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AN ALTERNATIVE APPROACH TO α-METHYLENE LACTONE

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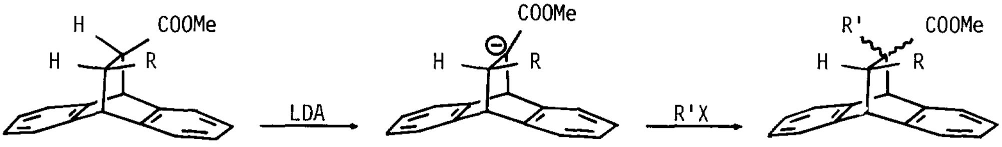
Summary Model syntheses of α-methylene-γ-butyrolactones have been achieved via an alkylation-lactonisation reaction of anthracene adducts 1a and 1b with epoxides followed by release of the methylene lactones through a retro Diels-Alder reaction

Numerous reports concerning the synthesis of α-methylene lactones have appeared in the literature and constructing the methylene group itself has claimed its own field of research(1) Lately, the masked acrylate anion has caught interest as a good candidate for the methylene synthon and its application is being studied by several groups(2)

We have formerly noticed that upon treatment with LDA (1 2 equivalent) at 0^0 in THF/TMEDA (8/1) adducts 1a and 1b(3) gave orange solutions of anions 2a and 2b which could then be alkylated with alkyl halides to give products 3a and 3b respectively

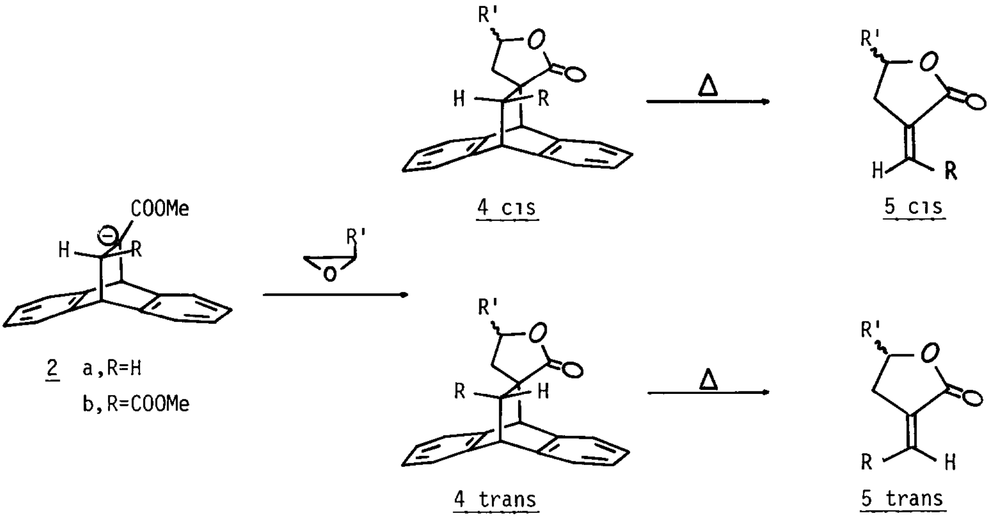


1 2 3

a, R = H b, R = COOMe

The sequence greatly appealed to us because the anion 2 is, in fact, an easily available form of masked acrylate anion, providing that 3 will undergo a retro Diels-Alder reaction. We have now proved this to be the case, and wish to report in this communication our findings(4)

The reaction of the anion 2a with gaseous ethylene oxide at room temperature for 5 hr. in THF/TMEDA (8/1) gave a good yield of 4a(5) (mp 112-4^0, m/e 276, ir.1750 cm^{-1}, 72%) Similarly, treatment of 2b with the same reagent produced a crude mixture, which, upon separation by preparative TLC (using $CHCl_3$/hexane=3/2 as the developing solvent) two isomeric products, assigned as 4b cis (mp. 257-259 5^0 sublimed, m/e 334, ir 1760,1730 cm^{-1}) and 4b trans (mp. 203-204 5^0, m/e 334, ir.1765,1720 cm^{-1}) were isolated in a ratio of 1 2 (80% purified yield)(6)



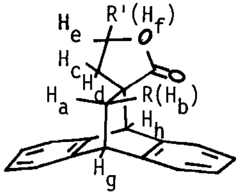
a,R,R'=H b,R=COOMe,R'=H c,R=H,R'=Me d,R=COOMe,R'=Me

Flash vacuum pyrolysis (250-300^{0}/0 1 torr) of 4a afforded anthracene and α-methylene-γ-butyrolactone 5a as a colourless liquid(7) in 77% yield Accordingly, 4b cis gave the lactone 5b cis (semi-solid, m/e 156, ir 1765,1730 cm^{-1}) and 4b trans gave 5b trans (mp 109-110.5^{0}, m/e 156, ir 1765,1720 cm^{-1}) in 74 and 61% purified yields respectively The nmr spectra of lacto-esters 5b cis and 5b trans are easily distinguishable since the olefinic and β-protons in 5b trans appear at much lower field than those in 5b cis, as shown in the table The isolation of both cis- and trans- 5b thus conclusively proved the structure assignment of 4b cis and 4b trans since comparable retro Diels-Alder reactions are known to operate with retention of stereochemistry(8)

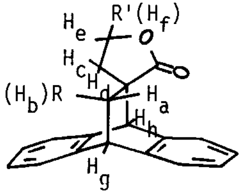
Treatment of 2a with propylene oxide yielded, surprisingly, only one racemate 4c, isolated as colourless prisms (mp 163-4^{0}, m/e 290, ir 1750 cm^{-1}) in very high yield (91%) The regiospecificity of the reaction and the absence of other stereoisomers were verified by high resolution 220 MHz nmr spectroscopy(9) This finding is rather interesting since it was expected that two pairs of enantiomers should, in principle, be obtained. Inspection of molecular models of the product 4c and of the approach of propylene oxide to the anion 2a failed to give any clear indication concerning the stereochemistry of the methyl group at the lactone ring of 4c

The methylene lactone 5c was obtained as a colourless liquid(10) (m/e 112, ir 1758 cm^{-1}, 81%) by the retro Diels-Alder reaction of the spirolactone 4c

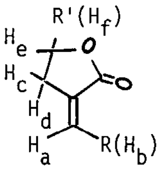
Similar reaction of the anion 2b with propylene oxide produced two, instead of four, pairs of isomers 4d cis (mp 195-7^{0}, m/e 348, ir.1755,1730 cm^{-1}) and 4d trans (mp 183-4^{0}, m/e 348, ir 1755,1712 cm^{-1}) in the ratio 3.5 1 (78% yield) after TLC separation(11) Again, the products were identified by their physical properties, especially their nmr data(12)



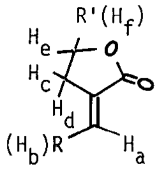
4 cis



4 trans



5 cis



5 trans

COMPOUND				Chemical Shift (ppm from TMS)		* 220 MHz nmr spectrum		
	H_a	$R(H_b)$	H_c	H_d	H_e	$R'(H_f)$	H_g	H_h
4a R=R'=H	1 58 (dd,J=12.5,3Hz)	2 29 (dd,J=12.5,3Hz)	1 56-1.97 (m)		4 08-4 43 (m)		4 32 (t,J=3Hz)	4.20 (s)
4b cis R=COOMe,R'=H	2 74 (d,J=2Hz)	3 55 (s)	2 14-2 43 (m)		4 28-4 54 (m)		4 77 (d,J=2Hz)	4 21 (s)
4b trans R=COOMe,R'=H	3.37 (d,J=2Hz)	3.58 (s)	1 78-2 01 (m)		4.06-4 52 (m)		4.56 (d,J=2Hz)	4.26 (s)
4c* R=H,R'=Me	1 52 (dd,J=12,2.5Hz)	2.38 (dd,J=12,2 5Hz)	1 54 (dd,J=13,10Hz)	2.04 (dd,J=13,5.5Hz)	4 77 (m)	1.32 (d,J=6.5Hz)	4 34 (t,J=2.5Hz)	4.25 (s)
4d cis* R=COOMe,R'=Me	2.64 (d,J=2Hz)	3.53 (s)	2 02 (dd,J=13,10Hz)	2 24 (dd,J=13,6Hz)	4.81 (m)	1 42 (d,J=6Hz)	4 65 (d,J=2Hz)	4 27 (s)
4d trans* R=COOMe,R'=Me	3 42 (d,J=2Hz)	3.58 (s)	1.48 (dd,J=13,10Hz)	1.92 (dd,J=13,6Hz)	4 83 (m)	1 35 (d,J=6Hz)	4 54 (d,J=2Hz)	4.31 (s)
5b cis R=COOMe,R'=H	6.37 (t,J=3Hz)	3 80 (s)	3 04 (dt,J=3,7Hz)		4.42 (t,J=7Hz)			
5b trans R=COOMe,R'=H	6.74 (t,J=3.5Hz)	3 78 (s)	3.35 (dt,J=3 5,7 5Hz)		4 45 (t,J=7.5Hz)			
5d cis R=COOMe,R'=Me	6.38 (t,J=3Hz)	3.80 (s)	2 59 (m)	3.20 (m)	4 67 (m)	1 42 (d,J=6Hz)		
5d trans R=COOMe,R'=Me	6 76 (t,J=3Hz)	3 82 (s)	2.98 (m)	3.65 (m)	4.82 (m)	1 46 (d,J=6Hz)		

Finally, flash vacuum pyrolysis of 4d cis yielded 5d cis (semi-solid, m/e 170, ir 1755,1728 cm^{-1}) while 4d trans yielded 5d trans (semi-solid, m/e 170, ir 1758,1718 cm^{-1}) in 78 and 81% yields respectively

We are currently engaged in exploring the scope of this procedure

References and Notes

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5 All new compounds have been characterised by spectroscopic and microanalytical methods

6 Upon equilibration (LDA 1 2 eq , room temp , 24 hr) both 4b cis and 4b trans yielded a mixture of cis trans=2 3 as indicated by nmr spectra

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11 Equilibration gave 4d cis 4d trans=3 7

12 At this stage of the work the stereochemistry of the methyl group in 4d cis and 4d trans is still uncertain (as discussed for 4c)

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