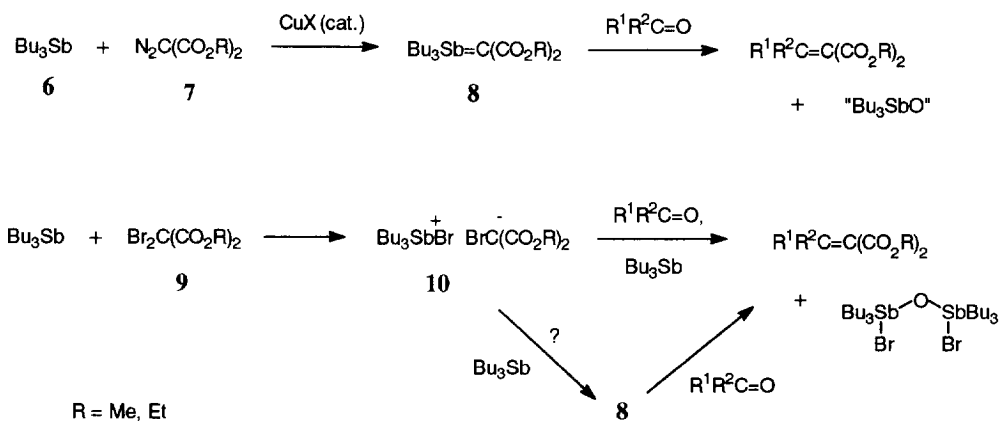
context of our own programme in particular, and of organic synthesis in general. We now describe our investigations in this area, including the successful malonylidenation of complex, highly functionalised ketones in high yields *via* a modified antimony-based procedure.

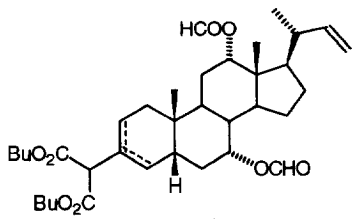
Results and Discussion

Due to problems in obtaining and handling organotellurium reagents, we decided to examine the antimony-based methods published by the Chinese group. One possibility involved treatment of the ketone with a diazomalonate **7** and tributylstibine **6** in benzene at elevated temperatures, in the presence of a copper (I) halide catalyst.[9] As shown in Scheme 2, this reaction is thought to proceed *via* stibonium ylide **8**, which is sufficiently reactive to accomplish a Wittig-style olefination of the carbonyl compound. In a second method, stibine **6** is added to a neat mixture of the carbonyl compound and a dialkyl dibromomalonate **9**.[10] In this case two equivalents of the stibine are required and, as shown in Scheme 2, the reaction is initiated by halophilic attack of the stibine on the dibromomalonate. This gives an ion pair **10**, which may react with the carbonyl compound directly or *via* ylide **8**.



Scheme 2

Our attempts to apply the first of these methods to ketone **5** produced an initial disappointment. Because of our interest in the ester groups as solubilising substituents, we used dibutyl diazomalonate (**7**, R = *n*Bu) as a malonyl donor. Following the literature procedure,[9] the ketone was treated with the diazomalonate (1.2 equiv.), copper (I) iodide (0.05 equiv.) and tributylstibine (1.2 equiv.) in benzene at 70 - 80 °C over a period of several hours. Although the reaction did afford the desired alkene **13** (*cf.* Scheme 3) the yield, at 30%, was unsatisfactory and the product was accompanied by one or both of the endocyclic regioisomers **11** (*ca.* 15%). A similar result was obtained when this procedure was applied to 4-*t*-butyl-cyclohexanone (**18**), the alkenes **19c** and **12** being obtained in 30% and 10% yield respectively.



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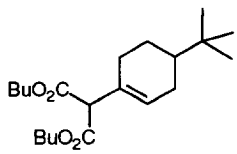

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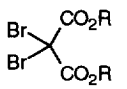
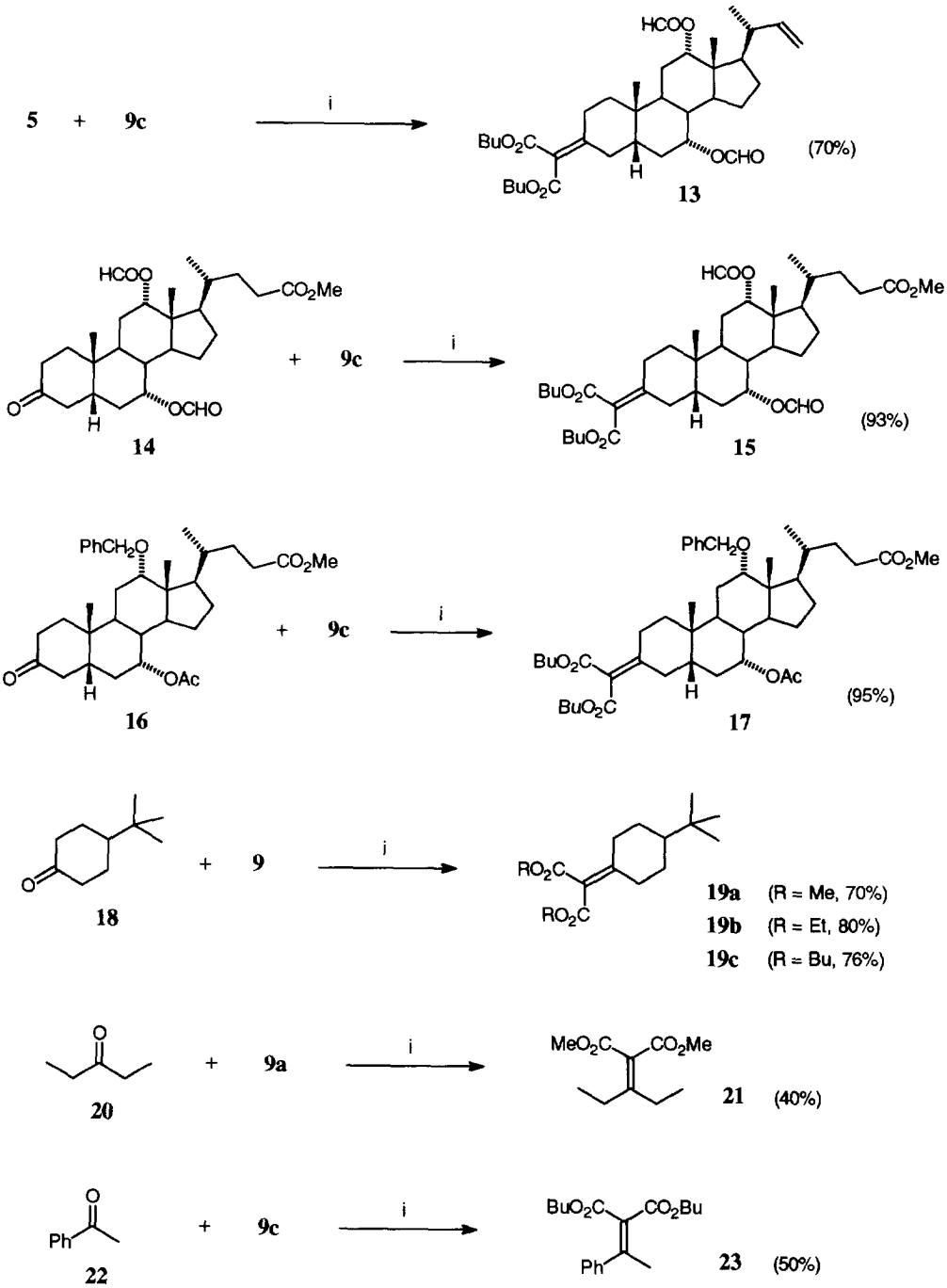


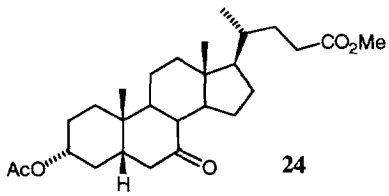
9a R = Me
9b R = Et
9c R = *n*Bu

We therefore turned to the second method in Scheme 2, in which the malonylidene group derives from a dibromomalonate ester. The published procedure,[10] involving addition of tributylstibine to a neat mixture of dibromomalonate and carbonyl compound, was unsuitable for complex substrates such as **5**. When benzene was added as solvent in trials employing dibutyl dibromomalonate (**9c**), the reaction still yielded the malonylidene derivative. However substantial quantities of endocyclic alkenes (e.g. **12**) were again produced.

On the other hand, as shown in Scheme 3, the use of THF as solvent produced some very satisfactory results. Treatment of a range of ketones with **9a-c** (1.2 - 1.5 equivalents) and tributylstibine (2.7 - 4.5 equivalents) in THF yielded the corresponding malonylidene compounds in yields of up to 96%. The reactions were conducted at temperatures of 60-70 °C and required 3 - 4 days to reach completion. Work-up involved exposure of the reaction mixture to air, to allow oxidation of excess stibine, followed by flash chromatography to separate the alkenes from the antimony-containing side products. The method was especially successful with the steroidal ketones **14** and **16**, demonstrating that various forms of ester protection (including formyl esters) are inert to the conditions. The slightly lower yield with **5** might suggest that simple alkenes are vulnerable to side reactions; for example, dibromomalonate esters have been shown to act as mild brominating agents in some circumstances.[12] The series of reactions involving *t*-butylcyclohexanone **18** demonstrated versatility with respect to group R in the ester. The reactions on **18**, **20** and **22** were unoptimised, and the lower yields may result largely from losses on work-up and purification. Separation of the product from antimony residues was a particular problem in the conversion of **20** to **21**, due to a coincidence of R_f values on silica gel. The method was not successful with benzophenone (which is, however, susceptible to Lehnert's conditions[7]) or with the more hindered steroidal ketones **24** - **27**.



Scheme 3. *Reagents and conditions:* i, Bu_3Sb (2-3 equiv.), THF, 60-70 °C, 72-82 h.



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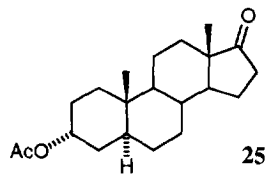

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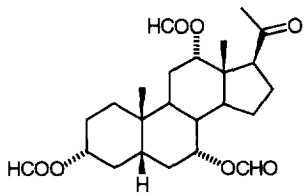

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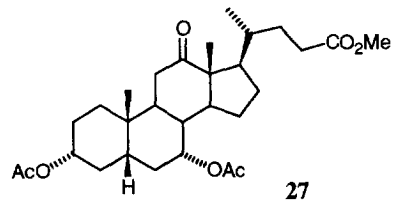

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In conclusion, having searched extensively for an efficient "Knoevenagel equivalent" for the malonylidenation of functionalised 3-keto steroids, we have established a set of conditions which are highly effective, compatible with several functional groups, and applicable to a range of steroidal and non-steroidal substrates. The methodology should complement that of Lehnert,[7] increasing the variety of malonylidene derivatives which are readily accessible. It has already contributed substantially to our "cholaphane" programme, and should be of assistance in other areas of synthetic organic chemistry.

Experimental

NMR spectra (^1H, ^{13}C) were recorded on Bruker MSL-300 at 300 and 75 MHz respectively with $CDCl_3$ as solvent, $SiMe_4$ (δ_H 0.00) as internal standard for proton spectra and the signal of the solvent (δ_C 77.00 ppm.) as reference for carbon spectra. ^{13}C assignments were made with the assistance of DEPT spectra. IR spectra were recorded as thin films on a Perkin Elmer 298 spectrometer. Flash chromatography was performed using Kieselgel 60 (400-230 mesh) purchased from Merck. Reactions were monitored by TLC on DC Alufolien Kieselgel 60 F254 (0.2 mm). Steroidal components were visualised as dark spots by heating the plates over a Bunsen flame. THF was dried by distillation from benzophenone ketyl. Tributylstibine was purchased from Aldrich or prepared using a method based on those of Seifter[13] and Dyke *et al.*[14] Dibutyl diazomalonate (**7**, R = *n*Bu)[15] was prepared from dibutyl malonate and *p*-toluenesulphonyl azide after the method of Regitz *et al.*[16] Dibromomalonates **9** were prepared by bromination of the corresponding malonates using the procedure of Teichmann.[17]

3 - [Bis - (butoxycarbonyl)methylidene] -7α,12α- bisformyloxy -24- nor -5β- cholan-22(23)-ene (**13**); *Method A [diazomalonate* **7** (R = *n*Bu) *as malonyl donor].-* Tributylstibine (**6**) (0.073 g, 65 ml, 0.25 mmol)

was added by syringe to a stirred solution of the ketone **5** (0.083 g, 0.2 mmol), dibutyl diazomalonate (**7**, R = *n*Bu) (0.06 g, 0.247 mmol) and copper (I) iodide (0.002 g, 0.01 mmol) in dry benzene (4 ml) under an inert atmosphere. The mixture was heated at 70 - 80 °C for 10 h, then exposed to the atmosphere and stirred for 1 - 2 h. Evaporation of the solvent yielded a gummy residue which was purified by flash chromatography using hexane-ethyl acetate (9:1) as eluent. The products emerged in the order: (a) *3-[Bis-(butoxycarbonyl)methyl]-7α,12α-bisformyloxy-24-nor-5β-cholan-2(3)/3(4),22(23)-diene* (**11**) as a viscous oil (mixture of isomers, 0.02 g, 15%); ν_{max} (film from $CDCl_3$)/cm^{-1} 2962, 2876, 1721 (C=O), 1648 (C=C), 1205, 1178; δ_H 8.16 and 8.15 (1 H, d, 12-formyl), 8.09 (1 H, s, 7-formyl), 5.67-5.56 (2 H, m, 22-H + endocyclic vinylic protons), 5.28 (1 H, br q, 12β–H), 5.11 (1 H, br q, 7β–H), 4.93-4.81 (2 H, m, 23-H), 4.17-4.14 (4 H, m, 2 x OCH_2), 3.50-3.36 (1 H, br d, malonyl C*H*), 2.86 (0.5 H, t, *J* = 13.4 Hz allylic protons), 2.59 (0.5 H, t, *J* = 14.24 Hz, allylic proton); δ_C (partial spectrum) 112.79 and 112.66 (endocyclic alkene), 75.25 and 75 (C-12 from both isomers), 70.95, 70.66, (C-7 from both isomers). (b) *Diene* **13**, as a low melting solid (0.040 g, 30%); ν_{max} (film from $CHCl_3$)/cm^{-1} 2963, 2876, 1731, (C=O), 1639 (C=C), 1463, 1385, 1274, 1237, 1204, 1179 (formate), 1099, 1065; δ_H 8.15 (1 H, s, 12-formyl), 8.08 (1 H, s, 7-formyl), 5.61 (1 H, br dd, *J* = 10, 7 Hz, 22-H), 5.28 (1 H, br s, 12β–H), 5.10, (br s, 7β–H), 4.87 (2 H, m, 23-H), 4.15 (4 H, t, *J* = 6.5 Hz, 2 x OCH_2), 2.75 (3 H, m), 0.79 (3 H, s, 18-Me); δ_C 165.75 and 165.53 (*C*OOBu), 160.92 (C-3), 160.40 (formyl), 144.10 (C-22), 121.62 [(O=C)$_2$*C*], 112.20 (C-23), 75.02 (C-12), 70.55 (C-7), 64.76 and 64.66 (OCH_2, malonyl), 46.8, 44.9 (C-13), 43.19, 42.87, 40.43, 37.67, 37.30, 34.80, 34.68 (C-10), 31.35, 30.45, 29.33, 27.21, 27.07, 25.75, 22.72, 21.76 (C-19), 19.51, 19.16 (C-21), 19.03, 18.94, 13.57, 12.33 (C-18). TLC R_f values for **11** and **13** with CH_2Cl_2 eluent were 0.39 and 0.35 respectively.

Method B [dibutyl dibromomalonate (**9c**) *as malonyl donor].-* Tributylstibine (**6**) (7.27 g, 6.5 ml, 24.8 mmol) was added dropwise to a stirred solution of ketone **5** (3.44 g, 8.26 mmol) and dibutyl dibromomalonate (**9c**) (3.86 g, 10.3 mmol) in anhydrous THF (30 ml) under nitrogen at room temperature. The reaction vessel was lowered into an oil bath maintained at 60-65 °C and stirring was maintained for 72 h. After this time interval TLC analysis (eluent CH_2Cl_2) of the reaction mixture indicated almost complete disappearance of the starting ketone (visualisation by 2,4-DNP) and appearance of the faster-moving product (visualisation by UV). The reaction mixture was cooled and stirred open to the atmosphere for 2 h. The solvent was evaporated and the residue dissolved in a minimum volume of hexane-ether (8:2). This solution was applied to a column of silica gel (2.5 x 20 cm) packed using hexane, and eluted with hexane (200 ml), hexane-ether (9:1, 200 ml), hexane-ether (8:2, 200 ml) and finally with hexane-ether (7:3) until no further product emerged. Fractions containing the product [R_f = 0.22 in hexane-ether (7:3)] were evaporated and dried under high vacuum to yield diene **13** (3.64 g, 70%), pure by TLC, IR and NMR.

Methyl 3-[Bis-(butoxycarbonyl)methylidene]-7α,12α-diformyloxy-5β-cholan-24-oate (**15**).- Ketone **14** (4 g, 8.39 mmol) was treated with dibutyl dibromomalonate (**9c**) (4.4 g, 11.75 mmol) and tributylstibine (**6**) (8.8 g, 7.7 ml, 29.4 mmol) in dry THF (30 ml) as described for ketone **5** above (Method B) to yield the malonylidene derivative **15** as a white solid (5.25 g, 93%); (Found: C 67.78; H, 8.79. $C_{38}H_{58}O_{10}$ requires C, 67.63; H, 8.66%); ν_{max}(film from $CHCl_3$)/cm^{-1} 2962, 2877, 1720 (C=O), 1635(C=C), 1273, 1238, 1201, 1175; δ_H 8.13 (1 H, s, 12-formyl), 8.09 (1 H, s, 7-formyl), 5.28 (1 H, br s, 12β–H), 5.11 (1 H, br s, 7β–H), 4.15 (4 H, t, *J* = 7 Hz, 2 x OCH_2), 3.65 (3 H, s, OMe), 0.95 (3 H, s, 19-Me), 0.84 (3 H, d, *J* = 6 Hz, 21-Me), 0.77 (3 H, s, 18-Me); δ_C 174.24 (*C*OOMe), 165.63 and 165. 41 (*C*OOBu), 160.83 (C-3), 160.29 (formyl),

121.49 [(O=C)$_2$*C*], 75.02 (C-12), 70.41 (C-7), 64.64 and 64.55 (O*C*H$_2$), 51.32 (O*C*H$_3$), 47.01 (C-17), 44.82 (C-13), 43.08, 42.73, 37.53, 37.17, 34.69, 34.55 (C-10), 34.55 (C-20), 31.23, 30.66, 30.46, 30.33, 29.09, 26.97, 25.59, 22.60, 21.64 (C-19), 18.92, 17.29 (C-21), 13.46, 11.96 (C-18). TLC R_f values for **14** and **15** with hexane-ether (1:1) eluent were 0.08 and 0.37 respectively.

Methyl 3-[Bis-(butoxycarbonyl)methylidene]-7α-acetoxy-12α-benzyloxy-5β-cholan-24-oate (**17**).- Ketone **16** [18] (2.49 g, 4.5 mmol) was treated with dibutyl dibromomalonate (**9c**) (2.36 g, 6.30 mmol) and tributylstibine (**6**) (4.60 g, 4.2 ml, 15.8 mmol) in dry THF (20 ml) as described for ketone **5** above (Method B) to yield the malonylidene derivative **17** as a white solid (3.19 g, 95%) (Found: C, 71.76; H, 8.86. $C_{45}H_{66}O_9$ requires C,71.96; H, 8.86%); ν_{max} (film from $CDCl_3$)/cm^{-1} 2961, 2877, 1739,(C=O), 1248, 1210, 1163; δ_H 7.35 - 7.27 (5 H, m, Ar*H*), 4.93 (1 H, br d, 7β–H), 4.58, 4.39 (2 H, ABq, J = 11.9 Hz, OCH_2Ph), 4.15 (2 H, t, J = 6.6 Hz, malonyl OCH_2), 3.72 (1 H, br s, 12β–H), 3.65 (3 H, s, OCH_3), 2.68-2.73 (3 H, m), 2.05 (3 H, s, OCOCH_3), 0.72 (3 H, s, 18-Me); δ_C 174.60 (*C*OOMe), 170.39 (OCOCH$_3$), 165.73 and 165.65 (*C*OOBu), 162.0 (C-3), 139.27, 128,22, 127.26, 127.08, 121.07 [(O=C)$_2$*C*], 80.53 (C-12), 70.78 (C-7), 70.26 (O*C*H$_2$Ar), 64.62 (O*C*H$_2$ malonyl), 51.37 (OMe), 46.52 (C-13), 46.05, 43.48, 42.58, 38.05, 37.56, 35.22, 35.05, 34.77 (C-10), 31.28, 30.80, 30.45, 29.06, 27.30, 27.17, 23.17, 23.01, 21.98 (C-19), 21.47 (OCO*C*H$_3$), 19.02, 17.45 (C-21), 13.56, 12.44 (C-18).

4-t-Butyl-1-[bis-(methoxycarbonyl)methylidene]-cyclohexane (**19a**).- Tributylstibine (**6**) (1.74 g, 1.46 ml, 5.6 mmol) was added dropwise to a stirred solution of 4-t-butylcyclohexanone (**18**) (0.29 g, 1.86 mmol) and dimethyl dibromomalonate (**9a**) (0.65 g, 2.24 mmol) in anhydrous THF (5 ml) under nitrogen at room temperature. The mixture was heated at 70 °C for 72 h after which TLC analysis (eluent CH_2Cl_2) of the reaction mixture indicated almost complete disappearance of the starting ketone (visualisation by 2,4-DNP) and appearance of the faster-moving product (visualisation by UV). The reaction mixture was cooled and stirred open to the atmosphere for 2 h. The solvent was evaporated and the residue subjected to flash chromatography in a column packed using hexane and eluted with hexane-ether (9:1), to give the malonylidene derivative **19a** as a viscous oil (0.348 g, 70%); ν_{max} (film from $CDCl_3$) 2920, 2830, 1720 (C=O), 1640 (C=C), 1440, 1220, 1180, 1150, 1045; δ_H 3.76 (6 H, s, OCH_3), 3.14-3.09 (2 H, br d, C-2 and C-6 equatorial *H*), 2.03-1.95 (4 H, br m), 1.28-1.20 (3 H, br m), 0.85 (9 H, s, CMe$_3$); δ_C 166.02 (*C*OOMe), 162.30 (C-1), 120.73 [(O=C)$_2$*C*], 51.89 (O*C*H$_3$), 47.39 (C-4), 32.30 (*C*Me$_3$), 32.28, 28.6, 27.4 (*C*H$_3$). TLC R_f = 0.48 with CH_2Cl_2 eluent.

4-t-Butyl-1-[bis-(ethoxycarbonyl)methylidene]-cyclohexane (**19b**).- 4-t-butylcyclohexanone (**18**) (0.23 g, 1.49 mmol) was treated with diethyl dibromomalonate (**9b**) (0.573 g, 1.8 mmol) and tributylstibine (**6**) (1.32 g, 1.2 ml, 4.5 mmol) in anhydrous THF (5 ml), as described above for **18** + **9a**, to yield the malonylidene derivative **19b** as a viscous liquid (0.361 g, 80%); ν_{max} (film from $CDCl_3$)/cm^{-1} 2960, 2872, 1725 (C=O), 1645 (C=C), 1360; δ_H 4.23 (4 H, q, J = 7.1 Hz, OCH_2), 3.16-3.11 (2 H, br d, C-2 and C-6 equatorial *H*), 2.03-1.95 (4 H, m), 1.29 (9 H, m), 0.85 (9 H, s, CMe$_3$); δ_C 165.60 (*C*OOEt), 161.10 (C-1), 121.15 [(O=C)$_2$*C*], 60.70 (O*C*H$_2$), 47.41 (C-4), 32.31 (*C*Me$_3$), 32.16, 28.57, 27.39 (3 x *C*H$_3$), 13.95 (*C*H$_3$). TLC R_f = 0.48 with CH_2Cl_2 eluent.

4-t-Butyl-1-[bis-(butoxycarbonyl)methylidene]-cyclohexane (**19c**).- 4-t-butylcyclohexanone (**18**) (0.100 g, 0.64 mmol) was treated with dibutyl dibromomalonate (**9c**) (0.359 g, 0.96 mmol) and tributylstibine (**6**) (0.59 g, 0.50 ml, 2.03 mmol) in anhydrous THF (3 ml), as described above for **18** + **9a**, to yield the malonylidene derivative **19c** a viscous oil (0.172 g, 76%); ν_{max}(film from $CDCl_3$)/cm^{-1} 2963, 2874, 1723, (C=O), 1639 (C=C), 1469, 1367, 1208, 1170, 1120; δ_H 4.16 (4 H, t, J = 6.6 Hz, CH_2), 3.16, 3.11 (2 H, br d, C-2 and C-6 equatorial *H*), 2.03-1.94 (4 H), 1.64 (4 H, m, 2 x CH_2), 1.40 (4 H, m, 2 x CH_2), 1.33-1.20 (3 H, cyclohexyl ring protons), 0.83 (9 H, s, CMe_3); δ_C 165.6 (*C*OOBu), 161.2 (C-1), 121.1 [(O=C)$_2$*C*], 64.50 (OCH_2), 47.42 (C-4), 32.27 (CMe_3), 32.13, 30.41, 28.54, 27.36 (3 x CH_3), 18.96, 13.49 (CH_3 malonyl); TLC R_f = 0.5 with CH_2Cl_2 eluent.

3-[Bis-(methoxycarbonyl)methylidene]-pentane (**21**).- Tributylstibine (**6**) (0.74 g, 0.62 ml, 2.52 mmol) was added dropwise to a stirred solution of pentan-3-one (**20**) (0.080 g, 0.95 mmol) and dimethyl dibromomalonate (**9a**) (0.33 g, 1.14 mmol) in anhydrous THF (5 ml) under nitrogen at room temperature. The mixture was heated at 70 °C for 82 h after which TLC analysis (eluent CH_2Cl_2) of the reaction mixture showed the presence of the product (visualisation by UV) accompanied by some of the slower-moving starting ketone (visualisation by 2,4-DNP). The reaction mixture was cooled and stirred open to the atmosphere for 2 h. The solvent was evaporated and the residue dissolved in a minimum volume of hexane-ether (9:1). This solution was applied to a column of silica gel packed using hexane, and eluted with hexane followed by hexane-ether (95:5). Fractions containing the product were evaporated to give malonylidene derivative **21** as an oil (40%, est. by GC), contaminated with byproducts presumed to derive from the tributylstibine; ν_{max}/cm^{-1} 2964, 2935, 2876, 1737 (C=O), 1661 (C=C), 1643, 1033; δ_H 3.76 (6 H, s, OCH_3), 2.09 (t, J = 6 Hz, $SbCH_2$), 2.38 (4 H, q, J = 7.6 Hz, allylic), 2.01 (CH_2 from antimony-containing byproduct), 1.11 (6 H, t, J = 7.6 Hz, CH_2CH_3), 0.94 (m, CH_3 from antimony-containing byproduct); δ_C 166.1 (*C*OOMe), 123 (C-3), 110 [(O=C)$_2$*C*], 51.93 (OCH_3), 43.7, 26.97, 24.76, 13.41, and 12.65.

1-[Bis-(butoxycarbonyl)methylidene]-1-phenylethane (**23**).- Acetophenone (**22**) (0.103 g, 0.80 mmol), was treated with dibutyl dibromomalonate (**9c**) (0.45 g, 1.2 mmol) and and tributylstibine (**6**) (1.04 g, 0.93 ml, 3.6 mmol) in anhydrous THF (5 ml) as described above for **20** + **9a** to yield the malonylidene derivative **23** as a viscous oil (0.08 g, 50%); ν_{max}/cm^{-1} 2964, 2877, 1725 (C=O), 1624 (C=C), 1222, 766; δ_H 7.31 - 7.21 (5 H, m, Ar*H*), 4.2 (2 H, t, J = 6.6 Hz, OCH_2), 3.87 (2 H, t, J = 6.6 Hz, OCH_2), 2.42 (3 H, s, C=C-CH_3), 1.65 (2 H, m, CH_2), 1.35 (4 H, m, CH_2), 1.11 (2 H, m, CH_2), 0.92 (3 H, t, J = 6.6 Hz), 0.78 (3 H, t, J = 7.3 Hz, CH_3); δ_C 166.29 and 164.73 (*C*OOBu), 155.41, 141.54, 128.34, 128.17, 126.53, 64.80 and 64.76 (OCH_2), 30.46, 30.11, 22.68 (=C-*C*H$_3$), 19.02, 18.79, 13.57, 13.49.

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