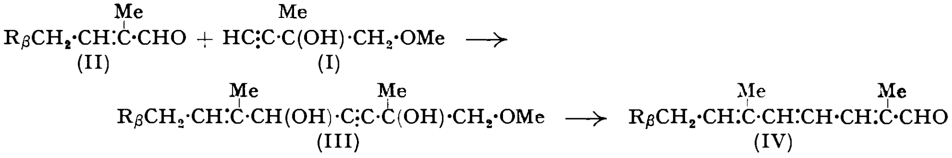
435. *Studies in the Polyene Series. Part XLIX.* Acetylenic Alcohols from Methoxyacetone, and their Conversion into Unsaturated Aldehydes.*

By Rashid Ahmad and B. C. L. Weedon.

A modification of the Inhoffen method has been used to prepare a number of $\alpha\beta$-unsaturated α-methyl-aldehydes.

A new method for the preparation of $\alpha\beta$-unsaturated α-methyl-aldehydes, valuable intermediates for polyene syntheses, was developed by Inhoffen and his collaborators who condensed 1-methoxy-2-methylbut-3-yn-2-ol (I) with the C_{14} aldehyde (II) to obtain a glycol (III) which, by anionotropic rearrangement, semihydrogenation of the triple bond, and dehydration, was converted into the C_{19} aldehyde (IV) (Inhoffen, Bohlmann, Bartram,



$$\underset{\text{(II)}}{R_\beta CH_2{\cdot}CH{:}\overset{Me}{C}{\cdot}CHO} + \underset{\text{(I)}}{HC{\vdots}C{\cdot}\overset{Me}{C}(OH){\cdot}CH_2{\cdot}OMe} \longrightarrow$$

$$\underset{\text{(III)}}{R_\beta CH_2{\cdot}CH{:}\overset{Me}{C}{\cdot}CH(OH){\cdot}C{\vdots}C{\cdot}\overset{Me}{C}(OH){\cdot}CH_2{\cdot}OMe} \longrightarrow \underset{\text{(IV)}}{R_\beta CH_2{\cdot}CH{:}\overset{Me}{C}{\cdot}CH{:}CH{\cdot}CH{:}\overset{Me}{C}{\cdot}CHO}$$

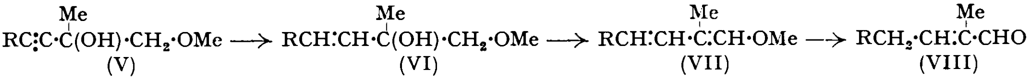
R_β = 2 : 6 : 6-trimethyl*cyclo*hexenyl.

---

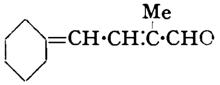
* Part XLVIII, *J.*, 1953, 1584.

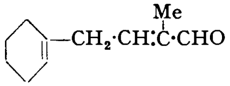
Rummert, and Pommer, *Annalen*, 1950, **570**, 54; Inhoffen and Leibner, *ibid.*, 1951, **575**, 105). A similar route has now been used for the preparation of other unsaturated aldehydes from typical, monosubstituted, acetylenes.

Reaction of methoxyacetone with the Grignard complexes of hex-1-yne, phenylacetylene, and 1-ethynyl*cyclo*hexene gave the acetylenic alcohols (V; R = Bu^n, Ph, and *cyclo*hexenyl) (*ca.* 70%). Partial reduction of the triple bond was accomplished, in good yield, either by catalytic hydrogenation (V; R = Bu^n and Ph), or by treatment with lithium aluminium hydride (V; R = Ph and *cyclo*hexenyl) (cf. Chanley and Sobotka, *J. Amer. Chem. Soc.*, 1949, **71**, 4140). Dehydration of the resulting ethylenic alcohols (VI), and



$$\underset{\text{(V)}}{\text{RC}{\vdots}\text{C}\cdot\overset{\text{Me}}{\text{C}}(\text{OH})\cdot\text{CH}_2\cdot\text{OMe}} \longrightarrow \underset{\text{(VI)}}{\text{RCH:CH}\cdot\overset{\text{Me}}{\text{C}}(\text{OH})\cdot\text{CH}_2\cdot\text{OMe}} \longrightarrow \underset{\text{(VII)}}{\text{RCH:CH}\cdot\overset{\text{Me}}{\text{C}}\text{:CH}\cdot\text{OMe}} \longrightarrow \underset{\text{(VIII)}}{\text{RCH}_2\cdot\text{CH:}\overset{\text{Me}}{\text{C}}\cdot\text{CHO}}$$

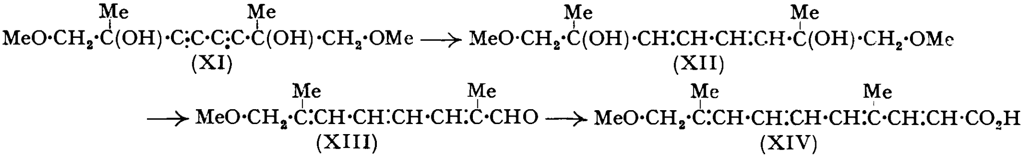
(IX) 

 (X)

subsequent hydrolysis of the crude ethers (VII), led to the aldehydes (VIII; R = Bu^n and Ph) and (IX), respectively. That these were αβ-unsaturated was shown by the ultra-violet light absorption properties of their crystalline derivatives. The aldehyde (VIII; R = Ph) has been prepared previously by a Darzens reaction with benzylideneacetone (Linnell and Shen, *J. Pharm. Pharmacol.*, 1949, **1**, 971); the m. p.s of the derivatives of the two specimens are in good agreement.

The spectrum (see Table) of the *cyclo*hexylidenealdehyde exhibited, in addition to the maxima characteristic of a conjugated diene-aldehyde, a band of low intensity at 2270 Å. This suggests that the product (IX) also contained some (*ca.* 20%) of the isomeric *cyclo*hexenyl-aldehyde (X), a lower homologue of the C_{14} aldehyde (II) [cf. equilibrium between *cyclo*hexylidene- and *cyclo*hexenyl-acetaldehyde (Aldersley and Burkhardt, *J.*, 1938, 545; *cf.* Dimroth, *Ber.*, 1938, **71**, 1333), and the corresponding acetone derivatives (Kon, *Ann. Reports*, 1932, **29**, 138)].

Finally, the new aldehyde synthesis was applied to the diacetylenic glycol (XI), formed in 70% yield by the oxidative coupling of the alcohol (I). Reduction of (XI) with lithium aluminium hydride (cf. Ahmad, Sondheimer, Weedon, and Woods, *J.*, 1952, 4089) gave the diene glycol (XII), as a crystalline solid in 80% yield, which, by dehydration and subsequent treatment with mineral acid, was converted into the triene aldehyde (XIII). This on condensation with malonic acid gave the tetraene acid (XIV).



$$\underset{\text{(XI)}}{\text{MeO}\cdot\text{CH}_2\cdot\overset{\text{Me}}{\text{C}}(\text{OH})\cdot\text{C}{\vdots}\text{C}\cdot\text{C}{\vdots}\text{C}\cdot\overset{\text{Me}}{\text{C}}(\text{OH})\cdot\text{CH}_2\cdot\text{OMe}} \longrightarrow \underset{\text{(XII)}}{\text{MeO}\cdot\text{CH}_2\cdot\overset{\text{Me}}{\text{C}}(\text{OH})\cdot\text{CH:CH}\cdot\text{CH:CH}\cdot\overset{\text{Me}}{\text{C}}(\text{OH})\cdot\text{CH}_2\cdot\text{OMe}}$$

$$\longrightarrow \underset{\text{(XIII)}}{\text{MeO}\cdot\text{CH}_2\cdot\overset{\text{Me}}{\text{C}}\text{:CH}\cdot\text{CH:CH}\cdot\text{CH:}\overset{\text{Me}}{\text{C}}\cdot\text{CHO}} \longrightarrow \underset{\text{(XIV)}}{\text{MeO}\cdot\text{CH}_2\cdot\overset{\text{Me}}{\text{C}}\text{:CH}\cdot\text{CH:CH}\cdot\text{CH:}\overset{\text{Me}}{\text{C}}\cdot\text{CH:CH}\cdot\text{CO}_2\text{H}}$$

EXPERIMENTAL

Light-absorption data, the majority of which are given in the Table, were determined in alcohol, unless otherwise stated.

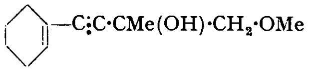
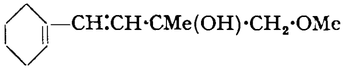
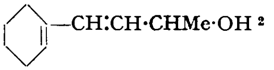
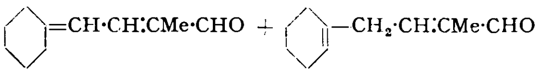
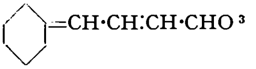
Methoxyacetone.—1-Methoxypropan-2-ol (Reeves and Sadle, *J. Amer. Chem. Soc.*, 1950, **72**, 1252) was oxidised by Mariella and Leech's method (*ibid.*, 1949, **71**, 3558). The product was fractionally distilled through a Stedman column (12 × 1″), and the fraction of b. p. 113—114° was collected. This was estimated, by conversion of an aliquot into the 2 : 4-dinitrophenylhydrazone (cf. Iddles and Jackson, *Ind. Eng. Chem.*, 1934, **6**, 456), to contain 85% of methoxyacetone, and was used without further purification.

Acetylenic Alcohols from Methoxyacetone.—A slight excess of the acetylene was added to a stirred solution (*ca.* 1M) of ethylmagnesium bromide in ether, and the mixture was heated under reflux for 3 hr. and then cooled. Methoxyacetone in ether (2 vols.) was added dropwise, and the mixture was heated under reflux for *ca.* 2 hr. and then cooled. The Grignard complex was decomposed by the addition of saturated aqueous ammonium chloride, and the product was isolated in the usual way.

Hex-1-yne (24 g.) and methoxyacetone (20 g.) gave 1-*methoxy*-2-*methyloct*-3-*yn*-2-*ol* (24 g.), b. p. 106—108°/18 mm., n_D^{24} 1·4474 (Found : C, 70·0; H, 10·35. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·7%).

Phenylacetylene (50 g.) and methoxyacetone (44 g.) gave 1-*methoxy*-2-*methyl*-4-*phenylbut*-3-*yn*-2-*ol* (48 g.), b. p. 148°/13 mm., n_D^{22} 1·5448 (Found : C, 75·9; H, 7·5. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%). Light absorption : see Table.

1-Ethynyl*cyclo*hexene (53 g.) and methoxyacetone (47 g.) gave 4-cyclo*hex*-1′-*enyl*-1-*methoxy*-2-*methylbut*-3-*yn*-2-*ol* (67 g.), b. p. 114—116°/2 mm., n_D^{22} 1·5032 (Found : C, 74·3; H, 9·6. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%). Light absorption : see Table.

	λmax., Å	ε max.
PhC⋮C·CMe(OH)·CH$_2$·OMe	2400	20,000
	2450	17,500
	2510	18,500
PhCH:CH·CMe(OH)·CH$_2$·OMe (*trans*)	2420	16,000
	2530	
PhCH:CH·CMe$_2$·OH [1]	2510	17,500
	2560	16,500
 —C⋮C·CMe(OH)·CH$_2$·OMe	2270	10,000
 —CH:CH·CMe(OH)·CH$_2$·OMe	2270	27,000
	2340 *	23,500
 —CH:CH·CHMe·OH [2]	2330	24,300
 =CH·CH:CMe·CHO + —CH$_2$·CH:CMe·CHO	2270	3,000
	2810	22,000
	2900	
 =CH·CH:CH·CHO [3]	2900	—
MeO·CH$_2$·CMe(OH)·C⋮C·C⋮C·CMe(OH)·CH$_2$·OMe	2280	450
	2420	
	2510	
HO·CHMe·C⋮C·C⋮C·CHMe·OH [4]	2320	320
	2425	330
	2560	210
MeO·CH$_2$·CMe(OH)·CH:CH·CH:CH·CMe(OH)·CH$_2$·OMe	2270	34,500
HO·CHMe·CH:CH·CH:CH·CHMe·OH [5] (m. p. 45°)	2270	32,000
	2340 *	24,500
MeO·CH$_2$·CMe:CH·CH:CH·CH:CMe·CHO	3230	28,500
CHMe:CH·CH:CH·CMe:CH·CHO [6]	3220	30,500
MeO·CH$_2$·CMe:CH·CH:CH·CH:CMe·CH:CH·CO$_2$H	3330	48,000
MeCH:CH·CH:CH·CH:CH·CH:CH·CO$_2$H [7]	3320 †	49,000

* Inflexion. † In hexane.

[1] Braude and Timmons, *J.*, 1950, 2001. [2] Chanley and Sobotka, *J. Amer. Chem. Soc.*, 1949, **71**, 4140. [3] Bohlmann, *Chem. Ber.*, 1951, **84**, 544. [4] Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 2003. [5] Ahmad, Sondheimer, Weedon, and Woods, *J.*, 1952, 4089. [6] Weedon and Woods, *J.*, 1951, 2687. [7] Hausser, Smakula, Kuhn, and Hoffer, *Z. physikal. Chem.*, 1935, **29**, *B*, 371.

1-*Methoxy*-2-*methyloct*-3-*en*-2-*ol* (VI; R = Bu^n).—A solution of 1-methoxy-2-methyloct-3-yn-2-ol (15 g.) in ethyl acetate (75 c.c.) was shaken in hydrogen in the presence of palladium–calcium carbonate (5 g.; 0·3% Pd). When 1 mol. of hydrogen (1980 c.c. at 15°/752 mm.) had been absorbed, the catalyst and solvent were removed and the residue was distilled, giving the *alcohol* (12·5 g.), b. p. 99°/16 mm., n_D^{18} 1·4402 (Found : C, 69·45; H, 11·7. $C_{10}H_{20}O_2$ requires C, 69·75; H, 11·65%).

2-*Methyloct*-2-*en*-1-*al* (VIII; R = Bu^n).—Toluene-*p*-sulphonic acid (60 mg.) was added to a boiling solution of the preceding alcohol (6 g.) in dry benzene (40 c.c.). A vigorous reaction occurred and the water liberated was removed by azeotropic distillation. The solution was heated under reflux for a further 15 min. and then cooled, washed with a saturated solution of sodium hydrogen carbonate, dried, and evaporated. Distillation of the residue gave the crude methoxy-diene (2·5 g.), b. p. 70—72°/15 mm., n_D^{18} 1·4587, which, in ether (15 c.c.), was shaken with N/5-hydrochloric acid (15 c.c.) for 1 hr. The crude aldehyde was isolated, and the main bulk was converted into the *semicarbazone* (1·7 g.) which crystallised from alcohol in plates, m. p. 159° (Found : N, 21·45. $C_{10}H_{19}ON_3$ requires N, 21·35%). Light absorption : maximum, 2650 Å; ε = 28,000. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in red needles, m. p. 121° (Found : C, 55·95; H, 6·4. $C_{15}H_{20}O_4N_4$ requires C, 56·25; H, 6·3%). Light absorption in $CHCl_3$ (main band only) : maximum, 3800 Å; ε = 28,000.

1-*Methoxy*-2-*methyl*-4-*phenylbut*-3-*en*-2-*ol* (VI; R = Ph).—(*a*) A solution of 1-methoxy-2-methyl-4-phenylbut-3-yn-2-ol (10 g.) in ether (75 c.c.) was added during ½ hr. to a stirred solution of lithium aluminium hydride (2·4 g.) in ether (200 c.c.). The mixture was heated under reflux for 3 hr. and then cooled. Ethyl acetate was added followed by a saturated aqueous solution of ammonium chloride. Isolation of the product with ether gave the trans-*alcohol* (8·9 g.), b. p. 114—115°/1 mm., n_D^{20} 1·5449 (Found : C, 75·0; H, 8·45. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·35%). Light absorption : see Table.

(*b*) A product (21 g.) which possibly contained some of the *cis*-isomer, was obtained by partial catalytic reduction of the acetylenic alcohol (25 g.) in ethyl acetate (120 c.c.) over a palladium–calcium carbonate catalyst (5 g.; 0·3% Pd). It had b. p. 104—106°/0·2 mm., n_D^{18} 1·5399 (Found: C, 74·55; H, 8·55%). Light absorption : maxima, 2420 and 2510 Å; ε = 12,000.

2-*Methyl*-4-*phenylbut*-2-*en*-1-*al*.—Toluene-*p*-sulphonic acid (150 mg.) was added to a boiling solution of 1-methoxy-2-methyl-4-phenylbut-3-en-2-ol (15 g.; prepared by method *b*) in toluene (110 c.c.). A vigorous reaction occurred, the water formed was removed by azeotropic distillation, and the mixture was then boiled for a further 15 min. Isolation and distillation of the product gave an oil (3·9 g.), b. p. 83—84°/1 mm. Light absorption : maxima, 2270, 2360, 2510, and 2800 Å; $E^{1\%}_{1\,\text{cm.}}$ = 650, 480, 350, and 350, respectively. Hydrolysis as described above yielded the aldehyde. This was converted into the semicarbazone (3·2 g.), which crystallised from alcohol in plates, m. p. 176° (Found : N, 19·35. Calc. for $C_{12}H_{15}ON_3$, N, 19·35%). Linnell and Shen, *J. Pharm. and Pharmacol.*, 1949, 1, 917, give m. p. 178—179°. Light absorption : maximum, 2640 Å; ε = 23,000. Inflexions, 2580, 2680, and 2760 Å; ε = 19,000, 19,000, and 14,500 respectively. (*Idem, loc. cit.*, give maximum, 2660 Å; ε = 34,000.) The 2 : 4-dinitrophenylhydrazone crystallised from alcohol as orange needles, m. p. 193° (Found : N, 16·25. Calc. for $C_{12}H_{16}O_4N_4$: N, 16·45%). (*Idem, loc. cit.*, give m. p. 188—190°.) Light absorption in $CHCl_3$ (main band only) : maximum, 3780 Å; ε = 35,500.

Similarly the alcohol (7 g.; prepared by method *a*) was converted into the aldehyde semicarbazone (1·2 g.), m. p. and mixed m. p. 176°.

4-cyclo*Hex*-1′-*enyl*-1-*methoxy*-2-*methylbut*-3-*en*-2-*ol* (VI; R = *cyclo*hexenyl).—Reduction of 4-*cyclo*hex-1′-enyl-1-methoxybut-3-yn-2-ol (62 g.) in ether (1 l.) with lithium aluminium hydride (15·5 g.), and isolation of the product, gave an oil (61 g.), n_D^{19} 1·5094. Light absorption : maxima, 2270 and 2360 Å; $E^{1\%}_{1\,\text{cm.}}$ = 1260 and 1180, respectively, indicating a purity of *ca.* 90%. Distillation of a small portion gave the *alcohol*, b. p. 104°/0·5 mm., n_D^{22} 1·5068 (Found : C, 73·1; H, 10·15. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·25%). Light absorption : see Table.

4-cyclo*Hex*-1′-*enyl*-2-*methylbut*-2 : 4-*dien*-1-*al* (VIII; R = *cyclo*hexenyl).—A saturated solution of toluene-*p*-sulphonic acid (250 mg.) in warm toluene (70 c.c.) was added to a solution of the preceding alcohol (7·5 g.) in toluene (60 c.c.). The mixture was rapidly boiled and then immediately cooled (ice-bath). Isolation and hydrolysis of the product in the usual way gave the *aldehyde* (2·5 g.), b. p. 87—90°/10^{-2} mm., n_D^{22} 1·5710 (Found : C, 80·15; H, 9·7. $C_{11}H_{14}O$ requires C, 80·5; H, 9·8%). Light absorption : see Table. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in dark red prisms, m. p. 214° (Found : N, 16·35. $C_{17}H_{20}O_4N_4$ requires N, 16·3%). Light absorption in $CHCl_3$ (main band only) : maximum, 4050 Å; ε = 41,500. The *semicarbazone* crystallised from alcohol in plates, m. p. 169° (Found : N, 19·0. $C_{12}H_{19}ON_3$ requires N, 19·0%). Light absorption : maximum, 3050 Å; ε = 51,500.

1 : 8-*Dimethoxy*-2 : 7-*dimethylocta*-3 : 5-*diyne*-2 : 7-*diol* (XI).—A solution of 1-methoxy-2-methylbut-3-yn-2-ol (10 g.) (Inhoffen, Bohlmann, Bartram, Rummert, and Pommer, *Annalen*, 1950, **570**, 54) in alcohol (10 c.c.) was added to one of cuprous ammonium chloride (from 2·5 g. of cuprous chloride and 8·0 g. of ammonium chloride) in 0·08N-hydrochloric acid (40 c.c.). The mixture was shaken in an atmosphere of oxygen until 1 mol. had been absorbed (cf. Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 2003). The inorganic green precipitate was dissolved by the addition of dilute hydrochloric acid, and the resulting solution was extracted with ether (constant ether extractor, 48 hr.). Evaporation of the extract and distillation of the residue gave the *glycol* (7·0 g.), b. p. 100—110° (bath-temp.)/10^{-4} mm., n_D^{22} 1·5095 (Found : C, 63·35; H, 8·15. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%). Light absorption : see Table.

The same yield of glycol was obtained by aerial oxidation of the alcohol at 55—60° in the presence of a large excess of aqueous cuprous ammonium chloride (cf. Bowden, Heilbron, Jones, and Sargent, *J.*, 1947, 1579).

1 : 8-*Dimethoxy*-2 : 7-*dimethylocta*-3 : 5-*diene*-2 : 7-*diol* (XII).—A solution of the preceding glycol (15 g.) in ether (200 c.c.) was added dropwise to one of lithium aluminium hydride (7·8 g.) in ether (800 c.c.), and the mixture was heated under reflux for 15 hr. Isolation of the product in the usual manner gave the *glycol* (12·5 g.), b. p. 100° (bath-temp.)/10^{-4} mm., m. p. 83—85°. Crystallisation from benzene gave needles, m. p. 84—86° (Found : C, 62·85; H, 9·65. $C_{12}H_{20}O_4$ requires C, 62·6; H, 9·55%). Light absorption : see Table.

8-*Methoxy*-2 : 7-*dimethylocta*-2 : 4 : 6-*trien*-1-*al* (XIII).—A solution of toluene-*p*-sulphonic acid (250 mg.) in warm toluene (100 c.c.) was added to one of the preceding glycol (10 g.) in toluene (200 c.c.). The mixture was rapidly boiled and then cooled immediately (ice-bath). Isolation of the product and hydrolysis gave the *aldehyde* (6·3 g.), b. p. 100—102°/0·5 mm., n_D^{25} 1·6015—1·6049 (Found : C, 72·9; H, 9·0. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%). Light absorption : see Table. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in dark red prisms, m. p. 171° (Found : N, 15·45. $C_{17}H_{20}O_5N_4$ requires N, 15·5%). Light absorption in $CHCl_3$ (main band only) : maximum, 4070 Å; $\varepsilon = 39,500$. The *semicarbazone* crystallised from alcohol in pale yellow plates, m. p. 180—182° (Found : N, 17·35. $C_{12}H_{19}O_2N_3$ requires N, 17·7%). Light absorption : maximum, 3280 Å; $\varepsilon = 51,000$.

4 : 9-*Dimethyl*-10-*methoxydeca*-2 : 4 : 6 : 8-*tetraenoic Acid* (XIV).—Malonic acid (0·9 g.) and a solution of the preceding aldehyde (0·9 g.) and freshly distilled piperidine (2 drops) in pyridine (9 c.c.) were heated on a steam-bath for 2 hr. The resulting dark red solution was cooled, acidified, and extracted with ether. Evaporation of the extract gave an oil which partly solidified when scratched. The solid (20 mg.), m. p. 150—153°, was crystallised from benzene, giving the *acid* as yellow needles, m. p. 159° (Found : C, 69·8; H, 8·35. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·15%). Light absorption : see Table.

The authors thank Dr. K. R. Bharucha for practical assistance, and one of them (R. A.) is indebted to the Royal Commission for the Exhibition of 1851 for an Overseas Scholarship.

Analyses and light-absorption measurements were carried out in the microanalytical (Mr. F. H. Oliver) and spectrographic (Mrs. A. I. Boston) laboratories of this Department.

DEPARTMENT OF ORGANIC CHEMISTRY, IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7.
[*Received, March 6th*, 1953.]