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ELECTROPHILIC ADDITION OF DICHLOROMETHYLMETHYL ETHER TO DIENES. A NEW ANNULATING PROCEDURE[1)]

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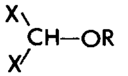
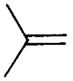
Dihalomethylethers (1) find application in a variety of reactions e.g. the formylation of aromatic systems,[3)] the preparation of acid halides,[4)] the synthesis of orthoformic acid derivatives,[5)] and the generation of cyclopropylmethyl ethers via methoxycarbene.[6)] We have attempted the formylation with dichloromethylmethyl ether (2) of methylpropene (3) and 2-methylbut-2-ene (4). In both instances the reaction products (5) (92%; δ_a1.63,s; δ_b2.0,d; δ_c3.31,s; and δ_d3.73, tt) and (6) (34%; δ_a1.03,d; δ_b1.60,s; δ_c3.35,s; δ_d3.91,br.dd) respectively originated from the condensation, irrespective of the relative concentrations of the reactants used in the Lewis acid catalysed condensation ($SnCl_4$; CH_2Cl_2).[7)] This observation indicated chloro-ether (7) to be more reactive than ether (2) in electrophilic addition reactions to olefins and suggested the use of dihalomethylmethyl ethers in the construction of carbocyclic ringsystems from suitable dienes.

Diene (8) was indeed successfully converted into cycloheptane derivatives by Lewis acid catalysed condensation with ether (2) ($SnCl_4$; solvent: CH_2Cl_2 or AcOMe). The crude product (8) was treated with base (^{t}BuOK/DMSO; 15h) to give (i) 19% of the dimethylcycloheptatrienes (11) (δ_a~1.98; δ_b2.30,br.d; δ_c5.34,m,J_{ce}9, J_{bc}7; δ_d5.87,br.d, J_{df}~6.5; δ_e5.97,br.d; δ_f6.3,br.d) and (12) (δ_a1.84; δ_b1.97,d,J_{bd}~1.5; δ_c2.24,br.d,J_{cd}7; δ_d5.14,br.t; δ_e~5.87,m; $\delta_{f\&g}$~6.36,m); (ii) 22% of the heptadienylethers (13) (δ_a1.82; δ_b~2.37,m; δ_c3.33; δ_d~3.60, m; δ_e5.56,br.s) and (14) (δ_a1.76,dd,J_{af}=J_{ad}=1; $\delta_{b'}$2.27,dd,$J_{b'b''}$13,$J_{b'd}$9; $\delta_{b''}$2.61,dd,$J_{b''d}$3.5; δ_c3.33; δ_d3.76,m,J_{df}3.5; δ_e4.76,m; δ_f5.56,m), as well as 9% of the cycloheptenylether (15) (δ_a~1.71; δ_b3.31; δ_c~3.67,m; δ_d~5.47,m).[9)] In some experiments the presence of small quantities of 1,2,4-trimethylbenzene was observed.[10)] Both ethers (13) and (14) were converted into dimethylcycloheptatrienes by acid catalysed (p-TsOH,


1: X = halogen; R = alkyl
2: X = Cl; R = Me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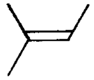
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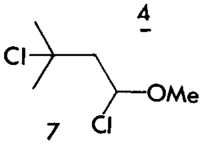
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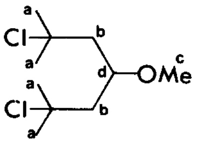
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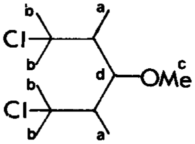
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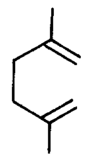

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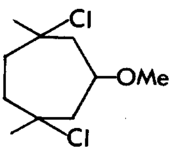

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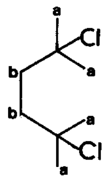

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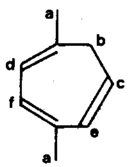

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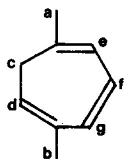

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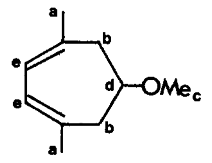

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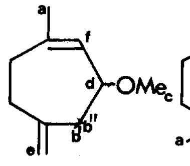

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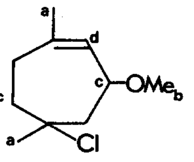

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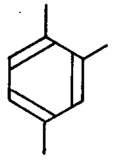

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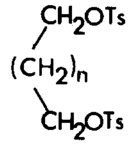

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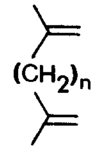
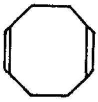


18: n=4
19: n=6
20: n=8

$CHCl_3$,Δ) methanol elimination. Cycloheptatriene derivatives have previously been obtained mostly by ring enlargement reactions of aromatic compounds with carbenoid reagents.[11] The attempted conversion into macrocyclic compounds[12] of dienes (18)-(20)[13] by condensation with dichloro-ether (2) failed. The dienes (18)-(20) were conveniently prepared from the corresponding tosylates (17) (n=2, 4 and 8 respectively)[13].

The dichloro-ether (2) was successfully condensed with the cyclic diene (21) to yield a mixture of stereo-isomeric dichloro-9-methoxybicyclo[3.3.1]nonanes e.g. (22).[14] The major isomer (40%) was isolated severally and according to pmr studies originated from a trans-addition to the first double bond of the 1,5-diene system of cyclo-octadiene (21), followed by an intramolecular attack on the second double bond to form the intermediate carbonium ion (22a), which rearranged before reaction with the chloride ion to yield the major isomer (22b) [$\delta_a 1.55, J_{ab} 6, J_{ad} -13.3, J_{af} 2, J_{ag} {\sim}1$; $\delta_b 1.74, J_{bd} 12, J_{bg} -13, J_{bm} 12$; $\delta_c 1.84, J_{cj} -14, J_{cm} {\sim}1, J_{cn} 12, J_{ci} 5$; $\delta_d {\sim}1.96, J_{df} {\sim}5, J_{dg} 7$; $\delta_e 2.02, J_{ef} {\sim}5, J_{eh} -14, J_{en} 12$; $\delta_f 2.09, J_{fh} 2.5$; $J_{fl} 2.3$; $\delta_g 2.17, J_{gm} 7$; $\delta_h 2.34, J_{hj} 2, J_{hn} 6$; $\delta_i 2.41$, $J_{ij} 2.5, J_{il} 3, J_{im} 4.5$; $\delta_j 2.83, J_{jn} 6$; $\delta_k 3.32$; $\delta_l 3.53$; $\delta_m 4.46$; $\delta_n 4.53$],[15] with both chlorine atoms in equatorial positions. The chemical reactivity of this isomer supports the structural assignment. Isomer (22b) readily undergoes elimination [cf. conformer (22c)][16] of one mole HCl/mole adduct on treatment with base (^{t}BuOK/DMSO, 50°, 1h) to yield the chloroderivative (23)($\delta_a 2.24$, $J_{ab} 18, J_{ai} 7.2, J_{ag} 3$, $J_{af} {\sim}1.5$; $\delta_b 2.68, J_{bg} 3, J_{bf} {\sim}1.5$; $\delta_c 3.33$; $\delta_d 3.61, J_{di} \simeq J_{dh} \simeq 3$; $\delta_e 4.48$, $J {\sim}4, 8\&8$; $\delta_f 5.56, J_{fg} 9.8, J_{fh} 6.8$; $\delta_g 5.83$). Conversion of the latter into the diene (24) ($\delta_a 3.42$, $\delta_b {\sim}3.48$, $\delta_c 5.35\text{-}5.95$) requires much more forcing conditions (^{t}BuOK/DMSO, 110°, 65h), in agreement with the assigned structure (23). In addition to bicyclic diene (24), the tricyclic ether (25) was also obtained as a minor product (ratio 10:1) on treatment of the crude condensation product under forcing conditions with excess base (^{t}BuOK/DMSO; 110°, 57h). The structural assignment of compound (25) ($\delta_a 1.07, J_{ag} 12, J_{ah} 6.5$; $\delta_b 2.86$; $\delta_{c'\&c''} 3.15$; $\delta_d 3.28$,s; δ_e,br.dd,$J_{ef} 8.2$;$J_{ec'} 6$, $J_{be} \sim 1$; $\delta_f 6.45$,m,$J_{bf} 7, J_{fc''} 2.2$) is based mainly on pmr and ^{13}C nmr spectroscopy (cf Table). Ether (25) does not originate from either compounds (22b) or (23).

The condensation of ether (2) with dimethylcyclo-octadiene (26) ($SnCl_4$; CH_2Cl_2; -80°) proceeds differently to yield the bicyclo-octane derivative (27) (9%; $\delta_a 0.97$; $\delta_b 3.52$,br.s) and the ether (28) (30%; m.p. 136.5°; $\delta_a 0.97$; $\delta_b 1.03$; $\delta_c 3.25$,m; $\delta_d 3.36$; $\delta_e 3.51$,br.s). For ^{13}C nmr - see Table. The stereo-isomerism of compound (28) was determined by X-ray crystallography cf.



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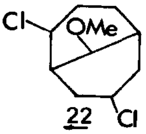

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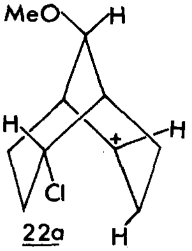
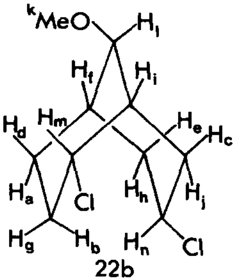
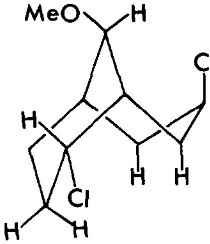


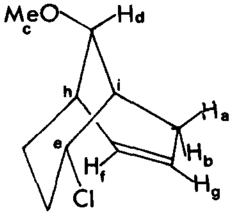
22a



22b



22c



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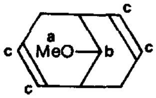

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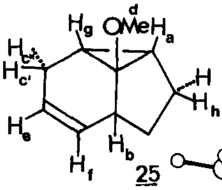

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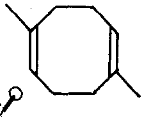

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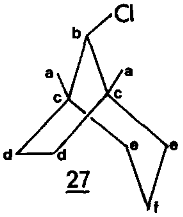

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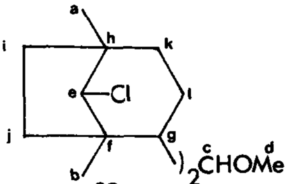

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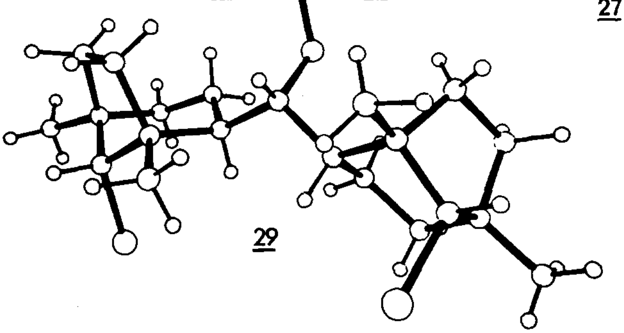

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formula (29). The identity of chloride (27) as the hydrochloric acid addition product of diene (26), is in agreement with the recent finding of Whitesell et al.[17] The bifunctional olefin (26), therefor effectively reacts like a mono-olefin.

TABLE

^{13}C-Nuclear Magnetic Resonance Data Recorded at 20 MHz in CDCl$_3$ with Tetramethylsilane (δ 0) as Internal Standard. [Details: δ-values (multiplicity, assignment, ^1J)]

Compound (23): 129.1(d,=CH-,157Hz); 127.3(d,=CH-,160Hz); 80.3(d,>CH-O,145Hz); 61.3(d,>CHCl, 152Hz); 55.7(q,OCH$_3$,141Hz); 38.6(d,>C-H,136Hz); 31.7(d,>C-H,135Hz); 28.3(t,>CH$_2$,132Hz); 27.1 (t,>CH$_2$,128Hz); and 24.2(t,>CH$_2$,132Hz)

Compound (24): 130.3(d,=CH-,157Hz), 127.7(d,=CH-,157Hz); 125.5(d,=CH-,158Hz); 125.1(d,=CH-, 158Hz); 77.6(d,>CH-O,143Hz); 55.9(q,-OCH$_3$,143Hz); 32.9(d,>C-H,132Hz); 32.1(t,>CH$_2$,125Hz); 31.8 (d,>C-H,130Hz); and 26.0(t,>CH$_2$,124Hz)

Compound (27): 76.2(d,C$_b$); 42.8(s,2C$_c$); 33.1(t,2C$_d$); 31.5(t,2C$_e$); 25.5(q,2C$_a$); and 19.7(t,C$_f$). (For the ^{13}C spectrum of the corresponding tosylate, see ref. 17)

Compound (28): 80.4(d,C$_c$, ~ 140Hz); 78.7(d,C$_e$, ~ 140Hz); 59.7(q,C$_d$,140Hz); 45.7(s,C$_f$); 43.1(d,C$_g$, 120Hz); 42.4(s,C$_h$); 33.4(t,C$_i$,135Hz); 32.2(t,C$_j$,125Hz); 30.0(t,C$_k$,130Hz); 25.1(q,C$_a$,125Hz); 24.3(q,C$_b$,125Hz); and 20.1(t,C$_\ell$, 130Hz)

REFERENCES AND FOOTNOTES

1. For a previous communication on electrophilic addition reactions of chloro-ethers to see C.F. Garbers and F. Scott, Tetrahedron Lett., 507 (1976).
2. Abstracted from part of Ph.D. thesis by H.E. Visagie, University of Stellenbosch (197
3. e.g. F. Straus and H.J. Weber, Ann., 498, 101 (1932); A. Rieche, H. Gross and E. Hö 93, 88 (1960); H. Gross, A. Rieche, and G. Mathey, Ber., 96, 308 (1963); A. Rieche, and E. Höft, Org. Syntheses, 47, 1 (1967).
4. A. Rieche and H. Gross, Ber., 92, 83 (1959).
5. H. Gross and A. Rieche, Ber., 94, 538 (1961).
6. U. Schöllkopf and J. Paust, Ber., 98, 2221 (1965).
7. Yields were not optimised. All new compounds or known compounds prepared by new met gave satisfactory combustion analyses. The spectral properties of all compounds ar accord with the assigned structures. Pmr spectra in $CDCl_3$. J values in Hz.
8. No attempts were made to isolate the addition product (9). However, the identificati compounds (11)-(15) infers the initial formation of the dichlorocycloheptane (9). T lation of dichloride (10) (δ_a1.58,s; δ_b1.94,s) from the condensation product suggest dehydrochlorination during the condensation of the formed chlorocycloheptanes.
9. In another experiment treatment of the condensation product with excess base (^{t}BuOK/I yielded the cycloheptatrienes (11) and (12) (30%), the ethers (13) and (14) (16%), b the chloro-ether (15).
10. The rearrangement of tropilidenes to benzene derivatives is known, cf. J.A. Berson a M.R. Wilcott, J. Amer. Chem. Soc., 88, 2494 (1966).
11. e.g. E. Müller, H. Kessler, H. Fricke and W. Kiedaisch, Ann., 675, 63 (1964); J. Nis J. Furukawa, N. Kawabata, and T. Fiyita, Tetrahedron, 26, 2229 (1970); S. Miyano, Y. Matsumoto, and H. Hasimoto, Chem. Commun., 364 (1975).
12. For recent alternative approaches to macrocyclic ringsystems see E.J. Corey and P. H Tetrahedron Lett., 4091 (1975); M. Karpf and A.S. Dreiding, Helv., 59, 1226 (1976); M. Baumann, W. Hoffmann, and N. Müller, Tetrahedron Lett., 3585 (1976); Yoshihiko It Takeo Saegusa, J. Org. Chem., 42, 2326 (1977), and references cited therein.
13. G.H. Posner, Organic Reactions, 22, 253 (1975); C.F. Garbers, J.A. Steenkamp, and H. Visagie, Tetrahedron Lett., 3753 (1975).
14. Total yield of condensation products: 32 %. The nature and stereochemistry of the o products are presently being investigated. Stereochemistry of ether (22b) at C-9 un
15. We thank Prof. F. Bohlmann, Technical University, Berlin, for kindly recording the 2 pmr spectrum of ether (22b) in $CDCl_3$ and C_6D_6, and for extensive spin decoupling exp The quoted δ-values were obtained with $CDCl_3$ as solvent.
16. J.A. Peters, J.M. van der Toorn, and H. van Bekkum, Tetrahedron, 31, 2273 (1975), an ferences cited therein.
17. J.K. Whitesell, R.S. Mathews, and P.A. Solomon, Tetrahedron Lett., 1549 (1976).