1,3-Migration of a Cyano-group in Substituted 3-Cyanopropyl Radicals

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The free radical addition of carbon tetrachloride to 2,2-dichlorobut-3-enonitriles gives both normal and rearranged addition products, namely hexachlorohexanonitriles and 3-cyanohexachloropentanes, respectively. The latter products are believed to be formed by migration of the cyano-group in the intermediate 3-cyanopropyl radical formed on addition of a trichloromethyl radical to the substrate. The migration is greatly assisted by methyl substituents in the 2-position, commensurate with migration through a four-membered cyclic intermediate radical. Some evidence is also presented for the formation of transient trichloroethylcyclopropanes when the initiating catalyst is benzoyl peroxide.

A large number of ring-closing and ring-opening reactions of organic radicals have been observed and their rates have, in many cases, been carefully measured.[1] From these studies it has become apparent that the ease of cyclisation of open chain radicals of the type shown in equations (1) and (2) decreases as the number of atoms in the subsequently formed cyclic radical changes in the sequence $5 > 6 > 3 \gg 4$. Examples of the first three types of ring closure abound, *e.g.* equation (3),[2] but the closure to four-membered rings is rare and has been observed only in a few rather special cases, *e.g.* equation (4).[3]

In those cases where four-membered cyclic radicals have been prepared directly from cyclic precursors, ring opening is believed to be very fast and only open chain products are obtained.[4] A relevant example is shown in equation (5).

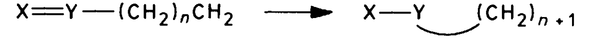
We now describe a study of the reaction of trichloromethyl radicals with 2,2-dichloropent-4-enonitriles which shows that the 1,3-migration of a cyano-group can take place *via* a four-membered cyclic radical intermediate, provided there is at least one, and preferably two, methyl substituents in the 3-position of the cyclic radical intermediate [equation (6)].

Results

Preparation of 2,2-*Dichloropent*-4-*enonitriles*.—Allylbis(dimethylglyoximato)pyridinecobalt(III) (1)[5] reacted with a little over one equivalent of trichloroacetonitrile in methylene chloride to give 2,2-dichloropent-4-enonitrile (5) and chlorobis(dimethylglyoximato)pyridinecobalt(III). The organic products were separated by chromatography and distillation. Similar reaction of 2-methylallyl-, but-3-enyl-, and 3-methylbut-3-enyl-bis(dimethylglyoximato)pyridinecobalt(III) (2)—(4), gave 2,2-dichloro-4-methyl-, 2,2-dichloro-3-methyl-, and 2,2-dichloro-3,3-dimethyl-pent-4-enonitrile[6] (6)—(8) [equation (7)].

Reactions with Carbon Tetrachloride.—2,2-Dichloropent-4-enonitrile (5) and copper(II) acetylacetonate[7] in carbon tetrachloride were sealed in a tube and heated to 100 °C for 12 h. The mixture was filtered and the organic products were separated by h.p.l.c. to give unchanged (5) and a single addition product 2,2,4,6,6,6-hexachlorohexanonitrile (9), identified by its ^{1}H n.m.r. and mass spectra (Table). Similar reaction of (6) gave substantial recovery of starting material together with 4-methyl-2,2,4,6,6,6-hexachlorohexanonitrile (10) (Table) and some unidentified elimination products. Similar reaction of (7) gave three main products, the two diastereoisomers of 3-methyl-2,2,4,6,6,6-hexachlorohexanonitrile (11) and (12), and an isomeric material identified as a single diastereoisomer of 3-cyano-1,1,1,5,5,5-hexachloro-2-methylpentane (13) (Table). The corresponding reaction of (8) however gave an 80% yield of 3-cyano-2,2-dimethyl-1,1,1,5,5,5-hexachloropentane (14) together with some 3-cyano-2,2-dimethyl-1,1,5,5,5-pentachloropentane (15), and 3,3-dimethyl-2,2,4,6,6,6-hexachlorohexanonitrile (16). When (8) reacted with carbon tetrachloride in the presence of a mixture of iron(III) chloride and butylamine[7] compound (14) was again the main product, but more substantial proportions of (15) and of the two diastereoisomers of 3,3-dimethyl-2,4,6,6,6-pentachlorohexanonitrile (17) and (18), respectively, were also formed.

Several products were formed in the reaction of (8) with carbon tetrachloride for 24 h at 101 °C in the presence of benzoyl peroxide but compound (14) could not be detected. The main products were (15) and a compound, $C_9H_9Cl_8N$,



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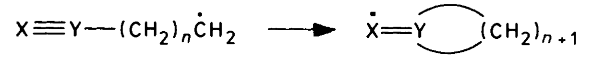

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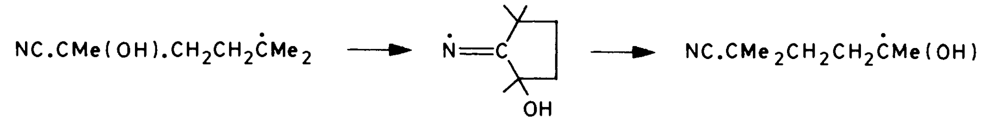

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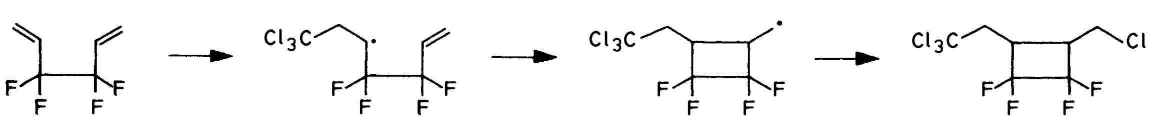

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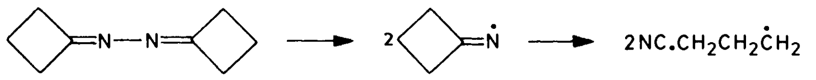

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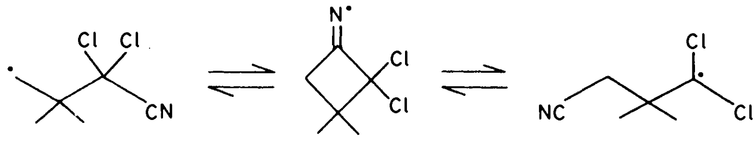

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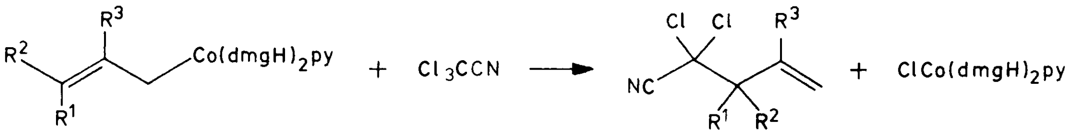

(7)

(1)	$R^1 = R^2 = R^3 = H$	(5)
(2)	$R^1 = R^2 = H, R^3 = Me$	(6)
(3)	$R^1 = R^3 = H, R^2 = Me$	(7)
(4)	$R^1 = R^2 = Me, R^3 = H$	(8)

^1H N.m.r. spectra of adducts $Cl_3C{\cdot}CH^4H^{4'}{\cdot}CR^3X{\cdot}CR^2R^1{\cdot}CYZCl$

	Substituents						Proton chemical shifts (δ)						Coupling constants (Hz)					
Formula	X	Y	Z	R^2	R^1	R^3	4-H	4'-H	3-H	R^2	R^1	Z	$J_{4,4'}$	$J_{4,3}$	$J_{4',3}$	J_{3,R^2}	J_{3,R^1}	J_{R^1,R^2}
(9)	Cl	CN	Cl	H	H	H	3.40	3.26	4.66	3.24	3.10		16.7	5.1	5.5	3.5	8.9	15.4
(10)	Cl	CN	Cl	H	H	Me	3.65	3.52		3.51	3.39		15.9					15.9
(11)	Cl	CN	Cl	H	Me	H	3.60	3.14	4.94	1.57	3.05		16.1	1.2	8.5	1.0		6.9
(12)	Cl	CN	Cl	Me	H	H	3.31	3.14	5.06	2.91	1.56		15.6	5.1	5.1		1.6	6.0
(13)	CN	Cl	Cl	H	Me	H	3.54	3.10	4.04	1.61	3.28		15.0	1.7	10.6	1.8		7.0
(14)	CN	Cl	Cl	Me	Me	H	3.53	3.20	3.64	1.59	1.67		15.0	1.6	9.8			
(16)	Cl	CN	Cl	Me	Me	H	3.44	3.21	4.51	1.50	1.52		16.2	1.5	7.3			
(17)	Cl	CN	H	Me	Me	H	3.32	3.20	4.35	1.24	1.78	4.88	16.1	1.9	6.8			
(18)	Cl	CN	H	Me	Me	H	3.26	3.17	4.41	1.30	1.40	4.94	16.0	2.7	6.1			
(15)	CN	Cl	H	Me	Me	H	3.12	2.93	3.34	1.30	1.31	6.00	14.7	9.4	1.4			
(19)	CCl_3	CN	Cl	Me	Me	H	3.45	3.22	3.76	1.78	1.77		15.1	1.8	9.5			

believed to be (19). These reactions are summarized in equations (8) and (9).

Discussion

The identification of compounds (9)—(19), with relatively few distinguishing features, requires justification. The mass spectra of compounds (14) and (16) are almost identical above *m/e* 198, showing characteristic patterns for sequential loss of six chlorine atoms, but the ^1H n.m.r. spectra are significantly different. The methine (CHCl) proton resonance of (16) is characteristically at δ 4.51,* whereas that (CHCN) of (14) is *ca.* 1 p.p.m. upfield at δ 3.64 (Figure). In contrast, the methylene proton resonances of (14) at δ 3.20 and 3.53 are very similar to those of (16) at δ 3.21 and 3.44,† each having one large and one small coupling to the respective methine protons, in accord with the chemical shifts of the addition products of carbon tetrachloride to unsubstituted n-terminal alkenes.

Similar consideration of the mass spectra and proton n.m.r. spectra of the monomethyl compounds (11) and (13), expecially the differences in chemical shift of the methine protons [CHCl at δ 4.94 in (11); CHCN at δ 4.04 in (13)], shows the similarity of their structures to those of (16) and (14), respectively, and suggests that they have the same configurations at the two chiral centres. Compound (12), which also has the expected methine (CHCl) proton resonance at δ 5.06, but quite different coupling constants, is the other diastereoisomer of (11).

Similar effects are apparent in the proton resonances of the methine protons of the reduction products (15), (17), and (18), *i.e.* the chemical shifts of the CHCl protons of (17) and (18) are at δ 4.35 and 4.41, respectively, whereas that of the CHCN proton of (15) is at δ 3.34. Similarly, the $CHCl_2$ proton resonance of (15) is at δ 6.0, whereas those of the CHCl(CN) protons of (17) and (18) are *ca.* 1 p.p.m. upfield at δ 4.88 and 4.94, respectively.

The mass spectrum of compound (19) clearly shows the presence of eight chlorine atoms, and its ^1H n.m.r. spectrum is very similar indeed to that of (14), as expected because of the similar proton chemical shifts of the CHCN and $CHCCl_3$ protons at δ 3.64 and 3.76, respectively.

Mechanism of Formation of the Products.—The formation of products (9)—(18) can be rationalised if the radical (20) (see Scheme), formed by attack of the trichloromethyl radical on

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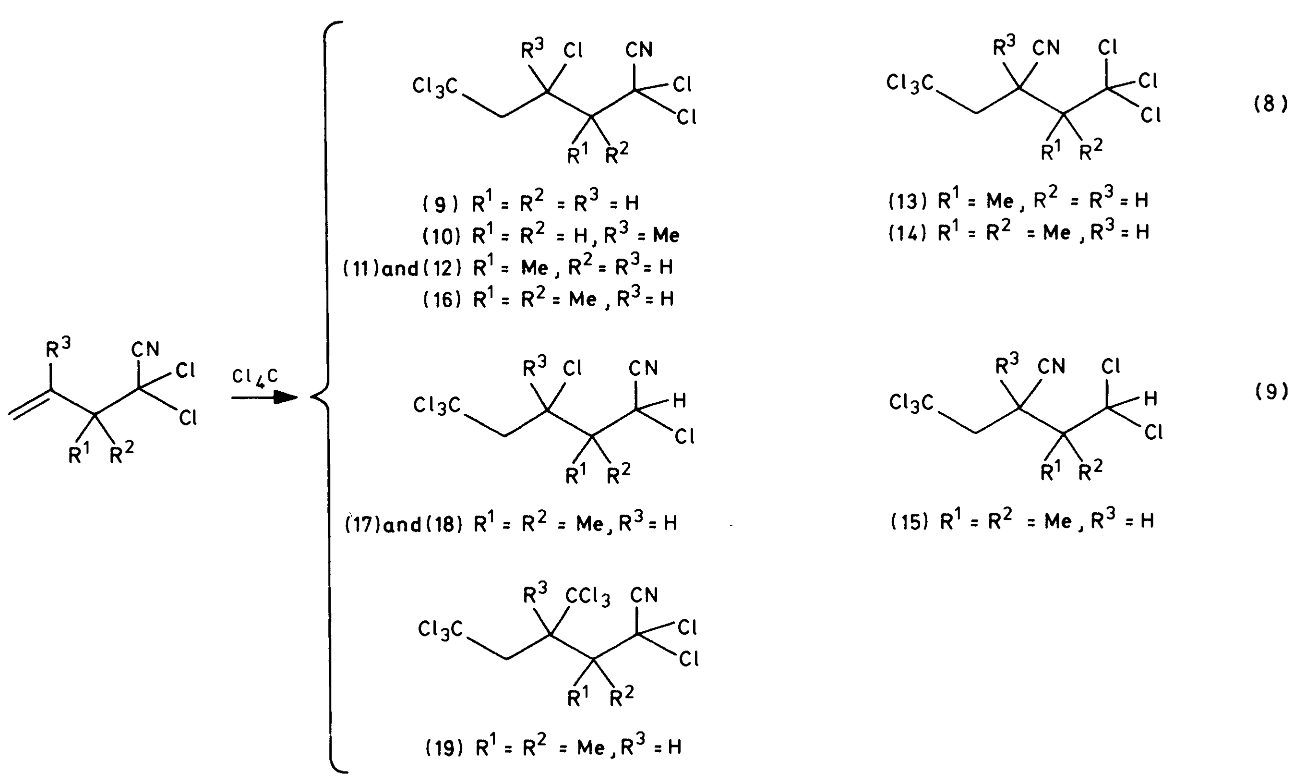
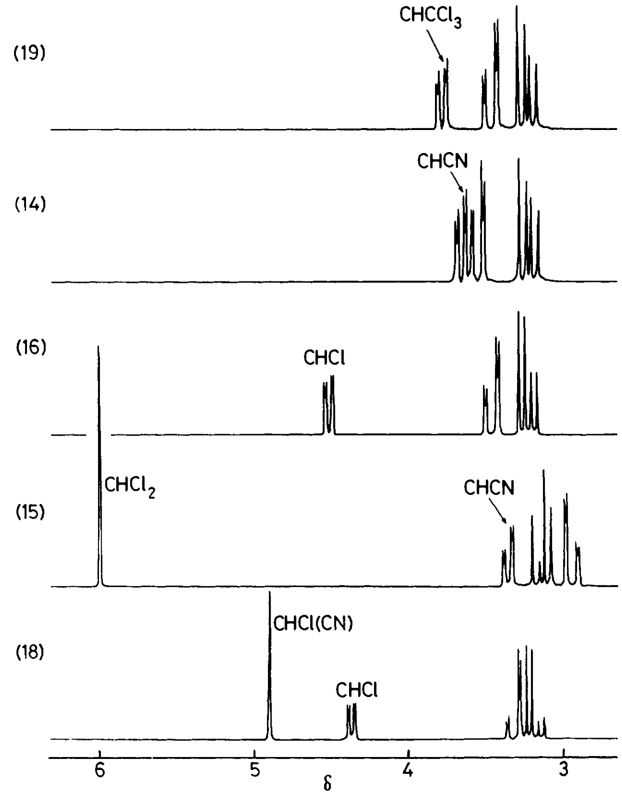
* The normal position of the CHCl resonance in CCl_4 adducts of terminal olefins is δ 4.2—4.3.

† The CH_2CCl_3 protons of the CCl_4 adducts of terminal olefins are diastereotopic, with a geminal coupling of 15—17 Hz and vicinal couplings of comparable magnitude in the range 4—8 Hz, at δ 4.2—4.3.



(8)

(9)



200 MHz ^1H N.m.r. spectra of compounds (19), (14), (16), (15), and (18). Methyl resonances are not shown

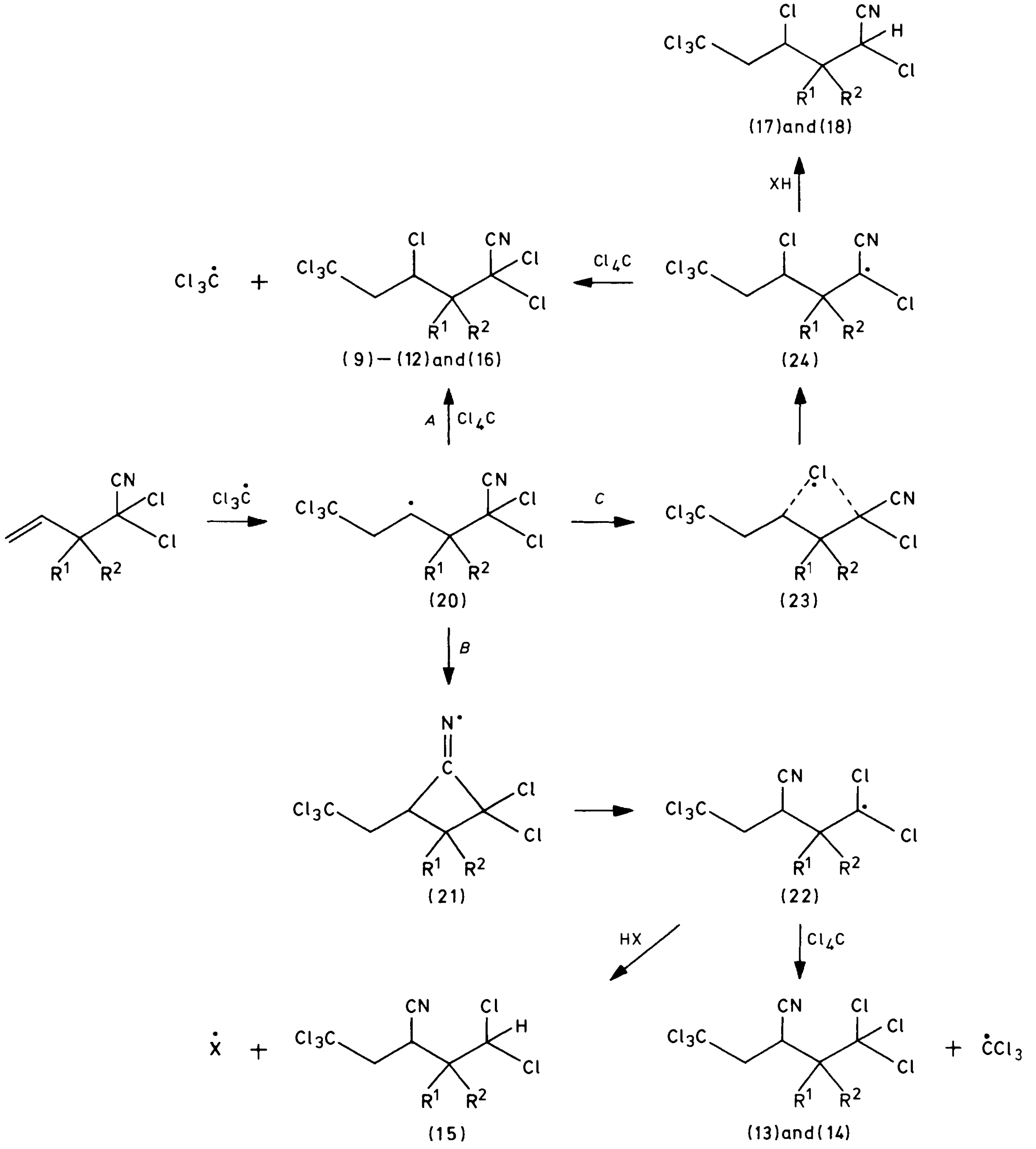
the terminal unsaturated carbon of the substrate, can react further in two main ways.

(1) It can abstract a chlorine atom from carbon tetrachloride to give the unrearranged, normal, addition product (9)—(12) or (16) *via* path *A*.

(2) It can rearrange to the dichloroalkyl radical (22) by migration of the cyano-group from C-2 to C-4 (path *B*) through a four-membered cyclic intermediate radical (21). The radical (22) can then abstract a chlorine atom from carbon tetrachloride to give the observed rearranged products (13) and (14), or it can gain a hydrogen atom from some other source to give the reduction product (15).

The formation of the reduction products (17) and (18) can be explained in two ways: *either* the substrate (8) is itself liable to chlorine abstraction by trichloromethyl radicals [equation (10)] and the substituted chloroacetonitrile radical (25) gains a hydrogen atom to give the reduced substrate (26) which can subsequently undergo a normal free radical addition of carbon tetrachloride, *or* the intermediate radical (20) rearranges *via* a chlorine-bridged transition state (23) to the chloroacetonitrile radical (24) (Scheme, path *C*) which subsequently reacts with carbon tetrachloride to provide another source of (9)—(12), or gains a hydrogen atom to give the diastereoisomeric reduction products (17) and (18). Whilst there is no evidence in the literature for a 1,3-migration of a halogen atom, the latter path seems the more likely, and we have previously suggested that a 1,3-migration of a bromine atom may account for the minor products of reaction of 2-bromopent-4-enonitrile with carbon tetrachloride.[8]

The rate of cyclisation of the unsubstituted 3-cyanopropyl radical would be expected to be appreciably less than that of the related 4-cyanobutyl radical for which a rate constant of $1.5 \times 10^3\ s^{-1}$ has been calculated for 278 K.[9] It is not surprising therefore that no rearrangement is observed with the 3-cyanopropyl radical (20), where $R^1 = R^2 = H$. However, the observation of slight rearrangement where R^1 *or* R^2 = Me and of substantial rearrangement where R^1 *and* R^2 = Me is indicative of a marked increase in the rate of cyclisation induced by such methyl substitution. This *gem*-dimethyl effect (also known as the Thorpe–Ingold effect) [10] has long been known to favour cyclisation to small carbocyclic rings. Whilst the

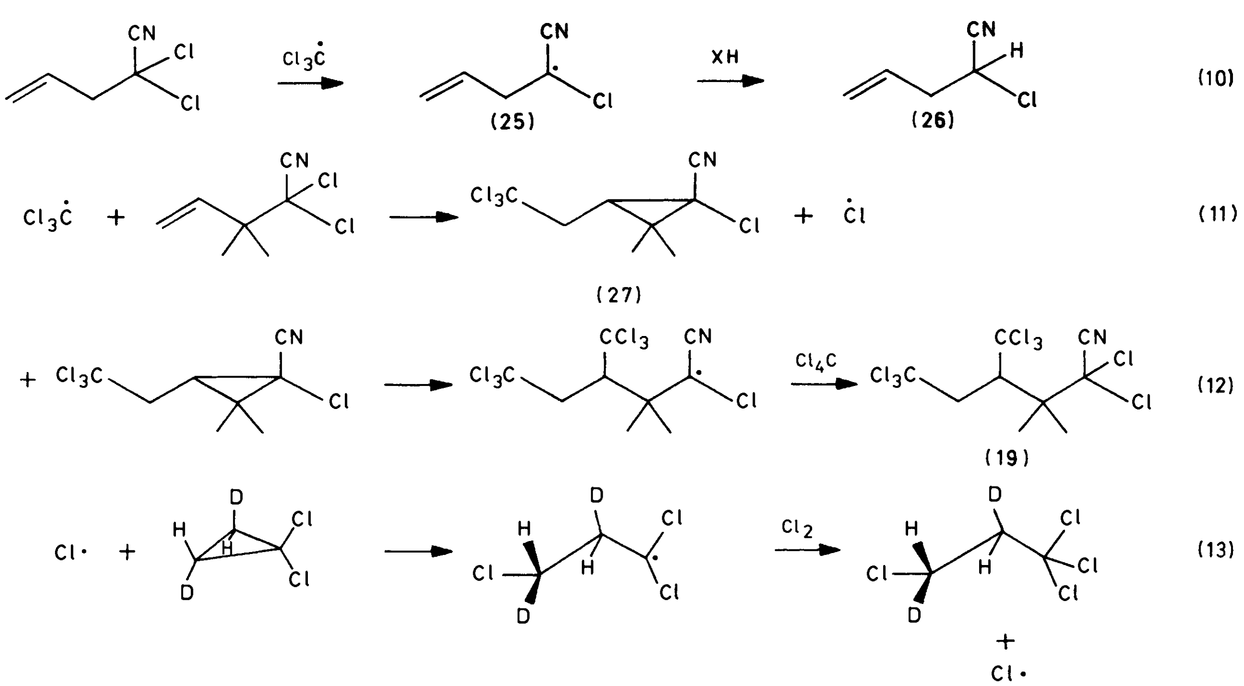


Scheme

1,3-migration of a chlorine atom (Scheme, path *C*) is by no means proven in this case, it is possible that the *gem*-dimethyl effect is also effective in its promotion.

The overall driving force in these rearrangements is clearly the much higher stability of the dichloroalkyl radicals (22) than of the initially formed secondary alkyl radical (20), but the part played by the metal catalyst, if any, in promoting the rearrangement of the cyano-group is not known. Stabilisation of the four-membered cyclic intermediate (21) by co-ordination to the metal cannot be ruled out especially as different products were obtained in the corresponding reaction of (8) with carbon tetrachloride in the presence of benzoyl peroxide. The butylamine–iron(III) chloride catalyst probably acts as an efficient hydrogen atom donor, but the source of hydrogen atoms in the presence of the other catalysts is obscure.

One of our aims in first studying the reactions of trichloromethyl radicals with the pentenonitriles was to prepare novel trichloroethylcyclopropanes, of interest as pyrethroid insecti-



cide precursors, by the intramolecular homolytic displacement shown in equation (11). We have previously detected such a reaction in the case of 2-bromo-3,3-dimethylpent-4-enonitrile,[8] but we were unable to detect any trichloroethylcyclopropanes in the products of the present reactions. However, the formation of the octachloro-compound (19) is indicative of the formation of a transient trichloroethylcyclopropane (27) which undergoes a bimolecular ring-opening on attack of trichloromethyl radicals at one of the cyclopropane carbon atoms [equation (12)]. A very similar bimolecular ring opening, by chlorine atoms, with inversion of configuration at carbon, has been investigated in detail elsewhere [equation (13)].[11]

Experimental

Allyl-, 2-methylallyl-, but-2-enyl-, and 3-methylbut-2-enylbis(dimethylglyoximato)pyridinecobalt(III) were prepared as described previously.[5] Trichloroacetonitrile, butylamine, methylene chloride, and carbon tetrachloride were commercial materials used without further purification. Copper(II) acetylacetonate was prepared by the method of Jones.[12]

Preparation of Pentenonitriles.—In a typical reaction, trichloroacetonitrile (8.5 g, 0.56 mol) was added to allylbis(dimethylglyoximato)pyridinecobalt(III) (20 g, 0.5 mmol) in methylene chloride (250 cm^3). The mixture was warmed to 40 °C and allowed to stand for 2 h. The volume was reduced *in vacuo* to *ca.* 80 cm^3 and the crude mixture was chromatographed on alumina, eluting the organic material with pentane–methylene chloride (10 : 1 v/v). The eluant was distilled to give *2,2-dichloropent-4-enonitrile* (5) (5.7 g, 0.33 mol, 66%), b.p. 66—68 °C at 40 mmHg (Found: C, 40.4; H, 3.3; Cl, 47.7; N, 9.6. C$_5$H$_5$Cl$_2$N requires C, 40.0; H, 3.3; Cl, 47.3; N, 9.3%), δ 3.05 (m, 3-H), 5.40 (d, *trans*-5-H), 5.50 (d, *cis*-5-H), 5.98 (m, 4-H); $J_{4,5}$ 10 and 18, $J_{3,4}$ 6 Hz. Similarly prepared were *2,2-dichloro-4-methylpent-4-enonitrile* (6), b.p. 82—86 °C at 40 mmHg (Found: C, 44.4; H, 4.75; Cl, 43.4; N, 8.8. C$_6$H$_7$Cl$_2$N requires C, 43.9; H, 4.3; Cl, 43.3; N, 8.5%), δ 2.00 (d, Me), 3.08 (s, CH$_2$), 5.21 and 5.30 (both s, :CH$_2$), *2,2-dichloro-3-methylpent-4-enonitrile* (7), b.p. 80—90 °C at 40 mmHg (Found: C, 43.9; H, 3.9; Cl, 42.7; N, 8.75. C$_6$H$_7$Cl$_2$N requires C, 43.9; H, 4.3; Cl, 43.3; N, 8.5%), δ 1.43 (d, Me), 3.08 (m, 3-H), 5.33 (d, *trans*-5-H), 5.42 (d, *cis*-5-H), 5.90 (m, 4-H); $J_{5,4}$ 10.3 and 18.0, $J_{3,4}$ 7.0, $J_{3,\mathrm{Me}}$ 6.5 Hz, and 2,2-dichloro-3,3-dimethylpent-4-enonitrile (8).[6]

Reactions with Carbon Tetrachloride.—In a typical reaction 2,2-dichloro-3,3-dimethylpent-4-enonitrile (8) (700 mg, 4 mmol) and copper(II) acetylacetonate (200 mg) in carbon tetrachloride (4 cm^3) were sealed in a glass tube and heated to 100 °C for 12 h. The crude product was chromatographed on silica gel (Mallinckrodt CC4) using methylene chloride–pentane (1 : 10 v/v) as eluant. The solvent was distilled off and a portion of the residue was analysed and separated by h.p.l.c. using 3 × 25 cm Partisil and methylene chloride–pentane (15 : 85 v/v) as eluant on a Waters ALC 100 instrument with an M60 pump and RI detection. The fractions eluted in the following order: (a) unchanged material; (b) 3,3-dimethyl-2,2,4,6,6,6-hexachlorohexanonitrile (16), *m/e* $(M + 1)^+$ 330, *332*, 334, 336; $(M - \mathrm{Cl})^+$ 294, *296*, 298, 300; $(M - 2\mathrm{Cl} - 1)^+$ 258, *260*, 262; $(M - 3\mathrm{Cl} - 2)^+$ *222*, 224, ^{1}H n.m.r. spectrum see Table; (c) A diastereoisomer of 3,3-dimethyl-2,4,6,6,6-pentachlorohexanonitrile (17), *m/e* $(M + 1)^+$ 296, *298*, 300, 302; $(M - \mathrm{Cl})^+$ 260, *262*, 264; $(M - 2\mathrm{Cl} - 1)^+$ *224*, *226*, 228; (d) another diastereoisomer of 3,3-dimethyl-2,4,6,6,6-pentachlorohexanonitrile (18), *m/e* $(M + 1)^+$ 296, *298*, 300, 302; $(M - \mathrm{Cl})^+$ 260, *262*, 264; $(M - 2\mathrm{Cl} - 1)^+$ *224*, *226*, 228; (e) 3-cyano-2,2-dimethyl-1,1,5,5,5-pentachloropentane (15), *m/e* $(M - \mathrm{Cl})^+$ 260, *262*, 264; $(M - 2\mathrm{Cl} - 1)^+$. *224*, *226*, 228; and (f) the main product, 3-cyano-2,2-dimethyl-1,1,1,5,5,5-hexachloropentane (14), *m/e* $(M + 1)^+$ 330, *332*, 334, 336; $(M - \mathrm{Cl})^+$ 294, *296*, 298, 300; $(M - 2\mathrm{Cl} - 3)^+$ 258, *260*, 262; $(M - 3\mathrm{Cl} - 4)^+$ *222*, *224*. A variety of other minor products was also formed, but in too small a yield for identification; complete separation from the above products was not achieved in every case.

The same products, but in different proportions, were formed in the reaction of (8) (0.2 g, 1.1 mmol) with iron(III) chloride (18 mg, 0.1 mmol) and butylamine (14 mg, 0.2 mmol) in carbon tetrachloride (8 cm^3) at 100 °C for 24 h. The main product was compound (14) but the proportions of (15), (17), and (18) were higher than in the previous experiment.

When the same reaction was carried out with compound (8) (0.2 g, 1.1 mmol) and benzoyl peroxide (0.1 g, 0.4 mmol) in carbon tetrachloride (2 cm^3) at 101 °C for 45 h, the two main fractions, separated by h.p.l.c., were compound (15) and 3,3-*dimethyl*-2,2,6,6,6-*pentachloro*-4-*trichloromethylhexanonitrile* (19) [Found: $(M + 1)^+$; 411.8413, 413.8314, 415.8363, 417.8165. $C_9H_9{}^{35}Cl_n{}^{37}Cl_{(8-n)}N$ requires 411.8504, 413.8335, 415.8463, 417.8098], ^{1}H n.m.r. spectrum in Table.

A similar reaction of 2,2-dichloro-3-methylpent-4-enonitrile (7) with carbon tetrachloride in the presence of copper(II) acetylacetonate gave, on separation by h.p.l.c., (a) unchanged (7); (b) one diastereoisomer of 3-methyl-2,2,4,6,6,6-hexachlorohexanonitrile (11), *m/e* $(M + 1)^+$ 316, *318*, 320, 322; $(M - Cl)^+$ 280, *282*, 284, 286; $(M - 2Cl - 1)^+$ 244, *246*, 248, 250; (c) the other diastereoisomer of 3-methyl-2,2,4,6,6,6-hexachlorohexanonitrile (12), *m/e* $(M + 1)^+$ 316, *318*, 320, 322; $(M - Cl)^+$ 280, *282*, 284, 286; $(M - 2Cl - 1)$ *244*, *246*, 248, 250; and (d) 3-cyano-2-methyl-1,1,1,5,5,5-hexachloropentane (13), *m/e* $(M + 1)^+$ 316, *318*, 320, 322; $(M - Cl)^+$ 280, *282*, 284, 286; $(M - 2Cl - 1)^+$ 244, *246*, 248, 250.

A similar reaction of 4-methyl-2,2-dichloropent-4-enonitrile (6) with carbon tetrachloride in the presence of copper(II) acetylacetonate gave (a) unchanged (6); (b) 4-methyl-2,2,4,6,6,6-hexachlorohexanonitrile, *m/e* $(M + 1)^+$ 316, *318*, 320, 322, 324; $(M - Cl)^+$ 280, *282*, 284, 286; $(M - 2Cl - 1)^+$ 244, *246*, 248; and (c) unidentified products containing olefinic proton resonances at δ 5.0 and 5.12.

A similar reaction of 2,2-dichloropent-4-enonitrile (5) with carbon tetrachloride in the presence of copper(II) acetylacetonate gave (a) unchanged (5) and (b) 1,1,3,6,6,6-hexachlorohexanonitrile (9), *m/e* $(M + 1)^+$ 302, *304*, 306, 308; $(M - Cl)^+$ 266, *268*, 270, 272; $(M - 2Cl - 1)^+$ 230, *232*, 234, 236; $(M - 3Cl - 1)^+$ *195*, *197*, 199.

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