## STEREOSELECTIVE ALKYLATION OF THE LITHIUM DI-ENOLATE OF BIS-2,3-CARBOMETHOXY BICYCLO[2 2 1]HEPT-5-ENE. A CONVENIENT SYNTHESIS OF MONO- AND DISUBSTITUTED FUMARATE ESTERS

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<u>Summary</u> The diesters formed by a Diels-Alder reaction between cyclopentadiene and methyle maleate or fumarate give the same lithium dienolate which is stereoselectively mono- or dialkylated. The products obtained are good precursors for substituted fuma-rate esters

The preparation of dimetallated vicinal diesters has been recently described (1) and the potential of theses species as synthetic intermediates has been shown (2) We wish to report that the lithium dienolate of bis-2,3-carbomethoxy  $bicyclo \begin{bmatrix} 2 & 2 & 1 \end{bmatrix}$  hept-5-ene can be used as a trans vinyl dianion equivalent (3) since the products coming from the stereoselective alkylations of this di-enolate are thermally cleaved into cyclopentadiene and mono- or disubstituted fumarate esters, not easily accessible by other methods (4).

The diesters <u>1</u> and <u>2</u>, obtained from a Diels-Alder reaction between cyclopentadiene and dimethyle maleate and fumarate, were readily deprotonated with two equivalents of lithium diisopropylamidure in THF to give a solution of the diester dieno'ate <u>3</u> (5)



The diamon <u>3</u> could be monoalkylated by reaction with one equivalent of an organic halide in the presence of HMPT and the results are summarized in the Table The alkylation appeared to be highly stereoselective (6) and only the exo alkylated isomers <u>4</u> could be detected in the reaction mixture either by GLC (column SE 30 20%, 3 m, 170°) or by <sup>1</sup>H NMR (7) The formation of only small amounts of dialkyled products showed that, as it could be expected, the dienolate is much more reactive to alkylation than the monoenolate. It must be noticed that methylation of the lithium enolate

		Alkyla	lon			Thermolysis	(c)
RX	T°C	Prod	ucts (%) <sup>(a)</sup>	Yield % <sup>(b)</sup>	Eb/0,05	Products (%)	Yield % <sup>(e)</sup>
ICH <sub>3</sub> (1 eq )	+ 10	2 (4),	<u>4a</u> (88), <u>5a</u> (8)	78	72-74	<u>7a</u>	95
IC <sub>2</sub> H <sub>5</sub> (1 eq )	+ 10	2 (7),	<u>4b</u> (90), <u>5b</u> (3)	52	82–83	<u>7</u> b	06
ICH <sub>3</sub> (2 eq )	- 78	<u>4a</u> (12),	<u>5a</u> (70), <u>6a</u> (18)	68	75–80	<u>8a</u> (80), <u>9a</u> (20)	95
	+ 10		<u>5a</u> (81), <u>6a</u> (19)	60			
IC2 <sup>H</sup> 5 (2 eq.)	+ 10	<u>4b</u> (3),	<u>5b</u> (90), <u>6b</u> (7)	77	93-97	<u>8b</u> (91), <u>9b</u> (9)	94
IC <sub>2</sub> H <sub>5</sub> <sup>(1 eq )</sup> + ICH <sub>3</sub> <sup>(1 eq )</sup>	+ 10		$\frac{5c}{5c}$ (82) <sup>(d)</sup> , $\frac{6c}{6c}$ (12)	72	82–85	<u>8c</u> (82), <u>9c</u> (12)	61
Br(CH <sub>2</sub> ) <sub>4</sub> Br	+ 10		10	35	95-96	п	92
a) Ratios detei	cmined by	GLC. on t	he crude reaction m	ixture			
b) Yields given	n for Isola	ted distilled	l products				
c) The thermo the hot zon	lyses were e.	carried c	ut à 650° in vapo	or phase w	/ith a short co	ntact time ( $\checkmark$ 50 m	ls) In
d) A small am	ount of a c	dıethylated	compound was also ]	present			

- Yields given for crude products  $\underline{2}$  or mixtures ( $\underline{8} + \underline{9}$ ) which are at least 95% pure (G L C.,<sup>1</sup> H NMR). e)

formed by addition of one equivalent of L D A. to the diester 2 gave up to 20% of dimethylated products. This result might be due to a rapid proton exchange between the monomethylated product 4a and the monoenolate



Addition of two equivalents of the same alkyl halide to the THF-HMPT solution of the dienolate 3 afforded in good yields a mixture of the dialkylated esters 5 and 6 Successive addition of one equivalent of ethyl iodide and one equivalent of methyl iodide allowed the formation of the mixed dialkylated diesters 5c and 6c Yields and relative ratios of 5 and 6 are reported in the Table. The second alkylation appeared also to be stereoselective since the diesters 5, in which the second alkyl groups is coming from an endo alkylation, were largely predominant (80% to 90%). The approach of the electrophiles from the endo face being sterically untavourable, the stereoselectivity observed can be best explained by assuming a product-like transition state where the two bulky carbomethoxy groups are in a trans position.

Mono- and disubstituted methyl fumarates  $\underline{7}$  and  $\underline{8}$  were then prepared with excellent yields (see Table) by thermolysis (9) of the diesters  $\underline{4}$  and  $\underline{5} + \underline{6}$ 



We next investigated the possibility of formation of cyclic unsaturated diesters by alkylation of  $\underline{3}$  with a bifunctionnal electrophile

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Treatment of the dianon  $\underline{3}$  with excess 1,4-dibromobutane gave the annelated ter  $\underline{10}$  in 35% yield. Only one isomer could be detected either by G L C or <sup>1</sup>HNMR ing of  $\underline{10}$  at 650° afforded dimethyl-cyclohexene-1,2-dicarboxylate 11 in 92% yield.

## REFERENCES

a) P J Garratt and R Zahler, J Amer Chem Soc, 100, 7753 (1978), b) N R Long and M W Rathke, Synth Comm., 11, 687 (1981) a) K G Bilyard, P J Garratt and R Zahler, Synthesis, 389 (1980), b) As this work was in progress, alkylation of the monoanions and the dianions derived from 5-norbornene-2,3-dicarboximides was described PJ Garratt and F. Hollowood, J Org. Chem, 47, 68 (1982) Such vinyl diamions could not be prepared directly BA Feit, U Melamed, R R. Schmidt and H Speer, J Chem Soc Perkin I, 1329 (1981) M P  $\,$  Cooke Jr., Tetrahedron Letters, 381 (1981) and references cited therein We believe that the dienolate formed from esters 1 or 2 is the same intermediate since identical results are observed after alkylation Predominant exo alkylation of the monoenolate of 2-carbomethoxy bicyclo [2 2 ] A P Krapcho and E A Dundulis, [ hept-5-ene has been recently reported Org Chem, 45, 3236 (1980) The exo position of the methyl substituant in 4a was determined by the chemical shift of the methyl singlet ( $\delta$  = 1,29 ppm) compared to the chemical shifts of the two methyl singlets in 5a ( $\delta$  = 1,30 and 1,05 ppm). Or it has been reported that in 2-methyl bicyclo 2 2 1 hept-5-enes, the endo methyl peak is shifted to high field by 0,2 - 0,3 ppm with respect to the signal of the corresponding exo methyl (see ref (8)) The exo position of the ethyl group in 4b was indirectly shown by the endo position of the methyl substituant appearing in 5c ( $\delta$  = 1,05 ppm) B C C Cantello and J M Mellor, Tetrahedron Letters, 5179 (1968) Thermolyses were carried out at 650° in a flow apparatus analogous to the one in reference (10) Samples of 200 mg to 1 g of diesters were distilled described through the hot tube in 20 to 40 minutes JF King, P De Mayo, C L Mc Intosh, K Piers and D J H Smith, Can J Chem, 48, 3704 (1970)

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