830. *Amides of Vegetable Origin. Part II.* Stereoisomeric* N-iso-*Butylnona*-1 : 5-*diene*-1-*carboxyamides and the Structure of Pellitorine.*

By L. Crombie.

Syntheses of the *trans*-1 : *trans*-5-, *trans*-1 : *cis*-5-, and *cis*-1 : *trans*-5-stereoisomers of *N-iso*butylnona-1 : 5-diene-1-carboxyamide have been effected. The *trans*-1 : *trans*-5-compound is identical with a previously described isomer of unproven configuration. Since the *cis*-1 : *cis*-5-compound is already known the four possible geometrical isomers are now available as in the *N-iso*butylundeca-1 : 7-diene-1-carboxyamide series. The configurations, assigned on a basis of reaction stereospecificity, are supported by spectroscopic investigation.

All of the compounds are poor sialogogues and have low insecticidal potencies. None is identical with natural pellitorine and the currently accepted structure, like that of herculin (Part I), is incorrect. Nevertheless, in contrast with herculin, it has been possible to re-isolate pellitorine and establish its identity with the material described by Jacobson (*J. Amer. Chem. Soc.*, 1949, **71**, 366).

The roots of *Anacyclus pyrethrum* D.C. (known in the older literature as *Anthemis pyrethrum*, Spanish chamomile, or pellitory of Spain) contain a sialogogue and stomachic principle which has been used in medicine for many centuries. When chewed, the effect is not immediate though the onset of a characteristic burning taste is rapid. It has been recommended for the alleviation of toothache and bronchitis and was prescribed by Arabian physicians for rigors. The compound responsible aroused the interest of various investigators (*inter al.*, Bucheim, *Arch. Exp. Path. Pharm.*, 1876, **5**, 455; Dunstan, *J.*, 1895, **67**, 100; Schneegans, *Pharm. Ztg.*, 1896, **41**, 669) and was isolated as a crystalline solid by Gulland and Hopton (*J.*, 1930, 6) who demonstrated that it was a diene which on

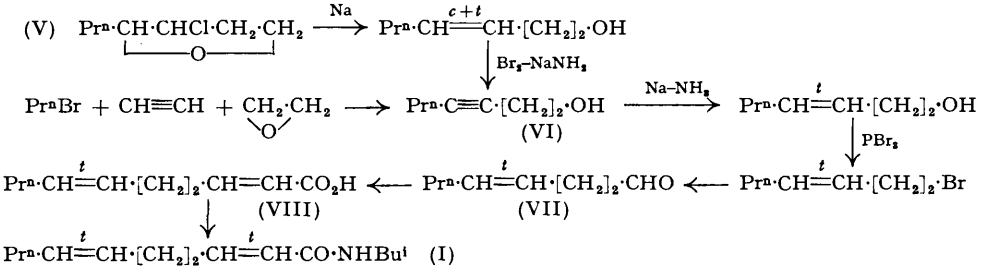
* Part I, *J.*, 1952, 2997.

hydrogenation yielded *N-iso*butylnonane-1-carboxyamide. As a result of degradative experiments with permanganate, Jacobson (*J. Amer. Chem. Soc.*, 1949, **71**, 366) assigned the unsaturation to the 1 : 5-positions, though no comment was made on the stereochemistry. Like a number of other sialogogue *iso*butylamides it is insecticidally active (Jacobson, *loc. cit.*; Crombie, Part I, *loc. cit.*).

The investigation recorded here was concurrent with that described in Part I and had similar objectives, *viz.*, the syntheses of the four possible geometrical isomers (I—IV). During its progress, preparations of the *cis*-1 : *cis*-5-stereoisomer (IV) (Raphael and Sondheimer, *J.*, 1950, 120) and a second compound of then uncertain configuration (Jacobson, Abstr. Papers presented at the 116th Meeting Amer. Chem. Soc., 1949; *J. Amer. Chem. Soc.*, 1950, **72**, 1489) were reported. Syntheses of the *trans*-1 : *trans*-5- (I), the *cis*-1 : *trans*-5- (II), and the *trans*-1 : *cis*-5-compound (III) are described below.

trans- and *cis*-Hept-3-enol were needed for the preparation of (I) and (III). A hept-3-enol is readily available from the mixed *cis*- and *trans*-3-chloro-2-*n*-propyltetrahydrofuran (V) (Normant, *Compt. rend.*, 1948, **226**, 773) by treatment with sodium but infra-red evidence and the melting point of its *p*-diphenylylurethane indicate that it is a mixture of *cis*- and *trans*-forms (cf. Crombie and Harper, *J.*, 1950, 1714). It must therefore first be converted into hept-3-ynol (VI), by bromination and dehydrobromination with sodamide in liquid ammonia. The latter alcohol was also made by a direct synthesis from acetylene (cf. Zoss and Hennion, *J. Amer. Chem. Soc.*, 1941, **63**, 1151; Sondheimer, *J.*, 1950, 877; Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1292), the pentyne not being isolated but converted directly into heptynol by addition of a further mol. of sodamide and excess of ethylene oxide. Besides the hept-3-ynol (3 : 5-dinitrobenzoate, m. p. 62°) there was isolated a higher-boiling acetylenic alcohol (3 : 5-dinitrobenzoate, m. p. 62°, but depressed on admixture with the former). Analysis of derivatives, microhydrogenation, and infra-red evidence show it to be the monohept-3-ynyl ether of ethylene glycol formed by reaction of hept-3-ynol with another mol. of ethylene oxide (cf. Leese and Raphael, *J.*, 1950, 2725).

Reduction of hept-3-ynol with sodium in liquid ammonia—a stereospecific process (Campbell and Eby, *J. Amer. Chem. Soc.*, 1941, **63**, 216, 2683)—gave *trans*-hept-3-enol (*p*-diphenylurethane, m. p. 105°) which was converted successively into the bromide, the Grignard reagent, and, by treatment with ethyl orthoformate, *trans*-oct-4-enal (VII) (2 : 4-dinitrophenylhydrazone, m. p. 110°). The Doebner reaction yielded nona-*trans*-1 : *trans*-5-diene-1-carboxylic acid (VIII), m. p. 43° [characterised like all other acids



described here as the *p*-bromophenacyl ester (see Table)]. This crystallinity is taken as evidence of its freedom from the small quantities of β-unsaturated acid sometimes encountered in such preparations and from other stereoisomers. Treatment with thionyl chloride and then *iso*butylamine produced the required *N-iso*butylnona-*trans*-1 : *trans*-5-diene-1-carboxyamide (I).

The amide (I) was identical (mixed m. p.) with the *iso*butylamide prepared by Jacobson (*loc. cit.*). Such a conclusion is to be expected as the oct-4-enal which he used was derived from oct-4-enol, in turn obtained from the ring fission of a mixture of *cis*- and *trans*-3-chlorotetrahydro-2-*n*-propylpyran with sodium. This reaction was subsequently shown (in the pyran series) to yield a *trans*-alcohol (Crombie and Harper, *J.*, 1950, 1707; *Nature*, 1949, **164**, 1053). Jacobson's yield at the Doebner stage was improved from 17% to 48%

by using a lower temperature and a longer reaction time (Boxer and Linstead, *J.*, 1931, 740) and the m. p. of this *trans-trans*-acid was 8° higher than his.

A convenient intermediate for the preparation of *N-iso*butylnona-*cis*-1 : *trans*-5-diene-1-carboxyamide is *trans*-non-5-en-1-yne (IX). The type of preparation used for its homologue, *trans*-undec-7-en-1-yne, in Part I, is here contra-indicated as sodium acetylide causes dehydrohalogenation of the hept-3-enyl halide to hepta-1 : 3-diene (Raphael and Sondheimer, *loc. cit.*). A coupling reaction between propargylmagnesium bromide and *trans*-hex-3-enyl bromide was therefore investigated. It is known (Young, Roberts, and Wax, *J. Amer. Chem. Soc.*, 1945, **67**, 841) that allylmagnesium halide gives almost entirely normal-chain diene hydrocarbon when allowed to react with but-2-enyl chloride, and even with pure 1-methylallyl chloride only 24% of branched-chain material is formed. The *trans*-hex-3-enyl bromide used in this work was prepared from 1-vinylbutyl carbinol by reaction with phosphorus tribromide and is therefore mainly primary (cf. Bouis, *Ann. Chim.*, 1928, **9**, 403; Winstein and Young, *J. Amer. Chem. Soc.*, 1936, **58**, 104). It was hoped that the coupling product would be essentially straight chain in this case too. The allylic bromide reacted vigorously with propargylmagnesium bromide (Prévost, Gaudemar, and Honigberg, *Compt. rend.*, 1950, **230**, 1186), yielding a product (b. p. 136—144°) still containing a considerable quantity of bromine. Infra-red examination confirmed the presence of $C{\equiv}CH$ and *trans*-$CH_2{\cdot}CH{=}CH{\cdot}CH_2$ groupings,* so the product was treated with an excess of ethylmagnesium bromide and carboxylated. The required *trans*-non-5-en-1-yne-1-carboxylic acid (X) was readily isolated from the product and purified by distillation (overall yield 25%). Its structure was confirmed by hydrogenation to nonane-1-carboxylic acid and by its infra-red spectrum : contamination with the branched-chain isomer (XI) was negligible [$C{\equiv}C{\cdot}CO_2H$ 2230 cm.$^{-1}$ (strong); C—H bending indicating internal *trans*-double bond 969 cm.$^{-1}$ (medium); absorption at 995 cm.$^{-1}$, indicating $CH_2{=}CH$, very weak; the other vinyl absorption region at 910 cm.$^{-1}$ could not be used decisively in the liquid film because of absorption here by the dimeric carboxylic acid grouping].

The coupling of a Grignard reagent from *trans*-hex-3-enyl bromide with propargyl bromide was avoided, as crotylmagnesium bromide and allyl bromide (Young, Roberts, and Wax, *loc. cit.*) yield a mixture of normal and branched-chain materials. Also much allene formation might be expected (Prévost *et al.*, *loc. cit.*). The components of the crude coupling product have not been further examined and no marked improvement of yield was noted by the addition of cuprous chloride catalyst.

$$Pr^n{\cdot}CH{=}CH{\cdot}CH_2Br + Br{\cdot}Mg{\cdot}CH_2{\cdot}C{\equiv}CH \longrightarrow Pr^n{\cdot}CH{=}CH{\cdot}[CH_2]_2{\cdot}C{\equiv}CH \quad (IX)$$

$$\downarrow$$

$$Pr^n{\cdot}CH{=}CH{\cdot}[CH_2]_2{\cdot}CH{=}CH{\cdot}CO{\cdot}NHBu^i \xleftarrow[3\ \text{stages}]{c} Pr^n{\cdot}CH{=}CH{\cdot}[CH_2]_2{\cdot}C{\equiv}C{\cdot}CO_2H$$

(II) (X)

$$Pr^n{\cdot}CH(CH{=}CH_2){\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CO_2H \quad (XI)$$

Partial catalytic hydrogenation of the enyne acid yielded nona-*cis*-1 : *trans*-5-diene-1-carboxylic acid which was converted into its *iso*butylamide, a liquid, by the oxalyl chloride method. Another specimen was made by the partial hydrogenation of *trans-N-iso*butylnon-5-en-1-yne-1-carboxyamide.

The reaction sequence for the preparation of *N-iso*butylnona-*trans*-1 : *cis*-5-diene-1-carboxyamide was similar to that for the *trans*-1 : *trans*-5-isomer except that the hept-3-ynol was converted into *cis*-hept-3-enol (*p*-diphenylylurethane, m. p. 85°). The intermediate *cis*-oct-4-enal was characterised as its 2 : 4-dinitrophenylhydrazone (m. p. 81°). A preliminary note on this synthesis has already been published (Crombie and Harper, *Nature, loc. cit.*). Data are given in the Table. A discussion of the stereospecificity of catalytic semihydrogenation is given elsewhere (Part I; Crombie, *Quart. Reviews*, 1952, **6**, 101), and the purity of the isomers made by this procedure is subject to the reservations mentioned there. The *cis-cis*-isomer was prepared by semihydrogenation of *N-iso*butyl-

* No absorption at *ca.* 1950 cm.$^{-1}$ was detected, indicating the absence of allenic material.

nona-1 : 5-diyne-1-carboxyamide by Raphael and Sondheimer (*loc. cit.*) who kindly made a specimen available for spectroscopic measurements.

Some support for the configurations assigned by the mode of synthesis comes from the order of melting points of the *p*-bromophenacyl esters of the three 1 : 5-diene-acids. These decrease (*trans*-1 : *trans*-5 > *cis*-1 : *trans*-5 > *trans*-1 : *cis*-5) as chain bending increases.

Nonadiene-1-*carboxylic acids and* iso*butylamides.*

			p-Bromophenacyl ester	*iso*Butylamide				
	B. p./mm.	n_D^{20} *	M. p.	B. p./mm.	n_D^{20} *	No. of C : C †	$\lambda_{max.}$ (mμ)	$\epsilon_{max.}$
trans-1 : *trans*-5... (I)	110°/0·4	(m. p. 43°)	87°	136—138°/ 4×10^{-2}	(m. p. 52°)	1·91	226	10,800
cis-1 : *trans*-5 (II)	105°/0·15	1·4718	58°	128°/8 × 10^{-4}	1·4830	1·98	226	9,400
trans-1 : *cis*-5 (III)	94—95°/ 8×10^{-2}	1·4746	45°	141°/5 × 10^{-2}	1·4836	1·86	226	10,700
cis-1 : *cis*-5 (IV) [1]	—	—	—	125—126°/ 5×10^{-4}	1·4856	—	227 [2]	10,300 [2]

[1] Data of Raphael and Sondheimer (*loc. cit.*). [2] Supplementary data.
* Adjusted to 20° by −0·0004 per degree within a range of ±5°.
† Double bonds determined by microhydrogenation.

A similar regularity was noted in the *S*-benzylthiuronium salts of the four geometrically isomeric undeca-1 : 7-diene-1-carboxylic acids in Part I.

Useful confirmation of the structure and stereochemistry of the four diene-*iso*butylamides springs from an interpretation of their infra-red spectra (see Figure). All four compounds show the N–H stretching frequency (3302—3293 cm.$^{-1}$) with the amide B absorption in the position expected for a monosubstituted amide (1555—1551 cm.$^{-1}$); the small band characteristic of amides at 3076 cm.$^{-1}$ is present. The position of the amide A absorption (1634—1631 cm.$^{-1}$, compared with 1644 cm.$^{-1}$ for *N-iso*butylnonane-1-carboxyamide) indicates the αβ-unsaturation. This is further confirmed by ultra-violet light absorption data (Table) which accord with previous observations (Part I).

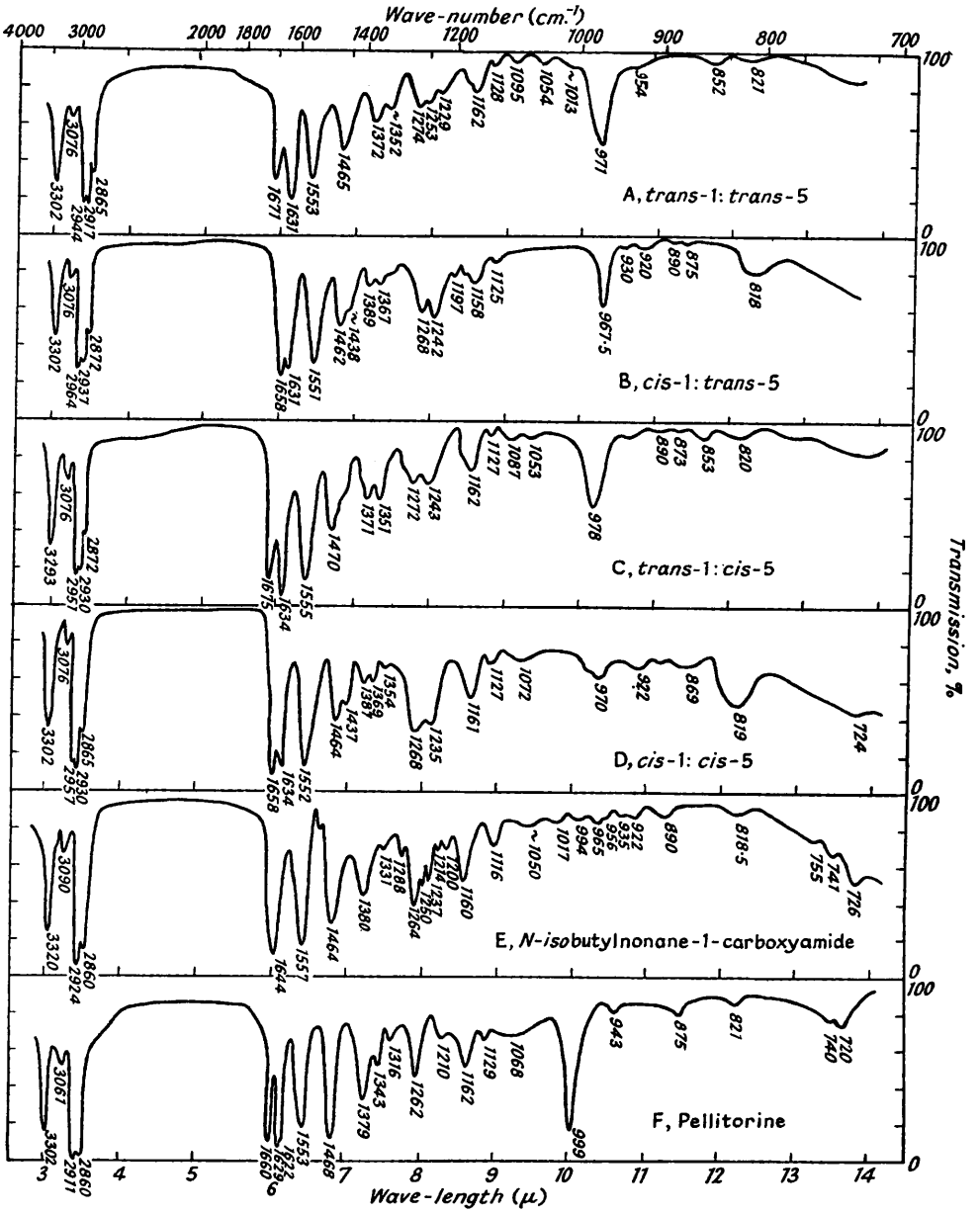
In Part I certain observations were made on the relation of geometrical stereochemistry to the infra-red absorption in the olefinic=C—H out-of-plane deformation region and in the C=C stretching region. The results obtained here may be interpreted along similar lines. The two isomers with *cis*-αβ-double bonds have the C=C stretching frequency at a lower value (1658 cm.$^{-1}$) than the *trans* (1675 and 1671 cm.$^{-1}$). In the region involving the deformation frequency of hydrogen atoms attached to an ethylenic linkage (Rasmussen, Brattain, and Zuco, *J. Chem. Physics*, 1947, **15**, 135; see also Part I), the *cis*-1 : *trans*-5- has absorption at lower frequencies (967·5 cm.$^{-1}$) than the *trans*-1 : *cis*-5-compound (978 cm.$^{-1}$). All this is as expected. The *cis-cis*-isomer shows some absorption in the latter region which is probably due to contamination with stereoisomers, arising because it is produced by partial catalytic (palladium) hydrogenation of a diyne (the extent of contamination, however, seems qualitatively greater than in the undeca-1 : 7-diene-1-carboxyamide series). Observations on *N-iso*butylnona-*trans*-1 : *trans*-5-diene-1-carboxyamide were somewhat disappointing; in the undeca-1 : 7-diene series two bands were resolved at 964·5 and 977 cm.$^{-1}$ due to the αβ- and the ηθ-double bonds respectively, but for the nonadiene only one band was obtained though its shape indicates that two unresolved bands are probably present. It is interesting that the qualitative fluctuations of intensity in the band at *ca.* 820 cm.$^{-1}$ and the two between 1230 and 1280 cm.$^{-1}$ (all of which are also present in the saturated analogue) parallel in this series of stereoisomers those observed in the undeca-1 : 7-diene series (Part I).

Since the general stereochemical assignments to the four *N-iso*butylnonadiene-1-carboxyamides can be accepted with some assurance, their relation to pellitorine may be examined. Direct comparison with a specimen of natural pellitorine, m. p. 73° (infra-red spectrum *F*), isolated from the root of *Anacyclus pyrethrum* showed that none was identical with it. Further, unlike pellitorine, they were comparatively stable substances and had low insecticidal potencies. Although they had a bitter taste and (particularly the

trans-1 : *cis*-5-isomer) some sialogogue activity these were not comparable with those of pellitorine. Jacobson's structure for pellitorine must be incorrect.

The situation therefore resembles that reached in Part I concerning Jacobson's structure

Infra-red spectra of N-iso*butylnona*-1 : 5-*diene*-1-*carboxyamides and related compounds.*



B—D, *Liquid films*; A, E, F, *paraffin mulls, paraffin absorption present.*

for herculin. However, there is one difference. Dr. Jacobson has kindly supplied the author with a sample of his natural pellitorine which on crystallisation had m. p. 73—74°. This was identical with the above specimen (mixed m. p.). We are thus certainly investigating the same material in this case.

Experimental

The ultra-violet light absorption data (in pure ethanol) were obtained by Mrs. I. M. Boston using a Hilger medium quartz instrument. Most of the analytical data and micro-hydrogenations are due to Mr. Oliver of the microanalytical laboratories of this College. The infra-red spectra were measured by the author on a single-beam instrument (see Part I) using liquid films or paraffin mulls; facilities for these measurements were kindly afforded by Dr. W. C. Price.

3-*Chlorotetrahydro*-2-n-*propylfuran*.—To a Grignard reagent prepared from magnesium (64 g.) and *n*-propyl bromide (328 g.) in anhydrous ether (600 ml.), cooled to 0°, freshly distilled 2 : 3-dichlorotetrahydropyran (250 g.) (Crombie and Harper, *J.*, 1950, 1714) diluted with an equal volume of ether was added slowly and with good stirring (particularly towards the end of the reaction when solid may separate). The reaction was controlled initially by cooling in ice but the temperature was later allowed to rise to that of the room. Next morning, ammonium chloride solution was added and as much of the ethereal layer as possible decanted. Sufficient concentrated hydrochloric acid was added to dissolve the basic magnesium halide (this caused some resinification) and the solution extracted with ether. The united ethereal solutions were washed with water and dried (K_2CO_3–Na_2SO_4). Removal of the ether and distillation (Dufton column) gave, after elimination of a small fore-run, *cis*- + *trans*-3-chlorotetrahydro-2-*n*-propyl furan (221 g., 83%), b. p. 65—80°/18 mm. (majority 74—77°). Normant (*Compt. rend.*, 1948, **226**, 733) gives b. p. 68—70°/12 mm.

Hept-3-*enol*.—Sodium (75 g.) was powdered under hot xylene, the xylene decanted, and the residue washed five times with ether. The metal was suspended in ether (700 ml.) and a few drops of 3-chlorotetrahydro-2-*n*-propylfuran were added. After a few minutes a vigorous reaction set in and the remainder of the chloro-compound (221 g. in all) was added dropwise at such a rate that steady refluxing was maintained. The surface of the sodium assumed a deep blue-purple colour. The product was set aside for 12 hours and then decomposed with water. Removal of the ethereal layer and extraction of the aqueous phase with ether gave a pale yellow solution which was washed and dried (Na_2SO_4). Distillation yielded hept-3-enol, b. p. 81—83°/19 mm., n_D^{20} 1·4425 (147·5 g., 87%) (presumed to be a mixture of *cis*- and *trans*-forms). Normant (*loc. cit.*) records b. p. 73°/12 mm. The *p*-diphenylylurethane (after one crystallisation) softened at 84° and melted at 87—92° to a turbid melt which cleared at 96°. On recrystallisation it had m. p. 97° after softening.

Hept-3-*ynol*.—(a) *Dehydrohalogenation procedure*. Bromine (185 g.) was added during 2 hours to hept-3-enol (132 g.) in ether (150 ml.) with vigorous stirring and cooling in ethanol–solid carbon dioxide (*ca.* 20°). The ether was then evaporated *in vacuo*. A solution of sodamide (from sodium, 100 g.; ferric nitrate, 2 g.) in liquid ammonia (2·5 l.) (Vaughn, Vogt, and Niewland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120) was treated rapidly with the 3 : 4-dibromoheptanol and the mixture stirred for a further 5 hours; ether (200 ml.) was added and the ammonia allowed to evaporate overnight; decomposition with water, extraction with ether (6 × 100 ml.), and distillation yielded crude hept-3-ynol (55·5 g., 42%), b. p. 86—111°/20 mm., n_D^{20} 1·4590, contaminated with monobromohept-3-enol. Fractionation gave pure hept-3-ynol (30 g., 23%), b. p. 86—88°/18 mm., n_D^{20} 1·4537.

(b) *From acetylene*. Sodium (46 g.) was added to liquid ammonia (2 l.) through which acetylene was passing at such a rate that a blue colour did not develop throughout the solution, whilst on the other hand a *considerable* excess of acetylene was never present. Towards the end of the reaction the blue colour was allowed to develop and just removed with acetylene by " titration " (Sondheimer, *J.*, 1950, 877). *n*-Propyl iodide (325 g.) in ether (300 ml.) was added dropwise and the product stirred for 4 hours. Then a solution of sodamide (from sodium 46 g., and liquid ammonia, 1·5 l.) was added and the whole stirred overnight. Excess of ethylene oxide (220 g.) was added in one portion and the mixture stirred for 30 hours. After addition of ether the excess of ammonia was allowed to evaporate and the residue decomposed with dilute hydrochloric acid. Extraction with ether and fractionation of the product (Stedman column) gave hept-3-yn-1-ol (48·6 g., 23%), b. p. 117—120°/83 mm., n_D^{20} 1·4550. Its 3 : 5-dinitrobenzoate crystallised from light petroleum in needles, m. p. 62°. Newman and Wotiz (*J. Amer. Chem. Soc.*, 1949, **71**, 1292) obtained a 30% yield from pentynylsodium and ethylene oxide in liquid ammonia, and report b. p. 111°/70 mm., n_D^{25} 1·4530, and a 3 : 5-dinitrobenzoate of m. p. 61°.

Ca. 70 g. of material of b. p. 240—242° were also isolated. Its infra-red spectrum indicated the presence of a primary hydroxyl grouping (3250 cm.$^{-1}$, broad; 1054 cm.$^{-1}$, medium-strong), a C≡C linkage situated internally (2222 cm.$^{-1}$, weak) and an ether linkage (1122 cm.$^{-1}$, strong).

Persistently low analyses for carbon were obtained (Found: C, 68·25, 68·15, 68·25; H, 10·3, 10·15, 10·25. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%). Microhydrogenation: 1·84 H_2. The p-*diphenylylurethane* crystallised from light petroleum (b. p. 60—80) in prisms, m. p. 88 (Found: C, 74·75; H, 7·35. $C_{22}H_{25}O_3N$ requires C, 75·2; H, 7·15%). A 3 : 5-*dinitrobenzoate* was also prepared, of m. p. 62° [needles from light petroleum (b. p. 40—60°)] (Found: C, 54·65; H, 4·85. $C_{16}H_{18}O_7N_2$ requires C, 54·85; H, 5·2%). Its appearance differed from that of the 3 : 5-dinitrobenzoate of hept-3-ynol (m. p. 62°) and on admixture the m. p. was depressed (partly melted 45°; turbid liquid 50°). It seems that the yield of hept-3-ynol could be considerably increased by using less ethylene oxide in this preparation.

trans-n-*Hept-3-en-1-ol*.—Hept-3-ynol (20 g.) was added in ether (25 ml.) to a solution of sodium (20 g.) in liquid ammonia (600 ml.) and stirred for 2 hours. After the addition of an excess of ammonium chloride, ether (50 ml.) was added and the ammonia evaporated. Water was added and the ethereal layer separated, washed, and distilled, to yield trans-n-*hept-3-en-1-ol* (17·2 g., 84%), b. p. 170—171°, n_D^{20} 1·4415 (Found: C, 74·1; H, 12·45. $C_7H_{14}O$ requires C, 73·6; H, 12·35%). The p-*diphenylylurethane* crystallised from light petroleum (b. p. 60—80°) as needles, m. p. 105° (Found: C, 77·6; H, 7·6. $C_{20}H_{23}O_2N$ requires C, 77·6; H, 7·4%).

trans-n-*Hept-3-enyl Bromide*.—Phosphorus tribromide (4·0 ml.) was added to a mixture of *trans*-hept-3-enol (13·0 g.) and pyridine (2·0 ml.) with stirring and cooling in ice. After stirring (30 minutes) the crude bromide was distilled directly from the flask at 100 mm. (b. p. 105—140°) and worked up as described for the *cis*-isomer (below). Distillation gave trans-n-*hept-3-enyl bromide* (13·2 g., 57·5%), b. p. 169—179°; on redistillation the main portion had b. p. 172—175°, n_D^{25} 1·4641 (Found: Br, 44·65. $C_7H_{13}Br$ requires Br, 45·15%).

trans-*Oct-4-enal*.—A Grignard reagent, prepared from *trans*-hept-3-enyl bromide (10·4 g.) and magnesium (1·4 g.) in ether (25 ml.) was treated with ethyl orthoformate (8·8 g.) and refluxed for 3·5 hours. The mixture was worked up as described for the *cis*-isomer and gave *trans*-oct-4-enal (2·75 g., 40%), b. p. 173°, n_D^{20} 1·4360 (Found: C, 76·15; H, 11·1. Calc. for $C_8H_{14}O$: C, 76·1; H, 11·2%). The 2 : 4-dinitrophenylhydrazone crystallised from ethanol in long golden-yellow needles, m. p. 110° (Found: C, 55·3; H, 6·2; N, 18·2. Calc. for $C_{14}H_{18}O_4N_4$: C, 54·9; H, 5·9; N, 18·3%). Jacobson (*loc. cit.*) gave b. p. 80—84°/13 mm., n_D^{25} 1·4463; 2 : 4-dinitrophenylhydrazone, m. p. 108°.

Nona-trans-1 : trans-5-*diene*-1-*carboxylic Acid*.—*trans*-Oct-4-enal (1·26 g.) was set aside with malonic acid (1·04 g.) and pyridine (1·0 ml.) for 4 days. All the solid had dissolved with effervescence and the mixture was then heated on the steam-bath for 2 hours to complete decarboxylation. Isolation of the acid (0·80 g., 48%) was effected as described for the *trans*-1-*cis*-5-isomer. The acid crystallised from the distillate in plates which, when dried between filter papers, had m. p. 42—43°. Jacobson (*loc. cit.*) records m. p. 35°.

The p-*bromophenacyl* ester formed plates (from ethanol–water), m. p. 87° (Found: C, 58·9; H, 6·05. $C_{18}H_{21}O_3Br$ requires C, 59·2; H, 5·8%). For further data see Table.

N-iso*Butyl*-trans-1 : trans-5-*diene*-1-*carboxyamide*.—The *trans-trans*-acid (350 mg.) was treated with thionyl chloride (0·25 ml.) and set aside for 90 minutes. The crude acid chloride was diluted with benzene (3 ml.), and excess of *iso*butylamine (0·8 ml.) added with cooling. Working up in the usual way and distilling gave the *trans-trans-iso*butylamide (292 mg., 63%), needles, m. p. 52°; when admixed with the specimen kindly supplied by Dr. Jacobson (m. p. 53—54°) its m. p. was raised to 53—54°. For further data see Table.

cis-*Hept-3-enol*.—Hept-3-ynol (23·5 g.) was hydrogenated without a solvent in the presence of 3% palladium–calcium carbonate until 4·5 l. of hydrogen had been absorbed (1 mol., 4·7 l.; volumes corrected to N.T.P.). Ether and filter-cel were added and the catalyst filtered off. cis-*Hept-3-enol*, isolated by distillation, had b. p. 80—82°/18 mm., n_D^{20} 1·4435 (22·0 g., 92%) (Found: C, 73·85; H, 12·75. $C_7H_{14}O$ requires C, 73·6; H, 12·35%). The p-*diphenylylurethane* crystallised from light petroleum (b. p. 80—100°) as needles, m. p. 84—85° (Found: C, 78·05; H, 7·55. $C_{20}H_{23}O_2N$ requires C, 77·6; H, 7·4%).

cis-*Hept-3-enyl Bromide*.—*cis*-Hept-3-enol (20·5 g.) was cooled in ice, and pyridine (4·1 ml.) added. Phosphorus tribromide (19·5 g.) was then added dropwise with stirring during 1·5 hours and the mixture allowed to warm to room temperature and left for a further hour. The crude bromide was isolated by direct distillation at 210 mm. (31·6 g.). It was washed with 10% sodium hydroxide solution, 10% hydrochloric acid, and water, separations being aided by the addition of light petroleum (b. p. 40—60°). cis-*Hept-3-enyl bromide*, isolated by removal of the solvent and distillation (26·6 g., 79%), had b. p. 68—72°/15 mm., n_D^{20} 1·4705 (Found: C, 47·8; H, 7·65. $C_7H_{13}Br$ requires C, 47·5; H, 7·4%).

cis-*Oct-4-enal*.—A Grignard reagent was prepared from *cis*-hept-3-enyl bromide (25·0 g.) and

magnesium (3·3 g.) in ether (40 ml.). After 20 minutes' refluxing freshly distilled ethyl orthoformate (20 g.; b. p. 146—148°) was added to the cooled reagent, the mixture refluxed for a further 6 hours, and the ether then distilled. Ice-cold 6% hydrochloric acid was added (90 ml.) and the emulsion which resulted was broken by the addition of 6% sulphuric acid (100 ml.). The upper acetal layer was separated. Steam-distillation of the aqueous acid phase showed that the amount of acetal or aldehyde contained in it was quite small.

The acetal was steam-distilled with 4% sulphuric acid (200 ml.), and the crude volatile aldehyde collected and purified by shaking it with sodium metabisulphite (20 g.) in water (60 ml.). Traces of undissolved material were rejected. cis-*Oct*-4-*en*-1-*al* (8·8 g., 58%), liberated by the addition of excess of sodium hydrogen carbonate and steam-distilled, had b. p. 173°, n_D^{20} 1·4353 (Found: C, 75·3; H, 11·15. $C_8H_{14}O$ requires C, 76·1; H, 11·2%). The 2 : 4-*dinitrophenylhydrazone* crystallised in yellow needles (from ethanol), m. p. 81° (Found: C, 54·65; H, 6·1; N, 17·7. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%).

Nona-trans-1 : cis-5-*diene*-1-*carboxylic Acid*.—*cis*-Oct-4-enal (4·2 g.) was added to an ice-cooled mixture of malonic acid (3·47 g.) and anhydrous pyridine (3·2 ml.). Two liquid phases were formed and much malonic acid remained undissolved. After 40 hours at room temperature the mixture became homogeneous; it was then heated for 2 hours on a water-bath. The product was cooled, acidified with 50% ice-cold sulphuric acid (Congo-red), and the acidic and the neutral material were isolated with light petroleum (b. p. 40—60°). The petroleum solution was thoroughly extracted with aqueous sodium hydrogen carbonate. The acid was liberated from the aqueous phase by just acidifying it under light petroleum (b. p. 40—60°). Drying (Na_2SO_4) and removal of the petroleum gave *nona*-trans-1 : cis-5-*diene*-1-*carboxylic acid* (2·32 g., 59%) (Found: C, 72·0; H, 9·85. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). A white to buff polymer fairly soluble in ether, remained in the distillation flask. The acid was characterised as its p-*bromophenacyl* ester which crystallised from ethanol–water as needles, m. p. 44—45° (Found: C, 59·4; H, 5·95%).

Nona-trans-1 : cis-5-*diene*-1-*carboxyl Chloride*.—Thionyl chloride (1·40 g.) was added slowly to nona-*trans*-1 : *cis*-5-diene-1-carboxylic acid (1·50 g.) and set aside overnight. Removal of the excess of thionyl chloride under vacuum and distillation gave the *acid chloride* (1·47 g., 88%), b. p. 118°/16 mm., n_D^{20} 1·4817 (Found: C, 64·4; H, 8·25; Cl, 19·75. $C_{10}H_{15}OCl$ requires C, 64·3; H, 8·1; Cl, 19·0%).

N-iso*Butylnona*-trans-1 : cis-5-*diene*-1-*carboxyamide*.—To the *trans*-1 : *cis*-5-acid chloride, (1·03 g.) in light petroleum (b. p. 40—60°) redistilled *iso*butylamine (1·00 g.) was added slowly. The solution was washed with water, dried, and evaporated, and the residue distilled, to give the required iso*butylamide*, as an almost colourless and rather viscous liquid (1·13 g., 92%) (Found: C, 75·0; H, 11·55; N, 6·05. $C_{14}H_{25}ON$ requires C, 75·25; H, 11·3; N, 6·25%).

trans-*Nona*-5-*ene*-1-*yne*-1-*carboxylic Acid*.—A Grignard reagent was prepared from propargyl bromide (23·0 g.; Kirrmann, *Bull. Soc. chim.*, 1926, **39**, 698) and magnesium (4·6 g.) in ether (60 ml.) a little mercuric chloride being used to start the reaction. It was cooled to 20° and *trans*-hex-2-enyl bromide (28·5 g.; Bouis, *Ann. Chim.*, 1928, **9**, 403) in ether (30 ml.) added dropwise. This caused gentle refluxing and two phases formed. The product was set aside for 18 hours, refluxed for 1 hour, cooled, and decomposed with water (vigorous reaction) followed by dilute hydrochloric acid. The ethereal layer was separated, the aqueous phases extracted, and the united ethereal extracts were dried and distilled. Six fractions were collected: (1) b. p. 55—105°, n_D^{21} 1·4430 (2·0 g.); (2) b. p. 105—125°, n_D^{21}·1·4541 (2·0 g.); (3) b. p. 125—136°, n_D^{21} 1·4528 (2·5 g.); (4) b. p. 136—141°, n_D^{21} 1·4520 (2·8 g.); (5) b. p. 141—144°, n_D^{21} 1·4522 (11·9 g. Found: Br, 23·6%); (6) temperature falling, n_D^{21} 1·4568 (2·1 g.). Fractions (2)—(4) and the first runnings of (5) were turbid, but slowly cleared. Fractions (4) and (5) were bulked and used below (Found: C, 67·3; H, 9·1; Br, 22·9%). Infra-red spectral examination showed a sharp band (medium-strong) at 3290 cm.$^{-1}$ (−C≡CH), a weak band at 2110 cm.$^{-1}$ attributable to the acetylenic carbon–carbon stretching frequency in an R·C≡CH environment, and the internal *trans*-olefin frequency (966 cm.$^{-1}$, strong). Johnson and McEwen's reagent gave a turbidity (yellow-green) with only slight precipitation, changing to greyish (cf. *trans*-undeca-7-ene-1-yne, Part I). Another preparation yielded crude material of b. p. 148—150°, n_D^{21} 1·4436.

The crude coupling product (13·1 g.) was added to a Grignard reagent prepared from ethyl bromide (23·4 g.) and magnesium (5·16 g.) in ether and refluxed for 4 hours. It was then sealed in an autoclave with a large excess of solid carbon dioxide for 18 hours. Decomposition with dilute hydrochloric acid, purification through sodium hydroxide solution in the usual way, and distillation yielded trans-*non*-5-*ene*-1-*yne*-1-*carboxylic acid* (6·2 g., 25% overall), b. p. 109—111°/0·2 mm., n_D^{20} 1·4778 (Found: C, 72·05; H, 8·6. $C_{10}H_{14}O_2$ requires C, 72·25; H, 8·5%).

Its p-*bromophenacyl* ester crystallised from ethanol in plates or needles, m. p. 82° (Found: C, 59·4; H, 5·5. $C_{18}H_{19}O_3Br$ requires C, 59·6; H, 5·3%).

Hydrogenation of the enyne-acid yielded a product which rapidly solidified (m. p. 31°). The m. p. was undepressed in admixture with authentic nonane-1-carboxylic acid (m. p. 31·5°).

Nona-cis-1 : trans-5-*diene*-1-*carboxylic Acid*.—The enyne-acid (1·57 g.) were hydrogenated in ethyl acetate over palladium–calcium carbonate until 220 ml. of gas was absorbed (1 mol. = 226 ml. at 20°/764 mm.). Filtration and distillation yielded the required *acid* (1·43 g.), n_D^{17} 1·4730 (Found: C, 71·0; H, 9·6%). Crystallisation of its p-*bromophenacyl* ester gave plates (from ethanol–water), m. p. 58° (Found: C, 58·6; H, 5·8%).

N-iso*Butylnona*-cis-1 : trans-5-*diene*-1-*carboxyamide*.—The above acid (850 mg.) was heated under reflux with oxalyl chloride (1·5 ml.) in benzene (5 ml.) for 1 hour and the solvent and excess of reagent were removed *in vacuo* at 20°. More benzene (3 ml.) was added and the process repeated. The crude acid chloride was diluted with ether and the *amide* prepared as described above. On distillation it (85%) had $n_D^{22\cdot5}$ 1·4820 (Found: C, 75·2; H, 11·0; N, 6·0%). The material did not crystallise.

A second specimen was made from *trans-N-iso*butylnon-5-en-1-yne-1-carboxyamide. The latter (b. p. 138°/4 × 10^{-3} mm., n_D^{23} 1·4858) was prepared by the oxalyl chloride method and semihydrogenated in the usual way, to give the *cis*-1 : *trans*-5-*iso*butylamide (n_D^{22} 1·4780, $\lambda_{max.}$ 227 mμ; $\varepsilon_{max.}$ 8250). It was probably less pure than the other specimen. During the preparation of the enyne-*iso*butylamide colourless needles were isolated which were almost insoluble in light petroleum (b. p. 40—60°) but crystallised readily from ethanol and then had m. p. 170° (Found: C, 59·9; H, 10·25. Calc. for $C_{10}H_{20}O_2N_2$: C, 59·95; H, 10·05%). It is the di*iso*butylamide of oxalic acid, indicating that the excess of oxalyl chloride had not been completely removed. Chablay (*Ann. Chim.*, 1914, **1**, 495) gives m. p. 169°.

Insecticidal Tests.—These were carried out through the kindness of Dr. C. Potter by Mr. M. Elliott and Mr. P. Needham of the Department of Insecticides and Fungicides, Rothamsted Experimental Station. Application of 0·004 ml. of the acetone solutions (below) was made dorsally between the prothorax and the mesothorax to adults of *Tenebrio molitor* (male and female). The results were as follows:

	Concn. (%, w/v)	Kill (%)		Concn. (%, w/v)	Kill (%)
trans-1 : *trans*-5	1·92	4	*cis*-1 : *cis*-5	2·64	8
cis-1 : *trans*-5	2·02	0	Natural pellitorine [1]	1·17	88
trans-1 : *cis*-5	1·92	4			

[1] Crude specimen, m. p. 59—63°.

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