

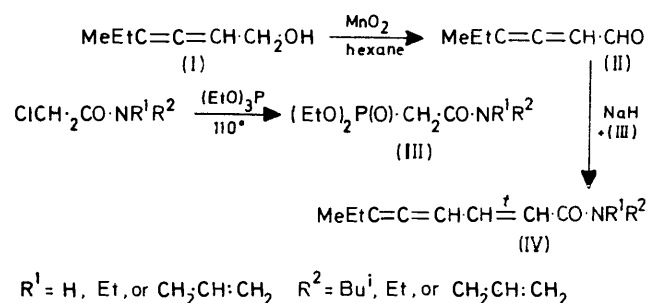
Allenes. Part 36.¹ Synthesis of 2,4,5-Trienamides as Potential Insecticides, by a Wittig Reaction

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N-Substituted 2,4,5-trienamides have been synthesised by the reactions of a 4,4-dialkylbuta-2,3-dienal with diethyl *N*-alkyl- and *NN*-dialkylcarbamoylmethylphosphonates, and characterised by i.r., u.v., and n.m.r. spectra. An attempted Wittig reaction of hepta-2,3-dienal and diethyl *N*-isobutylcarbamoylmethylphosphonate resulted in mainly nucleophilic attack at C-3 of the allenic aldehyde.

MANY natural products of plant origin contain an isobutylamide group conjugated with a *trans* double bond ($-\overset{\dagger}{\text{C}}\text{H}=\overset{\ddagger}{\text{C}}\text{H}\cdot\text{CO}\cdot\text{NHBu}^{\dagger}$), for instance affinin² and the isobutylamides from *Chrysanthemum frutescens* L.³ Most of these amides possess considerable insecticidal activity, and in some cases this is similar to that of the pyrethrins towards *Musca domestica*. We have, therefore, synthesised a number of conjugated *N*-substituted amides containing an allenic functional group in order to have these tested for insecticidal activity.

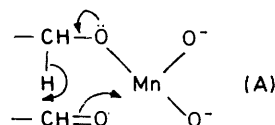
Previously allenic amides⁴ were prepared in our laboratory from allenic nitriles with hydrogen peroxide, and allenic *N*-*t*-butylamides were prepared by a Ritter reaction. This paper reports the synthesis of conjugated *N*-substituted 2,4,5-trienamides from an α -allenic alcohol (I),⁵ as outlined in Scheme 1.



SCHEME 1

The allenic alcohol (I) was oxidised with active manganese dioxide † in hexane and the reaction was monitored by i.r. spectroscopy to ascertain conditions for maximum yield of allenic aldehyde;⁶ the OH absorption decreased while a new band (conjugated C=O) at 1 690 cm⁻¹ increased. When no further change occurred the product was worked up and the crude aldehyde used in the next stage. The crude product consisted of a *ca.* 50 : 50 mixture of aldehyde (II) and alcohol (I), as shown by the integration of the allenic proton n.m.r. signals at τ 4.1 and 4.71, respectively, and u.v. absorption at λ_{max} 224 nm (ϵ 5 900) [cf. Me₂C:CH·CHO, λ_{max} 228 nm (ϵ 14 200)]. The yield of

oxidation product appeared to reach a maximum at this stage, and further addition of active manganese dioxide effected no change. Possibly an equilibrium involving complexing of alcohol and aldehyde with hydride transfer prevents further oxidation of the allenic alcohol [see (A)]. A series of *N*-substituted carbamoylmethylphosphonates (III) were prepared for use as modified



Wittig reagents in 65–73% yield from triethyl phosphite and the appropriate *N*-alkyl- or *NN*-dialkyl-chloroacetamide. The n.m.r. spectra showed a distinctive coupling constant, J 22 Hz, for $-\text{P}(\text{O})\text{CH}_2-$. The anion of the appropriate *N*-substituted carbamoylmethylphosphonate in dimethoxyethane was treated with 4-methylhexa-2,3-dienal to give a one-step Wittig synthesis of the trienamides (IV). Column chromatography on alumina gave the pure *trans*-amides, ν_{max} 1 940 (C:C), 1 650–1 640 (amide C:O), 1 610 and 980 (*trans*-C:C), and 1 510 cm⁻¹ (NH def.). High intensity u.v. absorption at λ_{max} 257–264 nm was comparable to that for alka-2,4-dienamides.⁷ The n.m.r. spectra resembled those of the *trans*-2,4,5-trienoates with $J_{2,3}$ 15 and $J_{3,4}$ 10 Hz.⁶

N-Isobutyl-6-methylocta-*trans*-2,4,5-trienamide was also prepared, in lower yield but spectroscopically identical with the previous sample, by using *N*-isobutylcarbamoylmethyl(triphenyl)phosphonium chloride³ as the Wittig reagent.

The known naturally occurring isobutylamides are straight-chain compounds, and in an attempt to prepare a similar allenic isomer we used hepta-2,3-dien-1-ol (VI) as starting material (Scheme 2). The allenic alcohol (VI) was prepared by a modification of our published route,⁵ *via* the acetylenic alcohol (V), obtained from the action of propyl-lithium followed by formaldehyde on 3-tetrahydropyran-2-yloxyhex-1-yne. This reaction was faster and cleaner than the Grignard method; reduction

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¹ Part 35, S. R. Landor, V. Rogers, and H. R. Sood, *Tetrahedron*, 1976, in the press.

² L. Crombie, A. H. Krasinski, and M. Manzoor-i-Khuda, *J. Chem. Soc.*, 1963, 4970.

³ F. Bohlmann and R. Miethe, *Chem. Ber.*, 1967, **100**, 3861.

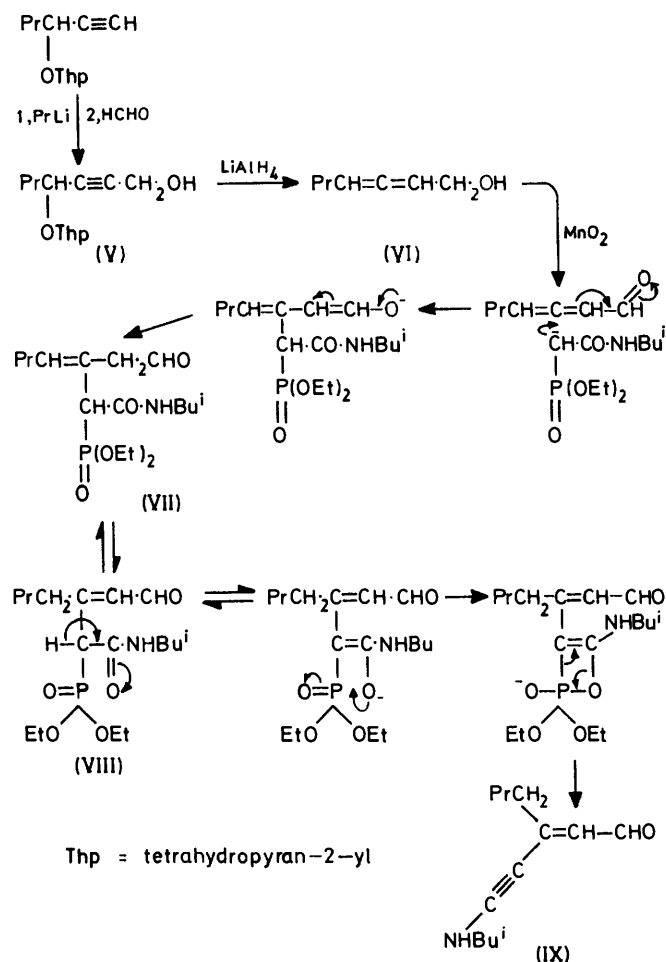
⁴ P. M. Greaves, P. D. Landor, S. R. Landor, and O. Odyek, *Tetrahedron*, 1974, **30**, 1427.

⁵ J. S. Cowie, P. D. Landor, and S. R. Landor, *J.C.S. Perkin I*, 1973, 720.

⁶ Preliminary report of a similar oxidation, P. D. Landor, S. R. Landor, and S. Mukusa, *Chem. Comm.*, 1971, 1638.

⁷ R. S. Burden and L. Crombie, *J. Chem. Soc. (C)*, 1969, 2477.

and oxidation then gave the corresponding crude allenic aldehyde. However on treatment with the anion of diethyl *N*-isobutylcarbamoylmethylphosphonate, work-up and chromatography, only traces of trienamidine were obtained, and the main product appeared to be formed



SCHEME 2

by a Michael addition at C-3 of the aldehyde [to give (VII) and (VIII) and degradation products such as (IX)]. Similar Michael additions of other ylides to two α -allenic ketones have been reported.⁸

EXPERIMENTAL

I.r. spectra were determined for liquid films with a Perkin-Elmer 257 spectrophotometer. U.v. spectra were obtained for ethanolic solutions with a Pye-Unicam 1800 spectrometer. N.m.r. spectra were determined with a Varian T60 spectrometer for solutions in deuteriochloroform, with tetramethylsilane as internal standard unless otherwise stated. Ethereal solutions were dried over MgSO_4 .

N-Isobutylchloroacetamide.—Chloroacetic acid (48.0 g, 0.5 mol) and benzoyl chloride (140.5 g, 1.0 mol) were heated under a fractionating column. The acid chloride was distilled off into an ice-cooled receiver and the distillate

refractionated to give chloroacetyl chloride (47.8 g, 86%), b.p. 106° (lit.,⁹ 105 – 107°), ν_{max} $1\ 800\ \text{cm}^{-1}$ (C=O).

The acid chloride (28.4 g, 0.25 mol), cooled to 0°C , was added to a solution of isobutylamine (29.2 g, 0.4 mol) in anhydrous ether (50 ml) at 0°C . The mixture was shaken vigorously and allowed to warm to room temperature overnight. The crystalline amide was dissolved in chloroform; the solution was washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water, dried, and evaporated to give *N*-isobutylchloroacetamide (27.4 g, 73%), m.p. 27 – 30° [recryst. twice from chloroform–light petroleum (b.p. 40 – 60°C)], ν_{max} $3\ 300$, $3\ 100$ (NH str.), $1\ 660$ (C=O), and $1\ 550\ \text{cm}^{-1}$ (NH def.), τ (CCl_4) 9.07 (6 H, d, Me_2CH), 8.20 (1 H, m, CHMe_2), 6.90 (2 H, t, collapses to a doublet on deuteration, $\text{NH}\cdot\text{CH}_2\cdot\text{CH}$), 6.00 (2 H, s, $\text{ClCH}_2\cdot\text{CO}$), and 2.78br (1 H, s, disappears on deuteration, NH); g.l.c. (t_R 10.5 min; 5% SE30 on Celite; 90°C) showed a single peak.

NN-Diethylchloroacetamide.—Diethylamine (29.2 g, 0.4 mol) and chloroacetyl chloride (28.4 g, 0.25 mol) in a similar manner gave *NN*-diethylchloroacetamide (23.2 g, 62%), b.p. 130° at 0.4 mmHg (Found: C, 48.0; H, 7.9; Cl, 23.6; N, 9.2. $\text{C}_8\text{H}_{12}\text{ClNO}$ requires C, 48.2; H, 8.0; Cl, 23.7; N, 9.4%), ν_{max} $1\ 655\ \text{cm}^{-1}$ (C=O), τ 8.82 (3 H, t, $\text{CH}_3\cdot\text{CH}_2$), 8.72 (3 H, t, $\text{CH}_3\cdot\text{CH}_2$), 6.53 [4 H, q, $\text{N}(\text{CH}_2\cdot\text{CH}_3)_2$], and 5.83 (2 H, s, $\text{CH}_2\cdot\text{CO}$).

NN-Diallylchloroacetamide.—Diallylamine (50.0 g, 0.52 mol) and chloroacetyl chloride (34.95 g, 0.31 mol) similarly gave *NN*-diallylchloroacetamide (30.51 g, 57%), b.p. 37° at 0.5 mmHg (Found: C, 55.5; H, 7.0; Cl, 20.4; N, 8.1. $\text{C}_8\text{H}_{12}\text{ClNO}$ requires C, 55.4; H, 6.9; Cl, 20.5; N, 8.1%), ν_{max} $1\ 660$ (C=O), $1\ 630$ (C=C), and 990 and $925\ \text{cm}^{-1}$ ($\text{CH}=\text{CH}_2$), τ 5.92 [6 H, m, $\text{CH}_2\cdot\text{CO}\cdot\text{N}(\text{CH}_2\cdot\text{CH}(\text{CH}_2)_2)_2$], 4.80 [2 H, dt, ($\text{CH}:\text{CHH}$)₂], 4.73 [2 H, dt, ($\text{CH}:\text{CHH}$)₂], and 4.13 [2 H, m, ($\text{CH}:\text{CH}_2$)₂].

Diethyl N-Isobutylcarbamoylmethylphosphonate.—Triethyl phosphite (10.0 g, 0.06 mol) was maintained at 110°C , and *N*-isobutylchloroacetamide (8.0 g, 0.053 mol) was added slowly. The mixture was then heated under reflux with stirring for 30 min. Low boiling material was distilled off at 1.0 mmHg and the residue crystallised on cooling to give the phosphonate (8.58 g, 65%), m.p. 40° , ν_{max} $3\ 290$ and $3\ 080$ (NH, str.), $1\ 660$ (C=O), and $1\ 550\ \text{cm}^{-1}$ (NH def.), τ 9.07 (6 H, d, Me_2CH), 8.63 [6 H, t, ($\text{CH}_3\cdot\text{CH}_2\cdot\text{O}$)₃P], 8.20 (1 H, m, CHMe_2), 7.10 (2 H, d, PCH_2 , J 22 Hz), 6.87 (2 H, t, collapses to d on deuteration, $\text{NH}\cdot\text{CH}_2\cdot\text{CH}$), 5.80 [4 H, dq, ($\text{CH}_3\cdot\text{CH}_2\cdot\text{O}$)₂P], and 2.87br (1 H, s, NH, disappears on deuteration).

Diethyl NN-Diethylcarbamoylmethylphosphonate.¹⁰—Triethyl phosphite (10.0 g, 0.06 mol) and *NN*-diethylchloroacetamide (7.5 g, 0.05 mol) similarly gave the phosphonate (9.2 g, 73%), b.p. 170° at 0.04 mmHg (Found: C, 47.8; H, 8.7; N, 5.5; P, 12.2. $\text{C}_{10}\text{H}_{22}\text{NO}_4\text{P}$ requires C, 47.8; H, 8.8; N, 5.6; P, 12.4%), ν_{max} $1\ 645\ \text{cm}^{-1}$ (C=O), τ 9.00–8.5 [12 H, m, ($\text{CH}_3\cdot\text{CH}_2$)₂N and ($\text{CH}_3\cdot\text{CH}_2\cdot\text{O}$)₂P], 6.97 (2 H, d, PCH_2 , J 22 Hz), 6.52 (2 H, q, $\text{N}\cdot\text{CH}_2\cdot\text{CH}_3$), 6.57 (2 H, q, $\text{N}\cdot\text{CH}_2\cdot\text{CH}_3$), 5.83 (2 H, q, $\text{CH}_3\cdot\text{CH}_2\cdot\text{O}$), and 5.72 (2 H, q, $\text{CH}_3\cdot\text{CH}_2\cdot\text{O}$).

Diethyl NN-Diallylcarbamoylmethylphosphonate.¹⁰—Triethyl phosphite (16.6 g, 0.1 mol) and *NN*-diallylchloroacetamide (15.62 g, 0.09 mol) similarly gave the phosphonate (16.6 g, 67%), b.p. 130° at 0.3 mmHg, ν_{max} $1\ 650$ (C=O) and

⁹ H. C. Brown, *J. Amer. Chem. Soc.*, 1938, **60**, 1325.

¹⁰ A. J. Speziale and R. C. Freeman, *J. Org. Chem.*, 1958, **23**, 1883.

⁸ G. Buono, G. Peiffer, and A. Guillemonat, *Compt. rend.*, 1970, **271**, 937.

1 640 cm^{-1} (C=C), τ 8.67 [6 H, t, $(\text{CH}_3\cdot\text{CH}_2\cdot\text{O})_2\text{P}$], 6.97 (2 H, d, $\text{P}\cdot\text{CH}_2$, J 22 Hz), 5.98 [8 H, m, $(\text{CH}_3\cdot\text{CH}_2\cdot\text{O})_2$ and $(\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2)_2$], 4.80 [4 H, m, $\text{N}(\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2)_2$], and 4.13 [2 H, m, $\text{N}(\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2)_2$].

4-Methylhexa-2,3-dienal.—Active manganese dioxide (18.0 g; Hoffmann-La Roche) was added to a solution of 4-methylhexa-2,3-dien-1-ol⁵ (1.8 g, 0.016 mol) in *n*-hexane (100 ml). The mixture was shaken at room temperature for 3 h, then filtered and washed with hexane. Manganese dioxide (18.0 g, 0.21 mol) was added to the combined filtrate and the oxidation was continued for a further 2 h. The reaction was monitored by i.r. spectroscopy. The mixture was filtered, the solid washed with hexane, and the filtrate evaporated at room temperature to give crude 4-methylhexa-2,3-dienal (1.2 g, 68%), ν_{max} 3 360 (OH), 1 945 (C:C:C), and 1 690 cm^{-1} (C:O), λ_{max} 224 nm (ϵ 5 900), τ 7.4 (0.5 H, s, OH), 5.97 (1 H, d, $\text{CH}_2\cdot\text{OH}$), 4.70 (0.5 H, m, $\cdot\text{CH}\cdot\text{CH}_2\cdot\text{OH}$), 4.17 (0.5 H, m, $\cdot\text{CH}\cdot\text{CHO}$), and 0.50 (0.5 H, d, $\cdot\text{CH}\cdot\text{CHO}$).

***N*-Isobutyl-6-methylocta-trans-2,4,5-trienamide.**—(a) Diethyl *N*-isobutylcarbamoylmethylphosphonate (1.8 g, 0.007 mol) was added to a slurry of sodium hydride (0.48 g, 0.02 mol) in 1,2-dimethoxyethane (50 ml) and the mixture was stirred for 30 min. Crude 4-methylhexa-2,3-dienal (0.4 g) obtained from oxidation of the alcohol (0.7 g, 0.006 mol) was added, and stirring was continued for 3 h at 40–50 °C. The mixture was diluted with water and the product extracted into ether and dried. The solvent was removed and the crude product (0.64 g) chromatographed on alumina (100 g; Woelm acid, activity II). Ether eluted *N*-isobutyl-6-methylocta-trans-2,4,5-trienamide (0.51 g, 40% based on the alcohol), m.p. 136–137° (Found: C, 75.0; H, 10.0; N, 7.1. $\text{C}_{13}\text{H}_{21}\text{NO}$ requires C, 75.3; H, 10.2; N, 6.8%), ν_{max} 3 450, 3 320 (NH str.), 1 940 (C:C:C), 1 650 (C:O), 1 610 (C:C), 1 510 (NH def.), and 980 cm^{-1} (*trans*-C:C), λ_{max} 257 nm (ϵ 24 700), τ 9.00 (9 H, m, $\text{CH}_3\cdot\text{CH}_2$ and Me_2CH), 8.20 (6 H, m, $\text{CH}_3\cdot\text{CH}_2$, Me_2CH , and $\text{CH}_3\cdot\text{C}$), 6.80 (2 H, t, collapses to d on deuteration), 4.10 (3 H, m, NH, $\cdot\text{CH}\cdot\text{CO}$, and C:C:CH, collapses to 2 H on deuteration), and 2.83 (1 H, dd, *trans*-CH:CH·CO, $J_{2,3}$ 15, $J_{3,4}$ 10 Hz), *m/e* 207.

(b) Crude 4-methylhexa-2,3-dienal [0.8 g; obtained from the oxidation of the alcohol (1.4 g, 0.012 mol)] in dry ethanol was added to a solution of *N*-isobutylcarbamoylmethyl(triphenyl)phosphonium chloride³ (3.4 g, 0.009 mol), followed by sodium ethoxide [1 ml of a solution from sodium (2.3 g) in dry ethanol (30 ml)]. The mixture was heated under reflux for 2 h, the solvent distilled off, and the crude amide (0.8 g) chromatographed on alumina (100 g). Ether eluted the 2,4,5-trienamide (0.62 g, 24% based on the alcohol), m.p. 137°, spectroscopically identical with the previous sample.

NN-Diethyl-6-methylocta-trans-2,4,5-trienamide.—Diethyl *NN*-diethylcarbamoylmethylphosphonate (5.4 g, 0.022 mol) and crude 4-methylhexa-2,3-dienal (1.5 g) obtained from oxidation of the alcohol (2.6 g, 0.023 mol) treated as in method (a) above gave the crude amide (4.5 g). Chromatography of the crude amide (1.9 g) on alumina (Woelm acid, activity II) and elution with isohexane–ether (4:1) gave

the *trienamide* (0.74 g, 36% based on the alcohol) (Found: C, 75.3; H, 10.3; N, 6.7. $\text{C}_{13}\text{H}_{21}\text{NO}$ requires C, 75.3; H, 10.2; N, 6.8%), ν_{max} 1 940 (C:C:C), 1 640 (C:O), 1 600 (C:C), and 980 cm^{-1} (*trans*-C:C), λ_{max} 263 nm (ϵ 30 000), τ 8.97 [6 H, t, $(\text{CH}_3\cdot\text{CH}_2)_2\text{N}$], 8.78 (3 H, t, $\text{CH}_3\cdot\text{CH}_2\cdot\text{C}$), 8.23 (3 H, d, $\text{CH}_3\cdot\text{C}$), 8.08 (2 H, m, $\text{CH}_3\cdot\text{CH}_2\cdot\text{C}$), 6.53 [4 H, q, $(\text{CH}_2\cdot\text{CH}_2)_2\text{N}$], 4.07 (1 H, m, C:C:CH), 3.75 (1 H, d, *trans*-C:CH·CO, $J_{2,3}$ 15 Hz), and 2.77 (1 H, dd, *trans*-CH=CH·CO, $J_{2,3}$ 15, $J_{3,4}$ 10 Hz).

NN-Diallyl-6-methylocta-trans-2,4,5-trienamide.—Diethyl *NN*-diallylcarbamoylmethylphosphonate (6.10 g, 0.022 mol) and crude 4-methylhexa-2,3-dienal (1.2 g) obtained from oxidation of the alcohol (2.5 g, 0.022 mol) similarly [method (a)] gave the crude amide (2.6 g). Chromatography of the crude amide (1.3 g) on alumina (Woelm acid, activity II) and elution with isohexane–ether (4:1) gave the *trienamide* (0.42 g, 16% based on the alcohol), ν_{max} 1 940 (C:C:C), 1 640 (C:O), 1 600 (C:C), 990 and 920 ($\text{CH}\cdot\text{CH}_2$), and 975 cm^{-1} (*trans*-C:C), λ_{max} 264 nm (ϵ 27 000), τ 8.97 (3 H, t, $\text{CH}_3\cdot\text{CH}_2$), 8.23 (3 H, d, $\text{CH}_3\cdot\text{C}$), 8.00 (2 H, m, $\text{CH}_3\cdot\text{CH}_2$), 5.93 [4 H, m, $\text{N}(\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2)_2$], 4.80 [2 H, dt, $(\text{CH}\cdot\text{CHH})_2$], 4.73 [2 H, dt, $(\text{CH}\cdot\text{CHH})_2$], 4.10 [3 H, m, C:C:CH and $\text{N}(\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2)_2$], 3.73 (1 H, d, *trans*-CH:CH·CO, $J_{2,3}$ 15 Hz), and 2.70 (1 H, dd, *trans*-CH:CH·CO, $J_{3,2}$ 15, $J_{3,4}$ 10 Hz), *m/e* 231.

4-Tetrahydropyran-2-yloxyhept-2-yn-1-ol. 3-Tetrahydropyran-2-yloxyhex-1-yne (59.7 g, 0.33 mol) in tetrahydrofuran (100 ml) was added dropwise to propyl-lithium [from 1-bromopropane (48.3 g, 0.4 mol) and lithium (5.5 g, 0.79 mol) in ether (160 ml) at –5 °C under oxygen-free nitrogen]. Gaseous formaldehyde generated from paraformaldehyde (16 g) was passed through a heated tube onto the surface of the stirred mixture. After 2 h the mixture was poured on aqueous ammonium chloride and the organic phase and ethereal extracts of the aqueous phase were dried (K_2CO_3 – MgSO_4). Evaporation left the heptynol⁵ (59 g, 85%).

Hepta-2,3-dienal.—Active manganese dioxide (35 g) and hepta-2,3-dien-1-ol⁵ (2.3 g, 0.02 mol) in *n*-hexane (60 ml) treated as described above gave crude hepta-2,3-dienal (0.8 g, 36%); ν_{max} 3 360 (OH), 1 945 (C:C:C), and 1 690 cm^{-1} (C:O), λ_{max} 220 nm (ϵ 10 400), τ 7.03br (0.5 H, s, OH), 5.97 (1 H, dd, $\text{CH}_2\cdot\text{OH}$), 4.78 (1 H, m, $\text{CH}\cdot\text{C}\cdot\text{CH}\cdot\text{CH}_2\cdot\text{OH}$), 4.28 (1 H, m, $\text{CH}\cdot\text{C}\cdot\text{CH}\cdot\text{CHO}$), and 0.60 (0.5 H, m, $\text{CH}\cdot\text{C}\cdot\text{CH}\cdot\text{CHO}$).

Reaction of Hepta-2,3-dienal with Diethyl *N*-Isobutylcarbamoylmethylphosphonate.—Diethyl *N*-isobutylcarbamoylmethylphosphonate (2.2 g, 0.01 mol) was added to a slurry of sodium hydride (0.2 g, 0.011 mol) in dry 1,2-dimethoxyethane (50 ml) and the mixture was stirred for 30 min. Crude hepta-2,3-dienal (1.5 g) was added dropwise with stirring for 1 h, and the mixture then heated at 40–50 °C for 2 h. Work-up as described above gave a crude product (1.2 g) which on chromatography afforded various fractions; spectroscopic examination showed only traces of allene (i.r. and n.m.r. spectra). The materials appeared to be mixtures of the Michael addition products (VII) and (VIII) and the degradation product (IX).