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VICINAL DIESTER DIANIONS. ANNELATION WITH ω-BROMOESTERS. A SIMPLE PREPARATION OF BICYCLO[4.4.0]DECAN-2-ONE DERIVATIVES VALUABLE IN SESQUITERPENE SYNTHESIS.*

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Summary: The dianion of dimethyl cyclohex-4-ene-1,2-dicarboxylate (1) can be annelated with ethyl 4-bromobutyrate (2) to give cis-dimethyl 1,2,3,5-tetrahydro-1-oxo-4a(4H), 8a (8H)-naphthalenedicarboxylate (5), which is readily transformed into 8a, a synthetic intermediate for a number of sesquiterpene syntheses.

Vicinal diester dianions are readily prepared and can be annelated with α,ω-dihalides and tosylates and with diethylphthalate.[1] We now report a novel annelation reaction between vicinal diester dianions and ω-bromoesters,[2] and illustrate the value of this reaction by a facile synthesis of 8a, a compound of considerable utility in sesquiterpene synthesis.

Addition of the dianion 1, prepared from dimethyl cyclohex-4-ene-1,2-dicarboxylate by treatment with $LiN(iPr)_2$, at -78 °C, to ethyl 4-bromobutyrate (2) at 20 °C gave compound 3, mp 122-123 °C, in 25% yield[3] and none of the desired product 5. The ^1H and ^{13}C NMR spectra[4] are consistent with structure 3, and dehydrogenation with DDQ gave the benzenoid system 4[3,4] quantitatively. We believe that 3 arises from the equilibrium of the dianion 1 with the monoanion resulting from deprotonation of 2,[5] and hoping to decrease this unwanted process we ran the reaction at lower temperature. When 1 was treated with 2 at -78 °C over 5 days the desired compound 5, mpt 103-105 °C, was isolated in 60% yield.[3] The ^1H and ^{13}C NMR spectra[4] are in accord with the assigned structure.

For conversion into into 8a,[6,7] 5 was first treated with NaCl in DMSO, H_2O under N_2[8] to give 6[6] as a mixture of trans : cis isomers (2 : 1).[9] This mixture was hydrolysed with KOH in aqueous EtOH to give 7 (trans : cis, 5 : 1).[6] Treatment of 7 with I_2, KI in aqueous $NaHCO_3$ gave 8 (trans : cis, 5 : 1), from which the trans isomer 8a could be crystallised.[6] Compound 8a could be prepared in 45-50% yield from 5 without purification

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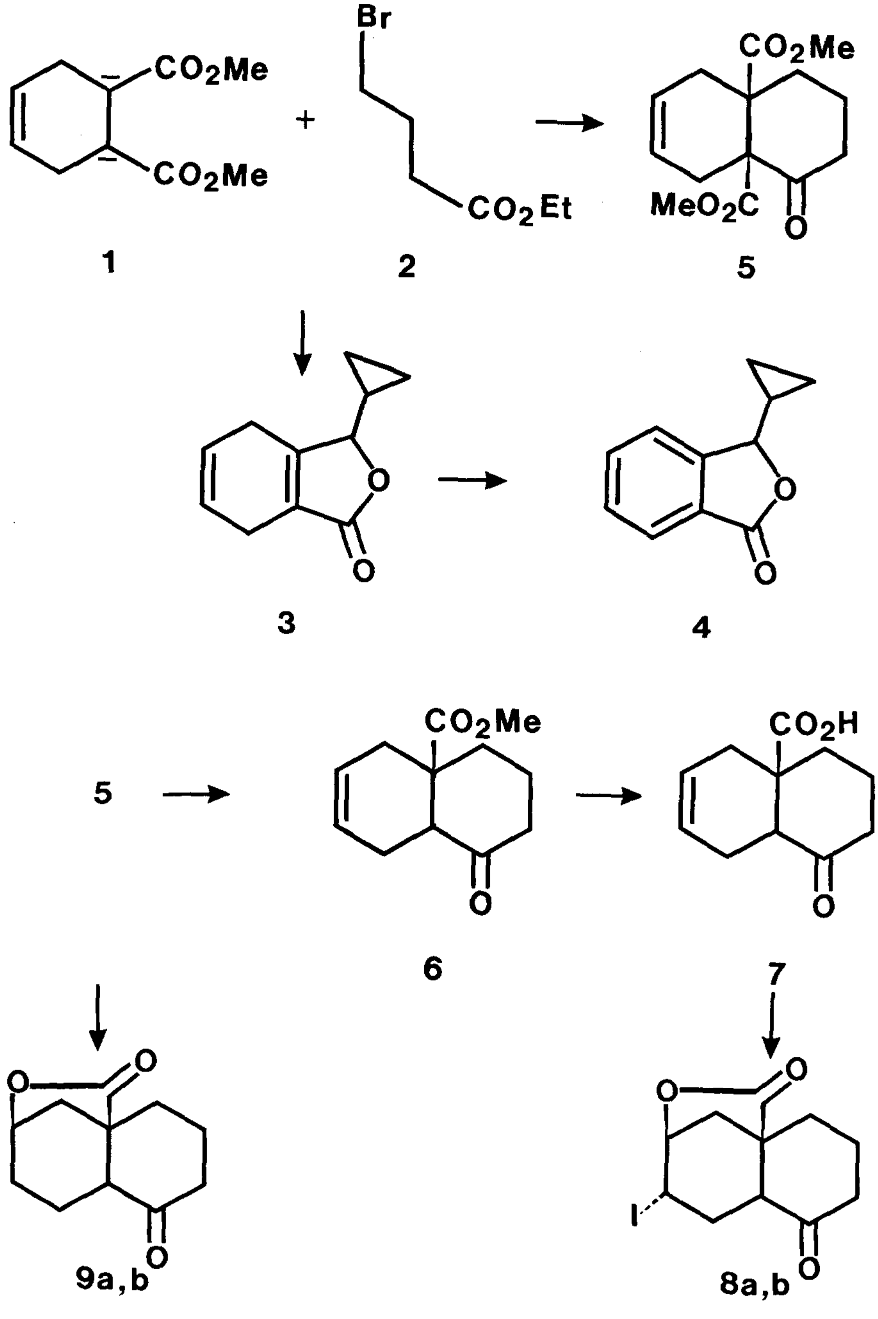
* Dedicated to the memory of Franz Sondheimer.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of any intermediates, and is thus available in 30% overall yield from 1.[10]

Compound 5 could also be converted directly into a mixture of 9a,b[3,4] (2 : 1) in 50-60% yield by treatment with conc. $HC\ell$ at reflux.[11] Compound 9a, previously prepared from 8a by treatment with nBu_3SnH,[6] has also been used as a synthetic intermediate in sesquiterpene synthesis.[7]

Preparation of 5: The bromoester 2 (0.1 mol) in THF (10 cm^3) was added over 18h (syringe pump) to a deep-red solution of the dianion 1[1] (0.1 mol) in THF (210 cm^3) containing HMPA (50 cm^3) at -78 °C under N_2. After stirring at -60 to -80 °C for a further 5 days the reaction mixture was quenched with aqueous acetic acid (150 cm^3, 33%) and extracted with ether to give an orange oil. Addition of ether : pentane (50 cm^3, 1 : 1,v : v) gave a white precipitate which was recrystallised ($CC\ell_4$) as 5, 16g, 60%.

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References and Footnotes

1. For our previous work on the preparation and reactions of vicinal dianions see Bilyard, K.G.; Garratt, P.J.; Zahler, R.; Synthesis, 1980, 389 and reference therein.
2. The scope of the reaction of dianions with ω-bromoesters will be described subsequently. The dianions of cyclic imides also react with both α,ω-dihalides and ω-bromoesters. Hollowood, F.; Hunter, R.; Lete, E.; unpublished observations.
3. Satisfactory analytical and high resolution mass spectral data have been obtained for this compound.
4. ^1H NMR spectra, δ, $CDCl_3$: 3, 0.44-1.0 (m,5H), 2.82-3.34 (m,4H), 4.17 (br.d.,1H), 5.76-6.0 (m,2H); 4, 0.57-0.93 (m,5H), 4.98 (br.d.,1H), 7.53-8.17 (m,4H); 5, 1.68-2.90 (m,10H), 3.66 (s,3H), 3.68 (s,3H), 5.58 (br.s.,2H); 9b, 1.47-2.87 (m,13H), 4.76 (t,1H). ^{13}C NMR spectra, ppm, $CDCl_3$: 3, 172.6, 160.4, 123.9, 123.6, 121.8, 86.6, 24.8, 21.6, 12.3, 1.93, 1.42; 5, 204.9, 174.7, 170.4, 124.2, 121.4, 62.0, 52.1, 51.5, 48.6, 35.1, 31.0, 29.0, 28.7, 20.3.
5. The mechanism of this reaction will be discussed subsequently.

6. Torii, S.; Kunitomi, T.; Okamoto, T., Bull. Chem. Soc. Japan, 1974, 47, 2349.
7. Sesquiterpenes synthesised from 8a include isopetasol; Torii, S.; Inokuchi, T.; Kawai, K.; Bull. Chem. Soc. Japan, 1979, 52, 861; arctiol, eudesma-4(14),7(11)-dien-8-one; Torii, S.; Inokuchi, T.; Yamafugi, T.; ibid, 1980, 53, 2642.
8. Krapcho, A.P.; Lovey, A.J.; Tetrahedron Letters, 1973, 957.
9. Compound 6 (trans isomer) has been converted into β-costol and β-costal.[7]
10. Torii et al[6] prepared 8a in 6% overall yield from methyl cyclohexene-1-carboxylate in a sequence involving a SeO_2 oxidation and a Diels-Alder reaction. By our method 0.03 moles of 8a can readily be prepared from 0.1 moles of 1.
11. These isomers are readily separated by chromatography on silica gel (EtOAc : pentane).

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