

938. *The Insertion of Dichlorocarbene in Ethers.*

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α -Dichloromethyl derivatives of ethers have been obtained in modest yields by generating dichlorocarbene in the presence of excess of ether. For allylic ethers, insertion did not compete effectively with the normal addition reaction except in the apparently anomalous case of 2,5-dihydrofuran (III).

OVER twenty years ago, Meerwein and his co-workers¹ irradiated an ethereal solution of diazomethane and obtained a mixture of n-propyl and isopropyl ethyl ethers; they thus showed that methylene could be inserted in carbon-hydrogen bonds. Since then,² the generality and comparative lack of specificity of the methylene insertion reaction have been clearly demonstrated. Examples of the insertion of substituted carbenes, notably ethoxy-carbonylcarbene, have been in the literature for many years³ but the first reports of the insertion of the much-studied dichlorocarbene appeared only quite recently.

Parham and Koncos⁴ treated 2*H*-1-benzothiopyran (I; R = H) with dichlorocarbene and obtained (I; R = CHCl₂), the isomeric 4-dichloromethyl-4*H*-1-benzothiopyran (II; R = CHCl₂), and an unidentified di-adduct. None of the expected tricyclic monoadduct

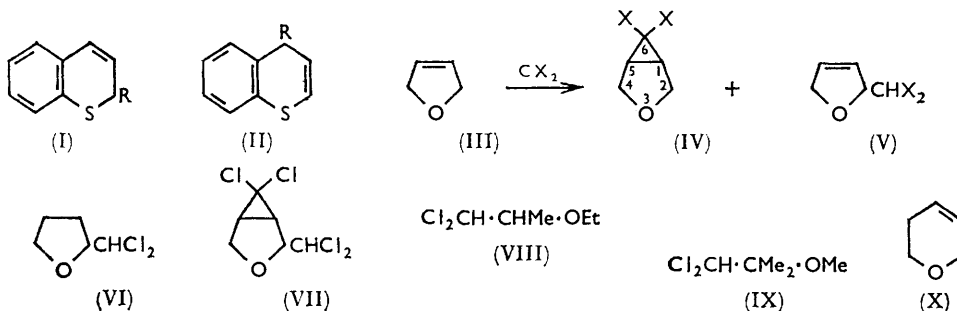
¹ Meerwein, Rathjen, and Werner, *Ber.*, 1942, **75**, 1610.

² Kirmse, *Angew. Chem.*, 1961, **73**, 161.

³ Buchner and Schulze, *Annalen*, 1910, **377**, 259.

⁴ Parham and Koncos, *J. Amer. Chem. Soc.*, 1961, **83**, 4034.

was found in the products. However, the chromene analogues⁵ of (I; R = H) and (II; R = H), and 4*H*-1-benzothiopyran itself⁴ all gave high yields of tricyclic adducts and no insertion product under similar conditions. Fields⁶ then reported that dichlorocarbene could be inserted in benzylic carbon-hydrogen bonds. This appeared to be a general reaction, but satisfactory yields of products were obtained only when dichlorocarbene was generated by the thermal decomposition of sodium trichloroacetate⁷ and not by the more usual low temperature methods. Very recently,⁸ the synthetic potential of this reaction has been increased by the use of phenyl(bromodichloromethyl)mercury as the dichlorocarbene source.



We have treated 2,5-dihydrofuran (III) with a slight excess of dichlorocarbene, generated from ethyl trichloroacetate and sodium methoxide,⁹ and obtained a 62% yield of a material with the composition of the expected adduct, 6,6-dichloro-3-oxabicyclo[3,1,0]hexane (IV; X = Cl), but which was shown by gas chromatography (g.l.c.) to be a 2 : 1-mixture of two compounds. The material was fractionated by preparative g.l.c. and the major, less volatile component shown by nuclear magnetic resonance (n.m.r.) spectroscopy to be the expected bicyclic adduct (IV; X = Cl). The other component was shown by n.m.r. spectroscopy to contain two vinyl protons, and was allocated the structure (V; X = Cl). This finding was confirmed chemically when the latter was reduced¹⁰ to 2-dichloromethyltetrahydrofuran (VI); it also formed a saturated adduct (VII) with dichlorocarbene.

An accurate g.l.c. analysis of the original mixture became possible after the isolation of the pure constituents (IV; X = Cl) and (V; X = Cl); it indicated 35% of insertion compound and 65% of bicyclic adduct. When dichlorocarbene was generated by the pyrolysis of sodium trichloroacetate,⁷ the corresponding mixture contained 47% of insertion compound (V; X = Cl) and 53% of adduct (IV; X = Cl), but the total yield was only 34%. Thus the competition of the insertion reaction became more pronounced at a higher temperature. A preliminary account of these findings has already been published.¹¹

We then examined the reaction between 2,5-dihydrofuran (III) and dibromocarbene, generated at *ca.* 0° from bromoform and potassium *t*-butoxide under the conditions described for 6,6-dibromobicyclo[3,1,0]hexane.¹² Surprisingly, only 8% of a 2 : 1-mixture of bicyclic adduct (IV; X = Br) and insertion compound (V; X = Br) was obtained.¹¹ The two components were separated by preparative g.l.c. and identified by n.m.r. spectroscopy. This appears to be the first reported case of an insertion reaction of dibromocarbene.

The mechanism of methylene insertion in allylic carbon-hydrogen does not¹³ proceed

⁵ Parham and Huestis, *J. Amer. Chem. Soc.*, 1962, **84**, 813.

⁶ Fields, *J. Amer. Chem. Soc.*, 1962, **84**, 1744.

⁷ Wagner, *Proc. Chem. Soc.*, 1959, 229.

⁸ Seyferth and Burlitch, *J. Amer. Chem. Soc.*, 1963, **85**, 2667.

⁹ Parham and Schweizer, *J. Org. Chem.*, 1959, **24**, 1733.

¹⁰ Dewey and van Tamelen, *J. Amer. Chem. Soc.*, 1961, **83**, 3729.

¹¹ Anderson and Reese, *Chem. and Ind.*, 1963, 575.

¹² Sonnenberg and Winstein, *J. Org. Chem.*, 1962, **27**, 748.

¹³ Doering and Prinzbach, *Tetrahedron*, 1959, **6**, 24.

via an actual carbonium-ion intermediate. However, it is helpful to consider a hypothetical transition state,¹⁴ resulting from the initial abstraction of a hydride ion by the electrophilic carbene, to account for preferential insertion at the centre where the most stable possible carbonium ion can be generated. This discrimination is not shown by methylene itself, but the known insertion reactions of dichlorocarbene occur at centres where hydride-ion abstraction would lead to resonance-stabilized carbonium ions. With 2,5-dihydrofuran (III), a carbonium ion generated at C-2 could be stabilized both by the double bond and by the unshared electrons of the heteroatom. Although allylic insertion would correspond with benzylic insertion, it has not been observed in the numerous reactions of dihalogenocarbenes with simple olefins. Presumably for dihalogenocarbenes, in contrast to methylene, insertion is considerably slower than normal addition. We thus observed that dichlorocarbene reacted with allylbenzene to give only 1,1-dichloro-2-benzylcyclopropane. No competitive insertion in the methylene group, which was both benzylic and allylic, was detected. Therefore it seemed likely that the apparently anomalous behaviour of 2,5-dihydrofuran might be due to its ether function.

We therefore treated tetrahydrofuran with dichlorocarbene, generated from ethyl trichloroacetate,⁹ and obtained the product of α -insertion (VI) but only in 2.5% yield. This compound was identical with that obtained by di-imide reduction¹⁰ of the insertion product (V; X = Cl), obtained from 2,5-dihydrofuran (III). No β -insertion was observed but this was not unexpected as, mechanistic considerations apart, even methylene inserted preferentially in the α -position of tetrahydrofuran.^{1,15} A marginally better yield (3.7%) of (VI) was obtained by the decomposition of sodium trichloroacetate⁷ in boiling tetrahydrofuran. However, the possibility that the insertion reaction of dichlorocarbene in α -carbon-hydrogen bonds of ethers might be of synthetic value was considered more seriously when a 20% yield (based on dichlorocarbene) of 1,1-dichloro-2-ethoxypropane (VIII) was obtained from addition of ethyl trichloroacetate to a cooled suspension of sodium methoxide in excess of diethyl ether. The structure allocated to the product followed from its n.m.r. spectrum, which exhibited a sharp doublet ($J = 4$ c./sec.) with a chemical shift of $\tau 4.3$, characteristic in our experience of a dichloromethyl proton, resulting from the insertion of dichlorocarbene in a methylene group.

In the same way, a 9% yield of 2-dichloromethyl-2-methoxypropane (IX) was obtained from the isomeric isopropyl methyl ether. The sharp singlet at $\tau 4.35$ and other features of the n.m.r. spectrum left no doubt that the main product was (IX) and not the other possible α -insertion product, 2,2-dichloroethyl isopropyl ether, which was perhaps the trace of impurity detected by gas chromatography in the crude products. It is noteworthy that two methyl groups should control the course of the insertion reaction so effectively when a statistical factor of 3 : 1 carbon-hydrogen bonds and possible steric considerations would favour the other product.

When it became apparent that the insertion of dichlorocarbene in ethers was a general reaction, the behaviour of 2,5-dihydrofuran (III) seemed less anomalous. However, when its homologue 5,6-dihydro-2*H*-pyran¹⁶ (X) was treated with one equivalent of dichlorocarbene, generated from ethyl trichloroacetate, the product was almost entirely the bicyclic adduct. Gas chromatographic analysis indicated a slight (*ca.* 2%) impurity, and n.m.r. spectroscopy supported the presence of a small amount of insertion product. Similarly, allyl ethyl ether was converted into 1,1-dichloro-2-ethoxymethylcyclopropane, contaminated with a small amount of an impurity which was probably insertion product.

It seems likely that competitive insertion will generally accompany cycloaddition in reactions between dichlorocarbene and allylic ethers, but only to a small extent. It seems that the behaviour of 2,5-dihydrofuran (III) is exceptional, although the difference between insertion : cyclo-addition ratios of approximately 1 : 2 and 1 : 50 could be brought

¹⁴ Doering and Knox, *J. Amer. Chem. Soc.*, 1961, **83**, 1989.

¹⁵ Doering, Knox, and Jones, *J. Org. Chem.*, 1959, **24**, 136.

¹⁶ Olsen, *Acta Chem. Scand.*, 1951, **5**, 1168.

about by relatively small changes in the activation energies of the reactions concerned. However, 2,5-dihydrofuran may owe its unusual properties to the ether oxygen atom, which can exert a negative inductive effect on the double-bond, thus decreasing its nucleophilic character, and at the same time can also activate the α -carbon-hydrogen bonds with respect to the insertion reaction.

EXPERIMENTAL

Nuclear magnetic resonance (n.m.r.) spectra of 10% solutions in carbon tetrachloride were measured by a Perkin-Elmer 40 Mc. n.m.r. spectrometer with tetramethylsilane as an internal standard. Gas chromatography (g.l.c.) was conducted on silicone oil (10 and 20% on Celite) columns.

Reaction of 2,5-Dihydrofuran (III) with Dichlorocarbene.—(a) To an ice-cold, stirred suspension of freshly prepared, finely divided sodium methoxide (16.8 g.) in a solution of 2,5-dihydrofuran (18.8 g., freshly distilled from lithium aluminium hydride) in dry pentane (200 c.c.), ethyl trichloroacetate (55 g.) was added rapidly. During the addition the pentane boiled vigorously. After the cooled mixture had been stirred under dry nitrogen for 3 hr., water (50 c.c.) was added, the organic layer separated, and the aqueous layer extracted with petroleum (b. p. 60–80°; 3 \times 50 c.c.). The combined organic layers were dried (Na_2SO_4), the solvent removed by evaporation, and the residue distilled to yield a fraction (25.6 g., 62%), b. p. 70–78°/20 mm. (Found: C, 39.3; H, 3.9. Calc. for $\text{C}_5\text{H}_6\text{Cl}_2\text{O}$: C, 39.25; H, 3.9%). G.l.c. analysis indicated the presence of two components, which were separated by preparative g.l.c.

The more volatile minor constituent, 2-dichloromethyl-2,5-dihydrofuran (V; X = Cl) had b. p. 72–74°/19 mm., n_D^{19} 1.4933 (Found: C, 39.1; H, 3.9. $\text{C}_5\text{H}_6\text{Cl}_2\text{O}$ requires: C, 39.25; H, 3.9%); τ 3.9, a multiplet, weight 2, assigned to C-3 and C-4 protons; τ 4.26, a doublet, weight 1, assigned to dichloromethyl proton; τ 4.85, a multiplet, weight 1, assigned to C-2 proton; τ 5.24, a multiplet, weight 2, assigned to C-5 protons. The less volatile major constituent, 6,6-dichloro-3-oxabicyclo[3,1,0]hexane (IV; X = Cl) had b. p. 76–78°/21 mm., n_D^{22} 1.4980 (Found: C, 39.3; H, 4.3; Cl, 45.9. $\text{C}_5\text{H}_6\text{Cl}_2\text{O}$ requires C, 39.25; H, 3.9; Cl, 46.4%); τ 6.0, a multiplet, weight 4, assigned to C-2 and C-5 protons; τ 7.49, a multiplet, weight 2, assigned to C-3 and C-4 protons.

The original mixture was estimated by g.l.c. to contain (IV; X = Cl) (65%) and (V; X = Cl) (35%) by comparison with standard solutions of the pure isomers.

(b) Sodium trichloroacetate (1.325 g.), 2,5-dihydrofuran (0.5 g.), and dioxan (5.5 c.c.) were heated in a sealed tube at 110° for 4 hr. G.l.c. indicated a total yield of 34% monoadduct, composed of insertion compound (V; X = Cl) (47%) and cycloadduct (IV; X = Cl) (53%).

Reduction of 2-Dichloromethyl-2,5-dihydrofuran (V; X = Cl) with Toluene-p-sulphonylhydrazine.—A solution of 2-dichloromethyl-2,5-dihydrofuran (V; X = Cl) (3.2 g.) and toluene-p-sulphonylhydrazine (14 g.) in diethylene glycol diethyl ether (60 c.c.) was heated under reflux for 25 min. Water (200 c.c.) was added and the solution was extracted with petroleum (b. p. 60–80°; 2 \times 100 c.c.). The combined organic extracts were extracted with water (15 \times 200 c.c.), 10% aqueous sodium hydroxide (2 \times 200 c.c.), and water (2 \times 200 c.c.), then dried (Na_2SO_4) and evaporated under reduced pressure to yield a residue, which distilled to give 2-dichloromethyltetrahydrofuran (VI) (29%), b. p. 70–71°/18 mm., n_D^{21} 1.4764 (Found: C, 39.0; H, 5.4; Cl, 45.8. $\text{C}_5\text{H}_6\text{Cl}_2\text{O}$ requires: C, 38.7; H, 5.2; Cl, 45.8%); τ 4.26, a doublet, weight 1, assigned to dichloromethyl proton; τ 6.12, a multiplet, weight 3, assigned to C-2 and C-5 protons; τ 8.0, a multiplet, weight 4, assigned to C-3 and C-4 protons.

Reaction of 2-Dichloromethyl-2,5-dihydrofuran (V; X = Cl) with Dichlorocarbene.—To a cold stirred suspension of sodium methoxide (3.2 g.) in a solution of 2-dichloromethyl-2,5-dihydrofuran {8.9 g. of material containing more than 50% of (V; X = Cl), contaminated with 6,6-dichloro-3-oxabicyclo[3,1,0]hexane (IV; X = Cl)} in dry pentane (100 c.c.), ethyl trichloroacetate (11.2 g.) was added rapidly. The experiment was conducted and worked up as for 2,5-dihydrofuran. G.l.c. of the crude product indicated that all (V; X = Cl) had been consumed. Distillation gave a main fraction of (IV; X = Cl), b. p. 68–69°/14 mm., and a less volatile, yellow-coloured fraction of 6,6-dichloro-2-dichloromethyl-3-oxabicyclo[3,1,0]hexane (VII) (0.93 g.), b. p. 68–70°/2 mm. (Found: C, 30.45; H, 2.75. $\text{C}_6\text{H}_6\text{Cl}_4\text{O}$ requires: C, 30.5; H, 2.6%); τ 4.25, a doublet, weight 1, assigned to dichloromethyl proton; τ 5.70, a double-doublet,

weight 3, assigned to C-2 and C-4 protons; τ 7.35, a multiplet, weight 2, assigned to C-1 and C-5 protons.

Reaction of 2,5-Dihydrofuran (III) with Dibromocarbene.—The procedure used by Sonnenberg and Winstein¹² for the reaction between cyclopentene and dibromocarbene was adopted except that 2,5-dihydrofuran (21.5 g., 0.30 mole) was used in place of the same molar proportion of cyclopentene. Distillation of the products yielded a liquid (6 g., 8%), b. p. 80–90°/1.5 mm., which was shown by g.l.c. to contain two components, in the approximate proportion of 1 : 2, which were separated by preparative g.l.c.

The more volatile, minor component was 2-dibromomethyl-2,5-dihydrofuran (V; X = Br), having b.p. 83–84°/1.5 mm. (Found: C, 25.0; H, 2.5. C₅H₆Br₂O requires C, 24.8; H, 2.5%); τ 3.8, a multiplet, weight 1, assigned to C-3 proton; τ 3.9, a multiplet, weight 1, assigned to C-4 proton; τ 4.35, a doublet, weight 1, assigned to dibromomethyl proton; τ 4.9, a multiplet, weight 1, assigned to C-2 proton; τ 5.25, a multiplet, weight 2, assigned to C-5 protons.

The less volatile component, 6,6-dibromo-3-oxabicyclo[3,1,0]hexane (IV; X = Br) had b. p. 88–90°/1.5 mm. (Found: C, 25.1; H, 2.5. C₅H₆Br₂O requires C, 24.8; H, 2.5%); τ 6.1, a multiplet, weight 4, assigned to C-2 and C-5 protons; τ 7.5, a multiplet, weight 2, assigned to C-3 and C-4 protons.

Reaction of Allylbenzene with Dichlorocarbene.—To an ice-cold, stirred suspension of sodium methoxide (5.4 g.) in a solution of allylbenzene (11.8 g.) in dry pentane (100 c.c.), ethyl trichloroacetate (19.1 g.) was added rapidly. After 30 min., sodium chloride was filtered off, and the filtrate concentrated to remove solvent and then distilled. The first fraction consisted of allylbenzene (4.3 g.), b. p. 22–24°/0.4 mm., and then 2-benzyl-1,1-dichlorocyclopropane (3 g., 30%), b. p. 68–72°/0.4 mm., was collected (Found: C, 59.7; H, 5.1; Cl, 33.8. C₁₀H₁₀Cl₂ requires C, 59.7; H, 5.0; Cl, 35.2%). G.l.c. indicated a single component; τ 2.8, a singlet, weight 5, assigned to aromatic protons; τ 7.15, a quartet, weight 2, assigned to benzylic protons; τ 8.4, a multiplet, weight 3, assigned to cyclopropyl protons. No signal was obtained by amplification of the region between τ 4.0 and 4.5.

Reaction of Tetrahydrofuran with Dichlorocarbene.—(a) To an ice-cold, stirred suspension of sodium methoxide (8.4 g.) in dry tetrahydrofuran (100 c.c.), ethyl trichloroacetate (37.5 g.) was added dropwise during 30 min. After a further 2 hr., sodium chloride was filtered off and the excess of tetrahydrofuran evaporated under reduced pressure. The residue was distilled (bath temp. 100°) and 2-dichloromethyltetrahydrofuran (VI) (0.7 g., 2.5%), b. p. 64–65°/14 mm. (Found: C, 38.3; H, 5.2. Calc. for C₅H₈Cl₂O: C, 38.7; H, 5.2%), was obtained. The n.m.r. spectrum was identical with that of the compound obtained by the reaction of 2-dichloromethyl-2,5-dihydrofuran (V; X = Cl) (see above).

(b) A suspension of sodium trichloroacetate (43 g.) in dry tetrahydrofuran (100 c.c.) was heated under reflux for 10 hr. The mixture was cooled and filtered, and the filtrate concentrated under reduced pressure to a residue (6 g.) which yielded 2-dichloromethyltetrahydrofuran (VI) (1.1 g., 3.7%), b. p. 84–87°/23 mm. The n.m.r. spectrum confirmed the assigned structure.

Reaction of Diethyl Ether with Dichlorocarbene.—To a cooled, stirred suspension of sodium methoxide (8.4 g.) in diethyl ether (200 c.c., distilled from lithium aluminium hydride), ethyl trichloroacetate (27.5 g.) was added rapidly. After 2 hr., the products were worked up (as for tetrahydrofuran, above). On distillation, the crude products yielded a homogeneous fraction (gas chromatographically) of 1,1-dichloro-2-ethoxypropane (VIII) (4.5 g., 20% based on dichlorocarbene), b. p. 42–43°/14 mm. (Found: C, 38.5; H, 6.2; Cl, 45.4. C₅H₁₀Cl₂O requires: C, 38.3; H, 6.4; Cl, 45.2%); τ 4.3, a doublet ($J = 4$ c./sec.), weight 1, assigned to dichloromethyl proton; τ 6.4, a multiplet, weight 3, assigned to protons attached to carbon atoms α to the ether function; τ 8.8, a multiplet (probably a superposed doublet and triplet), weight 6, assigned to methyl protons.

Reaction of Isopropyl Methyl Ether with Dichlorocarbene.—The experimental conditions were the same as above except that isopropyl methyl ether (100 c.c., distilled from lithium aluminium hydride) took the place of diethyl ether (200 c.c.). G.l.c. of the crude products indicated a principal component and a trace (ca. 1%) of a slightly more volatile material. Distillation gave 2-dichloromethyl-2-methoxypropane (IX) (2 g., 9%), b. p. 60–61°/24 mm. (Found: C, 38.2; H, 6.8; Cl, 46.1. C₅H₁₀Cl₂O requires: C, 38.2; H, 6.4; Cl, 45.2%); τ 4.35, a singlet, weight 1, assigned to dichloromethyl proton; τ 6.75, a singlet, weight 3, assigned to methoxyl protons; τ 8.7, a singlet, weight 6, assigned to C-methyl protons.

Reaction of 5,6-Dihydro-2H-pyran (X) with Dichlorocarbene.—To a cooled, stirred suspension

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of sodium methoxide (4.3 g.) in a solution of 5,6-dihydro-2*H*-pyran¹⁶ (6.6 g.) in dry pentane (100 c.c.), ethyl trichloroacetate (13.8 g.) was added rapidly. After 3 hours' stirring under nitrogen, the products were worked up as above [for 2,5-dihydrofuran (III)]. Distillation of the crude products gave a fraction (2 g., 25%), b. p. 63—66°/3 mm. (bath temp. 115°), of slightly impure 7,7-dichloro-3-oxabicyclo[4,1,0]heptane (Found: C, 42.7; H, 5.1; Cl, 42.5. Calc. for C₆H₈Cl₂O: C, 43.1; H, 4.8; Cl, 42.5%). G.l.c. indicated two components in the proportion of *ca.* 50 : 1, the minor component being the more volatile; τ 6.1, a doublet, weight 2, assigned to C-2 protons; τ 6.65, a multiplet, weight 2, assigned to C-4 protons; τ 8.15, a multiplet, weight 4, assigned to C-1, C-5, and C-6 protons. Amplification of the region τ 4.0—4.5 indicated a multiplet (τ 4.03) and a doublet (τ 4.27): this suggested an impurity containing olefinic and dichloromethyl protons.

Reaction of Allyl Ethyl Ether with Dichlorocarbene.—The experiment was conducted as above [for 5,6-dihydro-2*H*-pyran (X)] with sodium methoxide (8.4 g.), allyl ethyl ether (8.6 g.; distilled from lithium aluminium hydride), dry pentane (100 c.c.), and ethyl trichloroacetate (27.5 g.). Distillation of the crude products yielded a fraction (2.13 g., 12.7%), b. p. 64—66°/14 mm., which was found by g.l.c. to contain one principal and three minor components. The principal component, 1,1-dichloro-2-ethoxymethylcyclopropane (Found: C, 42.8; H, 5.9; Cl, 42.0. C₆H₁₀Cl₂O requires: C, 42.6; H, 6.0; Cl, 41.9%) was isolated by preparative g.l.c.; τ 6.45, a multiplet, weight 4, assigned to methylene protons α to ether oxygen; τ 8.3, a multiplet, weight 1, assigned to C-2 proton; τ 8.8, a multiplet, weight 5, assigned to remaining protons. The n.m.r. spectrum of the original fraction showed a weak signal in the region τ 4.2—4.5, which could indicate olefinic and dichloromethyl protons.

Two of us (J. C. A. and D. G. L.) thank the D.S.I.R. for the award of Research Studentships. One of us (D. G. L.) also thanks King's College, Cambridge, for the award of a Senior Studentship.

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[Received, January 16th, 1964.]