Amides of Vegetable Origin. Part XII.† A New Series of Alka-2,4-dienoic Tyramine-amides from *Anacyclus pyrethrum* D.C. (*Compositae*)

By **R. S. Burden** and **L. Crombie,***‡ Department of Chemistry, University College (University of Wales), Cathays Park, Cardiff

Anacyclus pyrethrum D.C. (Compositae) contains *N*-(2′-*p*-hydroxyphenylethyl) deca-, dodeca-, and tetradeca-*trans*-2, *trans*-4-dienamide, a new series of tyramine amides corresponding to isobutylamides which this plant produces. The tyramides, and the corresponding isobutylamides, are synthesised stereospecifically by phosphonate-anion synthesis. *Anacyclus pyrethrum* is found to contain the lignan (+)-sesamin and attention is drawn to the co-occurrence of lipid (and other) amides with lignans in a number of plants from three families (Compositae, Piperaceae, and Rutaceae).

LIPID isobutylamides with characteristic olefinic and acetylenic unsaturation patterns form a distinct group of natural products and have been isolated from members of the Compositae, Piperaceae, and Rutaceae families. The polyene members frequently possess sialogogue and insecticide activity. *Anacyclus pyrethrum* D.C. (Compositae) roots contain the dienamide (I) (and homologous relatives) in the pellitorine fraction,[1,2] together with anacyclin (II),[2] which has been synthesised.[3,4] The latter is neither a sialogogue nor an insecticide but takes on these properties after semihydrogenation of the acetylene linkages.[2] This plant also contains the enetriyne alcohol (III).[5] In this paper we report the occurrence and synthesis of a second series of lipid

$$Me[CH_2]_4\cdot CH{=}CH\cdot CH{=}CH\cdot CO\cdot NHBu^i \quad (I)$$

$$MeC{\equiv}C\cdot C{\equiv}C\cdot[CH_2]_2\cdot CH{=}CH\cdot CH{=}CH\cdot CO\cdot NHBu^i \quad (II)$$

$$MeC{\equiv}C\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH{=}CH\cdot[CH_2]_2\cdot CH(OH)Et \quad (III)$$

amides in *Anacyclus pyrethrum*, with tyramine replacing isobutylamine.

Chromatography of the less-soluble material from the light petroleum extracts of the roots gave a crystalline fraction, m.p. 112—114°, at first thought to be homogeneous (t.l.c.). It had $\lambda_{max.}$ 259 nm. ($E^{1\%}_{1\,cm.}$ 1000),

† Part XI, L. Crombie and M. Manzoor-i-Khuda, *J. Chem. Soc.*, 1963, 4984.

‡ *Present address:* Department of Chemistry, The University, Nottingham, NG7 2RD.

[1] L. Crombie, *J. Chem. Soc.*, 1952, 4338; *Chem. and Ind.*, 1952, 1034.

[2] L. Crombie, *Nature*, 1954, 174, 832; *J. Chem. Soc.*, 1955, 999.

[3] L. Crombie and M. Manzoor-i-Khuda, *Chem. and Ind.*, 1956, 409; *J. Chem. Soc.*, 1957, 2767.

[4] F. Bohlmann and E. Inhoffen, *Chem. Ber.*, 1956, **89**, 1276.

[5] F. Bohlmann and C. Arndt, *Chem. Ber.*, 1965, **98**, 1411.

$\nu_{max.}$ (mull) 3300, 3070 (NH, amide), 1635 (amide A), 1550 (amide B), 1660, 1615 (conj. diene), 995 cm.$^{-1}$ (without absorption at 960—965 cm.$^{-1}$: characteristic of a conjugated *trans–trans* diene [6]), suggesting that it was a conjugated monosubstituted dienamide. A broad band at 3200—3400 cm.$^{-1}$ was assigned to a hydroxy-group. As expected of such a *trans–trans*-conjugated dienamide, a maleic anhydride adduct formed readily (for structure *cf.* ref. 3), the high intensity absorption at 259 nm. being extinguished and replaced by a weaker maximum at 277 nm. ($E^{1\%}_{1cm.}$ 50). The latter was intensified and shifted to longer wavelength on addition of alkali, suggesting that the hydroxy-group was phenolic. Hydrogenation (Pd–C), followed by acid hydrolysis gave tyramine hydrochloride, identical with authentic material.

Analyses were unsharp, and mass spectral examination showed why. The substance m.p. 112—114° contained three parent peaks *m/e* 343, 315, and 287 corresponding to *N*-(2′-*p*-hydroxyphenylethyl)-deca-, -dodeca-, and -tetradeca-*trans*-2, *trans*-4-dienamide (VI; R = $Me[CH_2]_4$, $Me[CH_2]_6$, and $Me[CH_2]_8$), in the approximate ratio 40 : 50 : 10. ^{1}H N.m.r. data were in agreement, showing resonances at τ 2·2br (s, 1H, amide proton), 3·14 (q, 4H, J 8 Hz, two identical pairs of *o*-ArH), 2·8—4·5 (m, 4H, olefinic protons), 6·5 (m, 2H, C-1′-methylene), 7·3 (t, 2H, J 7 Hz, C-2′-methylene), 7·9 (m, 2H, C-6-methylene), 8·75 broad (s, *ca.* 9 methylene protons), 9·15 (t, 3H, terminal methyl). The count of *ca.* 9 methylene protons arises because of the mixture of chain-lengths.

Because of difficulties in separating the homologues, the three structures were confirmed by synthesis. All four geometrical isomers of deca-2,4-dienoic acid, and their methyl esters and isobutylamides had been prepared earlier [6] but a different technique for the *trans–trans*-stereoisomer is employed below. For this work we need a synthetic method whereby an homologous series can be constructed from one principal intermediate and we have used the phosphonate anion technique developed by Horner [7] and Wadsworth.[8] This method of double-bond construction is favourable to the formation of a *trans*-linkage [8] though conditions producing the *cis*-isomer arise when there is steric compression, especially when the phosphorus-bearing carbon of the phosphonate is branched.[9] Factors leading to production of much *cis*-material would not be expected in the present case.

The required phosphonate (IV) was prepared by a Michaelis–Arbuzov reaction [10] from methyl 4-bromocrotonate and triethyl phosphite. Condensation of the phosphonate anion with n-hexanal gave methyl deca-2,4-dienoate (V; R = $Me[CH_2]_4$, R^1 = OMe) which, from comparison with our earlier spectra of the four possible geometrical isomers,[6] was almost entirely *trans–trans*. Similarly n-octanal and n-decanal gave methyl dodeca- and tetradeca-*trans*-2, *trans*-4-dienoate. Reaction conditions are mild, work-up simple, and yields 25—30%. Though complete analysis of the n.m.r. data for the olefinic protons was not possible because of the close similarity in chemical shift of the 4- and 5-protons, the spectrum of the decadienoate was similar to that for methyl *trans–trans*-sorbate [11] with $J_{2,3}$ 15·8 and $J_{3,4}$ 10·5 Hz as expected.

$$(EtO)_2P(O)\cdot CH_2CH{=}CH\cdot CO_2Me \qquad (IV)$$

$$\downarrow \text{NaOMe–DMF, RCHO}$$

$$R\text{-}CH{=}CH\cdot CH{=}CH\cdot COR^2 \qquad (V)$$

$$\downarrow$$

$$RCH{=}CH\cdot CH{=}CH\cdot CO\cdot NH\cdot[CH_2]_2\cdot C_6H_4\cdot OH\text{-}p$$

or, $$RCH{=}CH\cdot CH{=}CH\cdot CO\cdot NH\cdot CH_2\cdot CHMe_2 \qquad (VII)$$

Hydrolysis gave the crystalline acids (V; R^2 = OH) which were converted into the acid chlorides (V; R^2 = Cl) with oxalyl chloride. Reaction with tyramine in diglyme gave the three tyramides (VI; R = $Me[CH_2]_4$) m.p. 132—133°, (VI; R = $Me[CH_2]_6$) m.p. 140—141°, and (VI; R = $Me[CH_2]_8$) m.p. 141·5—142·5°. Spectral information agrees with that obtained for the mixture, and a 4 : 5 : 1 mixture simulates the properties of the natural mixture isolated. Neither the natural mixture, nor the synthetic tyramides, are sialogogues. The three corresponding isobutylamides (VII; R = $Me[CH_2]_4$) m.p. 88—89°, (VII; R = $Me[CH_2]_6$) m.p. 89—90°, and (VII; R = $Me[CH_2]_8$) m.p. 86—87°, much less stable in light and air than the tyramides, were also made; they are sialagogues.

Apart from the occurrence of these amides in *Anacyclus pyrethrum*, *N*-isobutyldeca-*trans*-2, *trans*-4-dienamide occurs in *Fagara xanthoxyloides*,[12] *Piper longum* [13] and *Piper peepuloides* [13]: *N*-isobutyltetradeca-*trans*-2, *trans*-4-dienamide has been found in *Chrysanthemum frutescens* L.[14] Whilst our work was in progress Bohlmann and Miethe [15] described a Wittig synthesis of the latter in which the phosphorane derived from methyl 4-bromocrotonate was treated with decanal to give methyl deca-2,4-dienoate (mixed stereoisomers) which was converted into a mixture containing 55% *trans*-2,*trans*-4-dienamide and 45% of *trans*-2,*cis*-4-dienamide (overall yield 15%). The isomer mixture was

[6] L. Crombie, *J. Chem. Soc.*, 1955, 1007.
[7] L. Horner, H. Hoffmann, and H. G. Wippel, *Chem. Ber.*, 1958, **91**, 61; L. Horner, H. Hoffmann, H. G. Wippel, and G. Klahre, *ibid.*, 1959, **92**, 2499.
[8] W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1733; D. H. Wadsworth, O. E. Schupp, E. J. Seus, and J. A. Ford, *J. Org. Chem.*, 1965, **30**, 680.
[9] T. H. Kinstle and B. Y. Mandanas, *Chem. Comm.*, 1968, 1699.
[10] G. M. Kosolapoff, 'Organo Phosphorus Compounds,' John Wiley and Sons, Inc., New York, 1950, p. 121; P. J. vanden Tempel and H. O. Huisman, *Tetrahedron*, 1966, **22**, 293; K. Sato, S. Mizuno, and M. Hirayama, *J. Org. Chem.*, 1967, **32**, 177.
[11] J. A. Elvidge and P. D. Ralph, *J. Chem. Soc.* (*B*), 1966, 243.
[12] K. Bowden and W. J. Ross, *J. Chem. Soc.*, 1963, 3503.
[13] K. L. Dhar and C. K. Atal, *Indian J. Chem.*, 1967, **5**, 588.
[14] F. Bohlmann and C. Zdero, *Chem. Ber.*, 1967, **100**, 104.
[15] F. Bohlmann and R. Miethe, *Chem. Ber.*, 1967, **100**, 3861.

separated by chromatography. It thus appears that in work of this kind where the *trans–trans*-compound is the objective, phosphonate synthesis offers advantages in yield and convenience over the Wittig reaction.

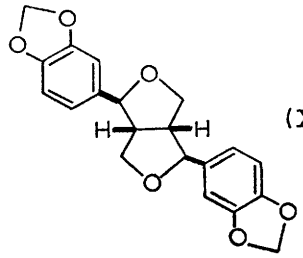
It seems likely the amide residues in the isobutylamide and tyramide series arise biogenetically from valine and tyrosine respectively. Although the fatty acid tyramides are novel, the tyramide residue occurs in an amide (VIII) recently isolated from *Evodia belahe* B.,[16] in *O*- and *N*-methylated form in herclavin (IX) which occurs together with the isobutylamide neoherculin in *Zanthoxylum clavaherculis*,[17,18] and in hydroxylated and *O*-methylated form in aegelin (X) from *Aegle marmelos*.[19] These are all members of the Rutaceae.

p-$HOC_6H_4CH{=}CH{\cdot}CO{\cdot}NH{\cdot}CH_2CH_2{\cdot}C_6H_4{\cdot}OH$-*p* (VIII)

$PhCH{=}CH{\cdot}CO{\cdot}NMe{\cdot}CH_2CH_2{\cdot}C_6H_4{\cdot}OMe$-*p* (IX)

$PhCH{=}CH{\cdot}CO{\cdot}NH{\cdot}CH_2CH(OH){\cdot}C_6H_4{\cdot}OMe$-*p* (X)

During the chromatographic examination of *Anacyclus pyrethrum* extractive, a compound $C_{20}H_{18}O_6$, m.p. 120° was encountered. It had $[\alpha]_D^{25}$ +67°, $\lambda_{max.}$ 236 (8200) and 286 (7800) nm., with i.r. bands assignable to aromatic and methylenedioxy-groups. This information led to recognition of the compound as (+)-sesamin (XI) which has been isolated from *Sesamum indicum* (sesame oil),[20,21] *Paulownia tomentosa*[22] and *Piper clusii*.[23] Its identity was confirmed by a study of the ^1H n.m.r. spectrum which was essentially as described by Becker and Beroza[24] and differed from spectra obtained for other geometrical isomers possible with this ring system. The absolute configuration of (+)-sesamin had been determined[25] and the racemate has been synthesised.[26]



(XI)

Co-occurrence of lipid isobutylamides (and other amides) with lignans seems frequent and may be of phytochemical interest: Some instances are summarised in the Table.

Co-occurrence of lipid amides and lignans *

Compositae	Amide	Lignan
Anacyclus pyrethrum	Anacyclin;[2] Pellitorine amides;[2] Tyramine amides †	(+)-Sesamin †
Heliopsis Scabra (*Heliopsis helianthoides var. scabra*)	Scabrin;[27] Heliopsin[28]	Helioxanthin;[29] (−)-Helianthoidin[29]
Piperaceae		
Piper longum	*N*-Isobutyldeca-*trans*-2,*trans*-4-dienamide;[13] Piplartine (Piperlongumine) [Piperlonguminine][30–32]	(+)-Sesamin[30]
Piper peepuloides	*N*-Isobutyldeca-*trans*-2,*trans*-4-dienamide;[13] [Peepuloidin][34]	(+)-Diaeudesmin[33]
Rutaceae		
Fagara xanthoxyloides (*Zanthoxylum senegalense*)	*N*-Isobutyldeca-*trans*-2,*trans*-4-dienamide[12]	(±)-Sesamin[35]
Zanthoxylum clava-herculis	Neoherculin;[17] Herclavin[17,18]	(−)-Asarinin[17]
Zanthoxylum piperitum	Neoherculin[36] (α-Sanshoöl)[36]	(−)-Sesamin[36]

* Synonyms in curved brackets: relevant amides of aromatic acids in square brackets. † Present work.

EXPERIMENTAL

Extraction of Pellitory Root and Fractionation of Components.—Dried, ground root (3·5 kg.) was extracted in a Soxhlet for 48 hr. with light petroleum (b.p. 40—60°). A small quantity of yellow oil was deposited. When the extract was concentrated (2 l.) and cooled to 0°, further yellow oil was obtained. The combined yellow oil samples (3 g.) were washed with light petroleum, dissolved in a little ether, and chromatographed on alumina (N III) [fractions monitored by t.l.c. (benzene–dioxan–acetic acid 90 : 25 : 4)]. Light petroleum–ether (1 : 1) eluted material shown to be homogeneous by t.l.c. Removal of the solvent

[16] J. Rondest, M. B. C. Das, and J. Polonsky, *Bull. Soc. chim. France*, 1968, 2411.
[17] L. Crombie, *J. Chem. Soc.*, 1952, 2997; 1955, 995.
[18] F. B. LaForge and W. F. Barthel, *J. Org. Chem.*, 1944, **9**, 250.
[19] A. Chatterjee, S. Bose, and S. K. Krinany, *J. Org. Chem.*, 1959, **24**, 687; R. N. Chakravarti and B. Dasgupta, *Chem. and Ind.*, 1955, 1632.
[20] W. M. Hearon and W. S. MacGregor, *Chem. Rev.*, 1955, **55**, 957.
[21] P. Budowski and K. S. Markley, *Chem. Rev.*, 1951, **48**, 125.
[22] K. Takahashi, Y. Tanake, K. Kobayayashi, and T. Nakagawa, *Yakugaha Zasshi*, 1963, **83**, 1101 (*Chem. Abs.*, 1964, **60**, 10,661).
[23] D. Hoensel and D. Zander, *Arch. Pharm.*, 1961, **294**, 699 (*Chem. Abs.*, 1962, **56**, 7423).
[24] E. D. Becker and M. Beroza, *Tetrahedron Letters*, 1962, 157.
[25] K. Freudenberg and G. S. Sidhu, *Tetrahedron Letters*, 1960, **20**, 3.
[26] K. Freudenberg and E. Fisher, *Chem. Ber.*, 1956, **89**, 1230.
[27] M. Jacobson, *J. Amer. Chem. Soc.*, 1951, **73**, 100.
[28] M. Jacobson, *J. Amer. Chem. Soc.*, 1957, **79**, 356.
[29] R. S. Burden, L. Crombie, and D. A. Whiting, *Tetrahedron Letters*, 1968, 1035; *J. Chem. Soc.* (*C*), 1969, 693.
[30] C. K. Atal, R. N. Girotra, and K. L. Dhar, *Indian J. Chem.*, 1966, **4**, 252.
[31] A. Chatterjee and C. P. Dutta, *Tetrahedron Letters*, 1966, 1797; *Tetrahedron*, 1967, **23**, 1769.
[32] B. S. Joshi, V. N. Kamat, and A. K. Saksena, *Tetrahedron Letters*, 1968, 2395.
[33] C. K. Atal, K. L. Dhar, and A. Pelter, *J. Chem. Soc.* (*C*), 1967, 2228.
[34] C. K. Atal, P. N. Moza, and A. Pelter, *Tetrahedron Letters*, 1968, 1397.
[35] B. Carnmalm, H. Erdtman, and Z. Pelchowicz, *Acta Chem. Scand.*, 1955, **9**, 1111; B. Carnmalm and H. Erdtman, *Chem. and Ind.*, 1955, 570.
[36] L. Crombie and J. L. Tayler, *J. Chem. Soc.*, 1957, 2760.

in vacuo and crystallisation from chloroform–light petroleum gave needles (280 mg., 0·008%), m.p. 118°, identified as anacyclin [lit.,[2] m.p. 121°] by spectroscopic comparison.

Elution by ether initially gave a mixture of two components: anacyclin and the tyramine amide complex of lower R_F. Further elution with ether gave the tyramine amides free from anacyclin. Concentration of the fractions and addition of light petroleum induced crystallisation (105 mg., 0·003%), m.p. 104—107°. Repeated recrystallisation gave m.p. 112—114°, homogeneous by t.l.c., and this sample was used for structure work.

The main, light petroleum extract was concentrated to 500 ml. and extracted with nitromethane. The nitromethane was removed under reduced pressure and the resulting yellow gum was dissolved in ether and chromatographed on alumina (N II). Light petroleum–ether (1 : 1) eluted a mixture of olefinic isobutylamides (4·3 g., 0·12%). No attempt to resolve this with polyamide and reverse-phase column and t.l.c. was completely successful.

Further elution with ether gave an anacyclin fraction but t.l.c. [benzene–ethyl acetate (8 : 2)] showed that this was not homogeneous and contained a small amount of a component of higher R_F. The latter could be separated from anacyclin by preparative layer chromatography (p.l.c.), or by fractional recrystallisation from ether–light petroleum, and was obtained as needles (30 mg., 0·001%), identified as (+)-sesamin. Anacyclin formed needles (1·4 g., 0·4%), m.p. 119°, spectroscopically identical with that above.

Tyramine Amide Complex.—This formed silky crystals, m.p. 112—114°; t.l.c. (benzene–dioxan–acetic acid 90 : 25 : 4) shows a single spot. Parent peaks in the mass spectrum were at *m/e* 287 (2·7), 315 (3·5), 343 (0·8).

Maleic Anhydride Adduct.—The tyramine amide mixture (10 mg.) and maleic anhydride (4·6 mg.) were heated in toluene (0·3 ml.) for 48 hr. in a sealed tube at 110°. The yellow solution was treated with charcoal, filtered, and evaporated. The crude product was crystallised from chloroform–light petroleum to give the adduct (2·5 mg.), m.p. 125° (unsharp): $\lambda_{max.}$ 277 ($E^{1\%}_{1\,cm.}$ 50) nm. $\lambda_{max.}$ (alkali) 294 ($E^{1\%}_{1\,cm.}$ 66) nm.

Hydrogenation and Hydrolysis of Tyramine Amides.—The tyramine amide mixture (20 mg.) was hydrogenated in ethyl acetate over 10% palladium–charcoal catalyst (10 mg.). The solution was filtered and the solvent was evaporated to yield a white solid which was dissolved in ethanol (1 ml.): concentrated hydrochloric acid (0·5 ml.) was added and the mixture was heated in a sealed tube at 100° for 24 hr. The solution was diluted with water and extracted with ether. The aqueous phase was evaporated to dryness and the resulting white solid crystallised from ethyl acetate–methanol to give tyramine hydrochloride (2 mg.), m.p. 260° (decomp.), undepressed on admixture with authentic tyramine hydrochloride. The i.r. spectra were identical.

Identification of (+)-*Sesamin.*—(+)-Sesamin formed needles, m.p. 120° (lit.,[20] m.p. 122—123°) (Found: C, 68·3; H, 5·09. Calc. for $C_{20}H_{18}O_6$: C, 67·8; H, 5·1%; mass spectrum parent ion, *m/e* 354·111. Calc. for $C_{20}H_{18}O_6$: 354·110); $[\alpha]_D^{25}$ +67° (*c*, 1·4%, $CHCl_3$) (lit.,[20] $[\alpha]_D^{21}$ +68·1°, $CHCl_3$); $\lambda_{max.}$ 286 (7800), 236 (8200) nm.; $\nu_{max.}$ (CCl_4) 2770 and 937 (methylenedioxy), 1608, 1500, and 1487 (Ar) cm.$^{-1}$; ^{1}H n.m.r. resonances ($CDCl_3$, 60 MHz) were at τ 3·0—3·2 (m, 6H, ArH), 4·01 (s, 4H, methylenedioxy protons), 5·25 (d, 2H, *J* 5 Hz, protons at C-2 and C-6), 5·55—6·25 (m, 4H, protons at C-4 and C-8), 6·8—7·1 (m, 2H, protons at C-1 and C-5).

Methyl 4-*Diethylphosphonocrotonate.*—Triethyl phosphite (100 g., 0·60 mol.) was maintained at 110° (oil bath) and methyl 4-bromocrotonate (100 g., 0·56 mole) was added dropwise to cause gentle reflux. When addition was complete, the mixture was heated to 150—160° for 30 min. Distillation gave methyl 4-diethylphosphonocrotonate (103 g., 72%), b.p. 115—130°/0·3 mm. (Found: C, 44·4; H, 7·65; P, 13·45. Calc. for $C_{15}H_{17}O_5P$: C, 45·7; H, 7·2; P, 13·2%).

Methyl Deca-trans-2,trans-4-*dienoate.*—Methyl 4-diethylphosphonocrotonate (20·0 g., 0·085 mol.) and hexanal (8·5 g., 0·085 mol.) in redistilled dimethylformamide (50 ml.) were vigorously stirred at room temperature and sodium methoxide (5·4 g., 0·1 mol.) in dry methanol was added dropwise during 1 hr. The solution was diluted with an excess of water and then extracted several times with light petroleum (ether tended to produce emulsions) and the extracts were washed with water. Evaporation and distillation gave methyl deca-*trans*-2, *trans*-4-dienoate (3·8 g., 25%), b.p. 71—73°/0·4 mm., n_D^{26} 1·4875 (lit.,[6,37] b.p. 70°/0·2 mm., n_D^{25} 1·4805, b.p. 69—70°/0·25 mm., n_D^{20} 1·4928) (Found: C, 72·2; H, 9·9. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·9%), $\lambda_{max.}$ 261 (27,400) nm.; $\nu_{max.}$ (liquid film) 1723 (ester), 1648 and 1620 (C=C), 1002 ($[CH{=}CH]_t$) cm.$^{-1}$; ^{1}H n.m.r. resonances (CCl_4, 60 MHz) were at τ 2·80 (dd, 1H, *J* 15 Hz, *J* 10 Hz, 3-H), 3·5—4·0 (m, 2H, 4-H and 5-H), 4·30 (d, 1H, *J* 15 Hz, 2-H), 6·32 (s, 3H, MeO), 7·82 (m, 2H, C-6 methylene), 8·63br (s, 6H, methylenes), 9·08 (t, 3H, terminal methyl).

Methyl Dodeca-trans-2,trans-4-*dienoate.*—This was prepared by the same procedure as the preceding compound, and had b.p. 106—108°/0·3 mm., n_D^{22} 1·4874 (Found: C, 74·35; H, 10·7. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·55%).

Methyl Tetradeca-trans-2,trans-4-*dienoate.*—This had b.p. 117—118°/0·2 mm., n_D^{20} 1·4862 (Found: C, 76·25; H, 11·15. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%).

Deca-trans-2,trans-4-*dienoic Acid.*—Methyl deca-*trans*-2, *trans*-4-dienoate (3·0 g.) was heated under reflux with potassium hydroxide (1·5 g.) in methanol (10 ml.) for 1 hr.; the acid was isolated as waxy crystals (2·3 g.). Recrystallisation from light petroleum at low temperature gave deca-*trans*-2, *trans*-4-dienoic acid, plates, m.p. 47—50° (lit.,[6,37] m.p. 49°, m.p. 49—50°). Dodeca-*trans*-2, *trans*-4-dienoic acid had m.p. 49—51°, and tetradeca-*trans*-2, *trans*-4-dienoic acid had m.p. 57—58°.

N-*Isobutyldeca*-trans-2,trans-4-*dienamide.*—Acid chlorides were prepared from the corresponding acids by treatment of the acid (1 mol.) with a slight excess of oxalyl chloride (*ca.* 1·3 mol.) in dry benzene. After being set aside overnight at room temperature, the mixture was heated under reflux for a short period; the solvent and excess reagent was then removed under reduced pressure and the acid chloride was purified by distillation.

Deca-*trans*-2, *trans*-4-dienoyl chloride (300 mg.) was dissolved in dry ether and isobutylamine (250 mg.) in ether was added slowly at 0° with shaking. After 30 min. at room temperature, the solution was poured into water, extracted with ether, and the extracts were washed successively with *N*-sulphuric acid, sodium hydrogen carbonate solution, and water; they were then dried.

[37] M. Jacobson, *J. Amer. Chem. Soc.*, 1953, **75**, 2584.

The solvent was evaporated and addition of light petroleum (b.p. 40—60°) at 0° to the residue induced crystallisation to give waxy plates (260 mg.). Crystallisations from light petroleum gave *N*-isobutyldeca-*trans*-2,*trans*-4-dienamide, plates, m.p. 88—89° (lit.,[6,37] m.p. 88°, m.p. 90°) (Found: C, 74·8; H, 11·3; N, 6·4. Calc. for $C_{14}H_{25}NO$: C, 75·3; H, 11·3; N, 6·25%), $\lambda_{max.}$ 260 (31,000) nm.; $\nu_{max.}$ (mull) 3295 and 3075 (NH), 1655 (C=C), 1626 (Amide A), 1615 (C=C), 1550 (Amide B), 995 ([CH=$\overset{t}{}$CH]$_2$) cm.$^{-1}$ ^{1}H n.m.r. (CCl_4, 60 MHz) were at τ 2·20br (s, 1H, amide proton), 2·92 (dd, 1H, *J* 15 Hz, *J* 10 Hz, 3-H), 3·6—4·2 (m, 3H, 2-H, 4-H, and 5-H, 6·90 (t, 2H, *J* 6 Hz, C-1′ methylene), 7·7—8·4 (m, 3H, 6-H and 2′-H), 8·7 (m, 6H, methylenes), 9·08 (d, 6H, *J* 7 Hz, *gem*-dimethyl at C-2′) 9·1 (t, 3H, terminal methyl).

N-*Isobutyldodeca*-trans-2,trans-4-*dienamide*.—This compound, prepared in the same manner to the preceding compound, had m.p. 89—90° (Found: C, 76·25; H, 11·55; N, 5·45. $C_{16}H_{29}NO$ requires C, 76·45; H, 11·65; N, 5·55%).

N-*Isobutyltetradeca*-trans-2, trans-4-*dienamide*.—This compound had m.p. 86—87° (lit.,[14,15] m.p. 84·5°, m.p. 88°) (Found: C, 77·0; H, 12·3; N, 5·05. Calc. for $C_{18}H_{33}NO$: C, 77·35; H, 11·9; N, 5·0%).

N-(2′-p-*Hydroxyphenethyl*)*deca*-trans-2,trans-4-*dienamide*.—Tyramine was prepared by the addition of saturated potassium carbonate solution to an aqueous solution of the hydrochloride: diglyme was dried by distillation over lithium aluminium hydride. Tyramine (600 mg.) was dissolved in diglyme with warming and the resulting solution was added dropwise to a solution of deca-*trans*-2,*trans*-4-dienoyl chloride (400 mg.) in diglyme. After being shaken at room temperature for 1 hr., the mixture was poured into a large volume of water and extracted with ether. The combined ether extracts were thoroughly washed with *N*-sulphuric acid, aqueous sodium hydrogen carbonate, and water; they were then dried. The solvent volume was reduced and addition of light petroleum (b.p. 40—60°) at 0° produced a silky crystalline precipitate (360 mg.). Crystallisation from ether–light petroleum gave N-(2′-p-*hydroxyphenylethyl*)*deca*-trans-2,trans-4-*dienamide*, prisms, m.p. 132—133° (Found: C, 74·85; H, 8·65; N, 4·75. $C_{18}H_{25}NO_2$ requires C, 75·2; H, 8·75; N, 4·85%); $\lambda_{max.}$ 260 (34,300), 229sh (14,000) nm.; $\nu_{max.}$ (mull) 3200—3400br (hydroxyl), 3280 and 3060 (NH), 1659 (C=C), 1633 (Amide A), 1616 (C=C), 1550 (Amide B), 1518 (Ar), 995 ([CH=$\overset{t}{}$CH]$_2$) cm.$^{-1}$; ^{1}H n.m.r. [$(CD_3)_2SO$, 60 MHz] were at τ 0·80 (s, 1H, hydroxyl proton), 2·00 (t, 1H, *J* 6 Hz, amide proton), 3·17 (q, 4H, *J* 8 Hz, ArH), 2·8—4·3 (m, 4H, olefinic protons), 6·7 (m, 2H, C-1′ methylene), 7·4 (m, 2H, C-2′ methylene), 7·9 (m, 2H, C-6 methylene), 8·75br (s, 6H, methylenes), 9·15 (t, 3H, terminal methyl). The signals at τ 0·80 and 2·0 disappeared on addition of deuterium oxide.

N-(2′-p-*Hydroxyphenylethyl*)*dodeca*-trans-2,trans-4-*dienamide*.—This was prepared in a similar way to the preceding compound, the *amide* had m.p. 140—141° (Found: C, 75·9; H, 9·75; N, 4·15. $C_{20}H_{29}NO_2$ requires C, 76·15; H, 9·25; N, 4·45%).

N-(2′-p-*Hydroxyphenylethyl*)*tetradeca*-trans-2,trans-4-*dienamide*.—This was prepared as the preceding compound and had m.p. 141·5—142·5° (Found: C, 77·2; H, 9·85; N, 4·4. $C_{22}H_{33}NO_2$ requires C, 76·9; H, 9·7; N, 4·1%).

One of us (R. S. B.) thanks the S.R.C. for a postgraduate award.

[9/808 *Received*, *May* 15*th*, 1969]