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An Unusual Condensation of Alkyl 3-oxo-4-(triphenylarsoranylidene)butanoate with Aldehydes; Synthesis of Symmetrical Substituted 1,3,5-Cycloheptatrienes.

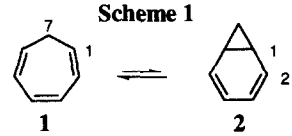
Cornelis M. Moorhoff*

Department of Chemistry, The University of Tasmania
GPO Box 252-75, Hobart, Tasmania, Australia 7001

Abstract: The unique preparation of 2-substituted 4,7-dihydroxycyclohepta-3,5,7-triene-1,3-dicarboxylates **5** from aldehydes **4** and two equivalents alkyl 3-oxo-4-(triphenylarsoranylidene)butanoate **3** is described. © 1997 Elsevier Science Ltd.

The valence tautomerism between derivatives of 1,3,5-cycloheptatriene **1** and bicyclo[4.1.0]hepta-2,4-diene (norcaradiene) **2** (Scheme 1), has attracted considerable attention for synthetic- and theoretical chemists.[1,2] The equilibrium of the parent system at room temperature is almost totally shifted to **1**.[3] However, structural modifications, steric effects[4] on the ringsystem **1** and an electron withdrawing-[5] or an electron donating[6] group in position 7 and 3 & 4,[7] respectively, appears to favour the equilibrium towards the norcaradiene tautomer **2**.

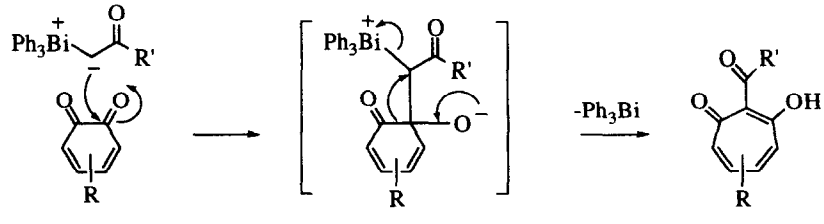
Scheme 1



1 **2**

1,3,5-Cycloheptatrienes are potentially useful intermediates in organic synthesis[8,9] and requires that suitable functionalised cycloheptatrienes are easily prepared.[10] A number of 1,3,5-cycloheptatriene syntheses starting from tropones[10] tropylium salts[5] or from cyclopropanation of quinones,[11,12] and other methods[13] have been developed. Recently, a novel ring enlargement of *ortho*-quinones to 3-hydroxytropones with stabilised bismuthonium ylides has been communicated (Scheme 2).[14]

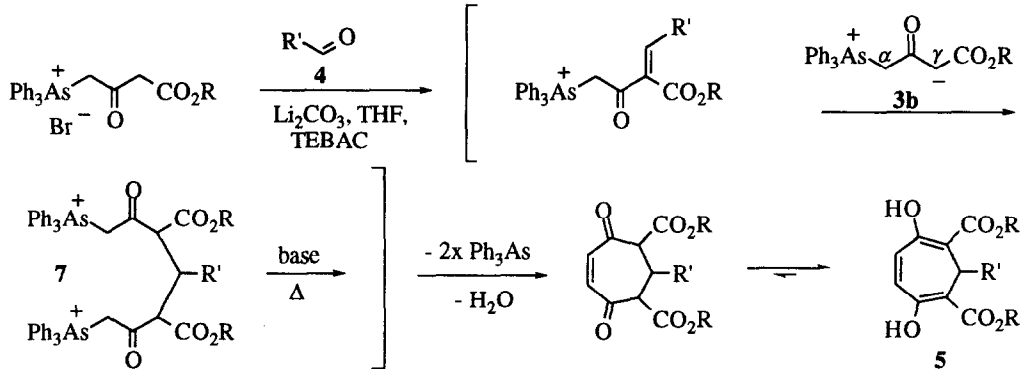
Scheme 2



In this paper we wish to describe a unique and useful synthetic method for the preparation of 2-substituted 4,7-dihydroxycyclohepta-3,5,7-triene-1,3-dicarboxylates **5**[7] from the reaction of two equivalents alkyl 3-oxo-4-(triphenylarsoranylidene)butanoate **3**[15] and one mole aldehyde **4** (Scheme 3, Table 1).

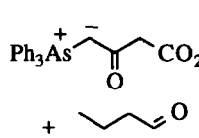
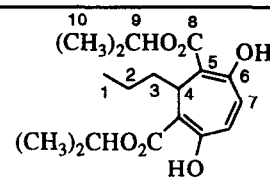
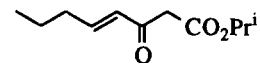
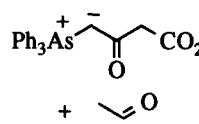
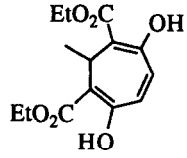
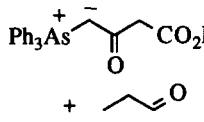
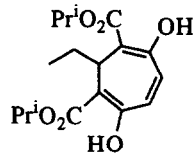
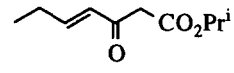
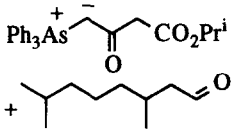
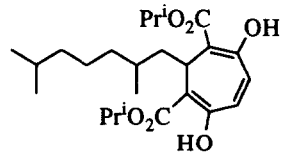
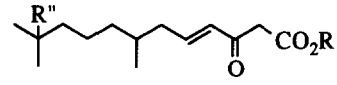
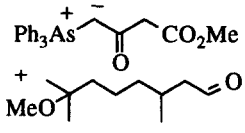
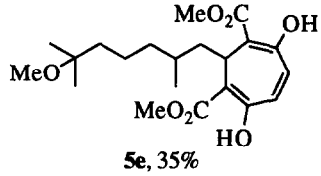
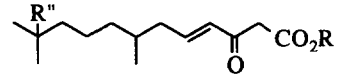
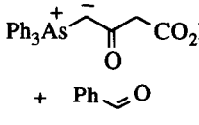
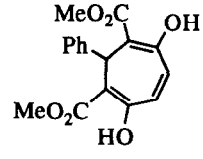
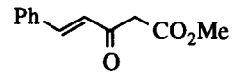
The arsonium ylide **3** was generated *in situ* from the corresponding arsonium salt[16] and lithium carbonate in THF at room temperature in the presence of triethylbenzylammonium chloride (TEBAC). Aldehyde **4** was added to the reaction mixture and stirred for almost 24 hours at room temperature. At that stage almost no condensation product could be detected. We can only assume that an intermediate arsonium species had formed (Scheme 3). The temperature was then raised to about 60 °C and the reaction mixture was stirred for another 48 hours to give, after purification, the substituted cycloheptatriene **5**. Raising the temperature at once seemed to dramatically lower the yield of substituted cycloheptatriene **5** and more of the acyclic Wittig product **6** had formed (Table 1). A plausible mechanism is given in Scheme 3. From our previous experience we know that the arsonium ylide **3** is in equilibrium with the γ-arsonium ylide **3b**.[15] Attack of **3b** on the aldol product of **3b** and **4** may have led to an intermediate, such as **7**, that decomposed under basic conditions and elevated temperatures. Triphenylarsine is a good leaving group and this seems to have been the driving force for the release of substituted 4,7-dioxocyclohept-5-ene-1,3-dicarboxylate; last mentioned species is totally in the 4,7-dihydroxycyclohepta-3,5,7-triene-1,3-dicarboxylate **5** tautomer. No trace of a substituted norcaradiene was found in $CDCl_3$ at room temperature and this in agreement with the literature.[9] Compounds **5a**, **5b** and **5c** displayed only one conformer, while **5d** and **5e** had two diastereomers. Our new unique method for the preparation of symmetrical substituted 3,5,7-cycloheptatriene-1,3-dicarboxylates could also be useful for the synthesis of substituted bridged annulenes.[19] We are investigating the optimum conditions for the preparation of cycloheptatrienes **5** and conducting mechanistic studies for this unique reaction.

Scheme 3



Typical experimental procedure: Redistilled aldehyde **4** (1.18 mmol)[17] was added to a suspension of finely powdered (3-alkoxycarbonyl-2-oxopropyl)triphenylarsonium bromide (1.20 mmol) and lithium carbonate (127 mg, 1.72 mmol) in anhydrous THF (10 mL) at room temperature in the presence of TEBAC (38 mg, 0.17 mmol), and stirred under nitrogen for 19 hours at room temperature, followed by 48 hours at 60 °C. A solution of ether:light petroleum (40 - 60 °C) (1:1) (20 mL) was added to the reaction mixture and the suspension filtered over silica gel and further eluted with ether:light petroleum (1:1). After evaporation of the solvents, the yellow viscous residue was chromatographed on silica gel and eluted with light petroleum, ether:light petroleum (1:19) to give triphenylarsine (CAUTION, TOXIC) followed by pale yellow substituted cycloheptatriene **5** and minor amounts of **6**. Polar arsonium- and polymeric residues were not analysed.

Table 1

Run	Arsonium ylide **3** and aldehyde **4**	Products and yield		
		Ph_3As	1,3,5-cycloheptatriene **5**[a]	other products[c]
a		*b*	 **5a**, 42%	 **6a**, 15% + *d*
b		78%	 **5b**, 53%	- **6b**, ~0% + *d*
c		57%	 **5c**, 47%	 **6c**, <5% + *d*
d		*b*	 **5d**, 20%	 **6d**, R = OPr^i, R" = H, ~10% + *d*
e		*b*	 **5e**, 35%	 **6e**, R = Me, R"= OMe, <5% + *d*
f		58%	 **5f**, ~8%	 **6f**, 27% + *d*

[a] For analyses of compounds **5**, see ref. 18. [b] Yield not analysed. [c] spectroscopic data of β-ketoesters are in agreement to spectroscopic data found in the literature. [d] Polar uncharacterised compounds.

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17. Excess aldehyde **4** was used. Stoichiometric amounts of reactants led to lower yields of **5**.
18. Spectrometric data [NMR, $CDCl_3$, ^1H = 200 MHz; ^{13}C = 50 MHz at 20 °C]:
    5a: Di-1-methylethyl 4,7-dihydroxy-2-propylcyclohepta-3,5,7-triene-1,3-dicarboxylate. mp. 30 - 35° C. Anal. Calcd. for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 63.91; H, 7.87. HRMS calcd for $C_{18}H_{26}O_6$ *m/z* 338.1729, found 338.1735. λ_{max} = 246, 327 nm (ε = 19100, 6250). ν_{max} (film) 2982 (w), 1711 (w), 1631 (s), 1581 (m), 1372 (s), 1315 (m), 1268 (m), 1216 (vs), 1105 (s), 829 (m) cm^{-1}. ^1H NMR: δ = 0.86 (3H, def.t, J = 7.0 Hz, CH_3-1), 0.91 - 0.85 (2H, m, CH_2-2), 1.08 - 1.19 (2H, m, CH_2-3), 1.34 (12H, d, J = 6.2 Hz, 4xCH_3-10), 4.41 (1H, t, J = 8.0 Hz, CH-4), 5.16 (2H, 2xh, J = 6.2 Hz, 2xCH-9), 6.55 (2H, s, CH-7), 12.46 (2H, s). ^{13}C NMR: δ = 13.78 (CH_3-1), 20.13 (CH_2-2), 21.84 (2x), 21.97 (2x, 4xCH_3-10), 27.08 (CH_2-3), 32.06 (CH-4), 68.64 (2xCH-9), 106.28 (2xC-5), 132.44 (2xCH-7), 164.07 (2xC-6), 171.88 (2xC-8).
    5b: ^1H NMR : δ = 0.96 (3H, d, J = 7.4 Hz), 1.37 (6H, t, J = 7.1 Hz), 4.28 and 4.33 (4H, 2xq, J = 7.1 Hz), 4.51 (1H, q, J = 7.4 Hz), 6.59 (2H, s), 12.31 (2H, 2xs). ^{13}C NMR: δ = 14.09 (2x), 15.38, 22.59, 61.15 (2x), 106.88 (2x), 132.47 (2x), 164.03 (2x), 171.92 (2x).
    5c: ^1H NMR: δ = 0.76 (3H, def.t, J =7.3 Hz), 0.9 - 1.0 (2H, m), 1.33 (12H, d, J = 6.2 Hz), 4.15 (1H, m), 5.18 (2H, 2xh, J = 6.2 Hz), 6.56 (2H, s), 12.50 (2H, s). ^{13}C NMR: δ = 11.71, 21.42 (2x), 21.73 (2x), 22.46, 35.53, 66.40 (2x), 105.75 (2x), 132.28 (2x), 163.86 (2x), 171.71 (2x).
    5d: HRMS (CI) calcd for $C_{24}H_{39}O_6$ *m/z* 422.2746, found 423.2731. ^1H NMR: δ = 0.86 (3H, d, J = 6.6 Hz), 0.87 (6H, s), 1.33, 1.35 (12H, 2xd, J = 6.2 Hz), 1.55-0.90 (9H, m), 4.46, 4.50(1H, 1:1 confomers, 2xd, J = 5.9 Hz and 6.1 Hz respectively), 5.16, 5.17 (2H, 2xh, J = 6.2 Hz), 6.56 (2H, s), 12.40, 12.47 (2H, 2xs).
    5e: HRMS (CI) calcd for $C_{21}H_{36}NO_7$ ($M+NH_4^{+\cdot}$) *m/z* 414.2492, found. MS 414.2506 ($[M+NH_4]^{+\cdot}$, 80), 382 (15), 365 (10), 260 (30), 239 (100). ^1H NMR: δ = 0.84 (3H, d, J = 5.6 Hz), 1.13 (6H, s), 1.5-0.8 (9H, m), 3.17 (3H, s), 3.76 (6H, s), 4.44 (1H, dm, J = 6.8 Hz), 6.58 (2H, s), 12.28, 12.31 (2H, 2xs). ^{13}C NMR: δ = 19.63, 21.00, 24.86, 24.90, 25.86, 30.26, 37.22, 37.51, 40.13, 49.03, 52.29 (2x), 74.55, 105.51, 106.25, 132.50, 132.68, 164.24, 164.30, 172.51, 172.70.
    5f: ^1H NMR: δ = 3.89 (6H, s), 5.72 (1H, brs), 6.40 (2H, s), 7.7 - 7.3 (5H, m), 12.41 (2H, s).
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