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1-HALOCYCLOPROPENES AND PROPARGYLIC HALIDES FROM THE REACTION OF TRIHALOCYCLOPROPANES WITH METHYL LITHIUM

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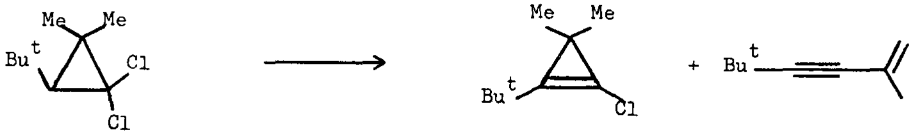
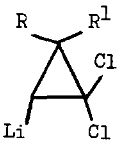
Abstract: 1,1,2-Trihalocyclopropanes (halogen = chlorine or bromine) undergo 1,2-dehalogenation on reaction with methyl lithium, and in a number of cases the product is a 1-halocyclopropene. In the reactions of (20, X = Br, Cl) and (25) a rearrangement occurs even at low temperatures and propargylic halides are isolated, while (16) is converted to 2-chlorocyclohex-2-enylidene which may be trapped by furan.

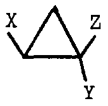
The dehydrohalogenation of 2-alkyl-1,1-dihalocyclopropanes with potassium alkoxide in alcohol or dimethylsulphoxide has been widely postulated to lead initially to 1-halocyclopropenes.[1] In general, these compounds have not been isolated, but undergo very rapid prototropic shifts to 2-methylene-1-halocyclopropanes followed by further dehydrohalogenation. In particular cases where the prototropic shift is blocked the halocyclopropene has been isolated, but can be accompanied by products in which the ring has opened:[2]



An alternative route to 1-halocyclopropenes involves the addition of an alkyl lithium (RLi) to a 1,1-dihalocycloprop-2-ene to give (1), followed by elimination of lithium halide.[3] The ready availability of 1,1,2-trihalocyclopropanes,[4] and the known fast lithium-halogen exchange in 1,1-dihalocyclopropanes[5] suggests an alternative process involving 1,2-elimination of LiX from compounds of type (2, Z = lithium).[6]



(1)



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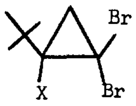

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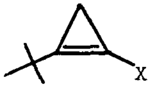
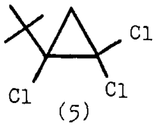


(4)

Treatment of dibromochloride (3, X = Cl) with one equivalent of methyl lithium in ether at -40° for 5 min, followed by quenching with water, leads to a single major product (52%) characterised as (4, X = Br), b.p. 31-32° at 14 mm Hg (δ_H 1.2 (9H, s), 1.5 (2H, s); δ_C 124.8s, 89.4s, 31.05s, 28.9q, 16.4t; ν_{max}1805 cm^{-1}); the structure of this compound was confirmed by reaction with bromine in carbon tetrachloride, when the tribromide (3, X = Br) was obtained

(92%).[7] In the same way the trichloride (5) reacted with MeLi-ether in 5 min at 25-35° to give the cyclopropene (4, X = Cl) (29%)(δ_H 1.2 (9H, s), 1.5 (2H, s); δ_C 117.8s, 103.7s, 30.7s, 27.4q, 15.8t; ν_{max} 1835 cm^{-1}). Moreover, the corresponding trihalides (6, X = Cl) and (6, X = Br) in which the 2-halogen is bromine react in analogous manner to produce (7, X = Cl, Br). Thus the various combinations of halogen in compounds (2, X = Br or Cl, Y = Z = Br or Cl) all undergo 1,2- rather than 1,1-elimination on reaction with MeLi. The stereochemistry of this process is at present under investigation, but by analogy with addition of an alkyl lithium to a cyclopropene may involve a cis-elimination.[8]



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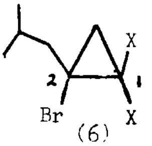

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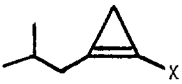

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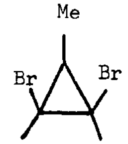
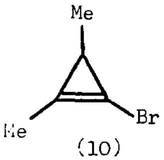


(9)

Vinylic hydrogens in cyclopropenes are known to be relatively acidic, and undergo lithiation on reaction with an alkyl lithium. However, this is a relatively slow process; thus (8) requires 40 hr at 20° to undergo lithiation with methyl lithium.[9] By contrast, lithium-halogen exchange in (4, X = Br) is complete in 2 min at 20°;[10] the lithio-derivative (4, X = Li) may be efficiently trapped by addition of carbon dioxide to produce (4, X = CO_2H) (91%), m.p. 194-6°. The lithiation of (4, X = Cl) with MeLi is much slower, requiring 3 h at 20°.



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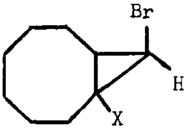

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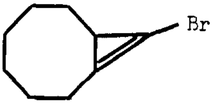

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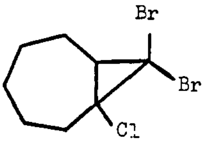
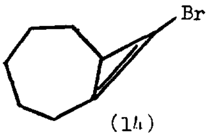


(13)

Cyclopropenes are also obtained when 1,1,2-trihalo-2,3-dialkylcyclopropanes are treated with methyl lithium. Thus (9) is converted to (10), and the bicyclic dibromochloride (11, X = Cl) leads to (12). The latter can be purified by rapid column chromatography over alumina and kept at 0° in solution, but decomposes rapidly when neat. The lower homologue (13) also reacts with MeLi in ether at -40° to give a single major product, presumably (14); this was too unstable to isolate pure at 20°, but immediate addition of t-butylmercaptan[11] to (14) leads to the thioether (15) (54%), confirming that the cyclopropene is again present in solution.[12]



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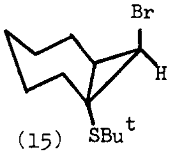

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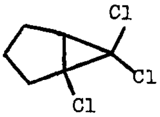

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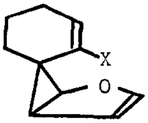
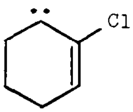


(17)

The trichloride (16) reacts with methyl lithium in ether at 25° in 15 min in the presence of furan to give (17, X = Cl) (64%), together with less volatile products. The overall ring structure of (17, X = Cl) was confirmed by its ^{13}C and ^1H n.m.r. spectra,[13] and in particular by the presence of signals in the latter very similar to those in other 2-oxabicyclo[3.1.0]hex-3-enes.[14] The spectra indicated that (17, X = Cl) was not a mixture of diastereoisomers. Moreover, reduction with lithium-t-butanol-tetrahydrofuran led to (17, X = H)[15] in which the cyclohexene hydrogen at position X appeared at δ 4.6 (d, J = 10.5 Hz); the small chemical shift of this hydrogen is in agreement with the isomer shown, in which X would be in the shielding zone of the enol-ether. A reasonable route to (17, X = Cl) would involve dehydrochlorination of (16) to (18) and ring-opening of this to 2-chlorocyclohexenylidene (19) which could be trapped by the furan.[16] The trapping of carbenes by furan is unusual in that it often does not lead to a mixture of diastereoisomers about the cyclopropane.[14]

When the trihalide (20, X = Br) was treated with a slight excess of methyl lithium at -40°, followed by quenching with water, a single product was again obtained (58%). However, this was not the cyclopropene (21, X = Br) but instead was shown to be the propargylic bromide (22, X = Br). One possible route to the latter would involve a 1,1-elimination of bromine from (20) to produce the cyclopropylidene (23) which might be expected to rearrange to allene (24) in the normal manner;[17] an allylic rearrangement could then lead to (22).

(18)



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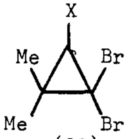

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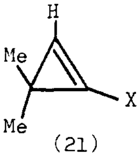

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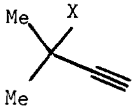
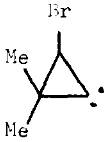


(22)

However, the normal direction of this rearrangement is from alkyne to allene, in the presence of halide ions or copper halides;[18] indeed, treatment of (24) with a deficiency of methyl lithium under the reaction conditions did not produce any (22). An alternative route to (22) would involve 1,2-dehalogenation, and rearrangement of the resulting halocyclopropene (21, X = Br).* Support for such a process was obtained in the reactions of (20, X = Cl) and (25) with methyl lithium when the halogen remaining in products (22, X = Br) and (26) respectively, indicated a 1,2- rather than a 1,1-elimination. Indeed, when (20, X = Br) was treated with MeLi-ether for 1 min. at -95° and quenched with water at that temperature a



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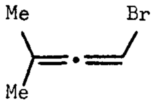

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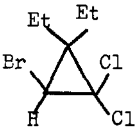

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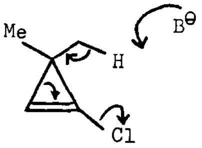

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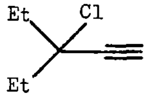

(26)

product was obtained which rearranged above ca. -80°, but which was trapped at -95° by addition of bromine to give (20, X = Br) (60%); the most reasonable structure for the intermediate is (21, X = Br).[19] The chloride (21, X = Cl) has been postulated as an intermediate in the dehydrochlorination of 1,1-dichloro-2,2-dimethylcyclopropane with potassium t-butoxide in dimethylsulphoxide, one product of which is isopropenylacetylene.[20] The formation of the latter was explained in terms of base induced elimination as in (27). In view of the ready rearrangement of (21, X = Br) to (22, X = Br), it seems possible that isopropenylacetylene may be derived from (22, X = Cl) produced by rearrangement of (21, X = Cl).

Various synthetic and mechanistic aspects of the above reactions are under examination.

We wish to thank the S.E.R.C. for a research studentship (to W.N.) and Dr. I. Sadler (Edinburgh) for running the n.m.r. spectra of (17).

1. See e.g., J. Prestien and H. Gunther, Angew.Chem.Int.Edn., 13, 276 (1974); W.E. Billups K.H. Leavell, W.Y. Chow and E.S.Lewis, J.Amer.Chem.Soc., 94, 1770 (1972); W.E. Billups and A.J. Blakeney, ibid., 98, 7817 (1976); W. Eymann and M. Hanack, Tetrahedron Letters, 1972, 4213.
2. T.C. Shields, B.A. Loving, and P.D. Gardner, J.Chem.Soc.,Chem.Commun., 1967, 556.
3. R. West and W. Goyert, Tetrahedron Letters, 1970, 4067.
4. See e.g., M.S. Baird and P.D. Slowey, Tetrahedron Letters, 1982, 3795.
5. D. Seyferth, R.L. Lambert and M. Massol, J.Organometal.Chem., 88, 255 (1975).
6. Dechlorination of 1,2-dichlorotetrafluorocyclopropane to tetrafluorocyclopropene by reaction with zinc in bis-(2-methoxyethyl)ether has been reported (G. Camazzi and F. Gozzo, J.Chem.Soc.(C), 1970, 178).
7. Addition of bromine to cyclopropenes is reported to occur in a trans-manner (K.B. Wiberg and W.J. Bartley, J.Amer.Chem.Soc., 82, 6375 (1960)).
8. J.G. Welch and R.M. Magid, J.Amer.Chem.Soc., 89, 5300 (1967).
9. G.L. Closs and L.E. Closs, J.Amer.Chem.Soc., 83, 1003 (1961); ibid., 85, 99 (1963).
10. The reaction of 1,1-dibromo-2-halocyclopropanes with MeLi occurs extremely rapidly at -50°; under these conditions the bromocyclopropene (4, X = Br) showed no appreciable lithiation after 15 min.
11. (13) was treated with MeLi (2 m. equiv.) at -40°, followed after 1 min by addition of excess t-butylmercaptan at that temperature, and quenching with water after 5 min.
12. W.E. Billups, L.P. Lin and W.Y. Chow, J.Amer.Chem.Soc., 96, 4026 (1974); T.C. Shields and P.D. Gardner, ibid., 89, 5427 (1967).
13. δ_H 6.36 (1H, dd, J = 0.6, 3 Hz), 5.92 (1H, t, J = 4.25 Hz), 5.15 (1H, t, J = 3 Hz), 4.74 (1H, br. d, J = 6 Hz), 2.78 (1H, dd, J = 6, 3 Hz), 2.17 (m, 2H), 1.6 (m, 2H), 1.33 (1H, ddd, J = 14, 8.5, 4 Hz), 1.41 (1H, ddd, 14, 7, 4 Hz); δ_C 148.1 d, 133.9s, 124.3d, 101.2d, 69.3d, 32.9d, 27.0t, 21.2t, 20.6t, 18.0s.
14. H.R. Kricheldorf, Angew.Chem.Int.Edn., 9, 526 (1970); M. Franck-Neumaun and C. Dietrich-Buchecker, Tetrahedron, 34, 2797 (1978); ibid., Tetrahedron Letters, 1973, 2875; J. Wolfhugel, A. Maujen and J. Chuche, ibid., 1635; G.O. Schenck and R. Steinmetz, Annalen, 668, 19 (1963).
15. δ_H 6.1 (1H, t, J = 3 Hz), 5.55 (1H, ddd, 3, 6, 10.5 Hz), 4.9 (t, J = 3 Hz), 4.6 (d, J = 10.5 Hz), 4.05 (d, J = 6 Hz), 1.8 - 2.1 (3H, m), 1.0 - 1.8 (4H, m). Compound (17, X = H) is unusual in forming a bright blue coloration on reaction with iodine, for example on iodine development of a t.l.c. plate.
16. The halocyclopropene - vinylcarbene rearrangement could lead either to (19) or to cyclopentenyl chlorocarbene; a rearrangement in the latter sense has been reported for a related 7-chloro-bicyclo[4.1.0]hept-1(7)-ene (see ref. 12).
17. L. Skattebøl, Acta.Chem.Scand., 17, 1683 (1963).
18. V.J. Shiner and J.S. Humphrey, J.Amer.Chem.Soc., 89, 622 (1967).
19. When (20, X = Cl) was treated with methyl lithium at -95° complete reaction again occurred in less than 1 min. Quenching of the products in water at that temperature, followed by addition of bromine again led to (20, X = Br), but in this case together with (20, X = Cl); the latter is presumably formed by anion exchange during the halogenation.
20. L. Crombie, P.J. Griffiths and B.J. Walker, J.Chem.Soc.,Chem.Commun., 1969, 1206.

[*] Possibly via 2-bromo-3-methylbut-2-enyl-1-idene.

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