98. *Fungicidal Activity and Chemical Constitution. Part X.*[1] *Preparation of 2-Alkyl-4,6-dinitrophenyl Esters.*

By (Mrs.) M. Clarke and D. Woodcock.

Fourteen 2-alkyl-4,6-dinitrophenyl esters have been prepared for testing against spores and mycelium of *Podosphaera leucotricha* (Ell. and Everh.) Salm., the causal agent of powdery mildew of apple.

Formulations based on 2-1′-methylheptyl-4,6-dinitrophenyl crotonate,[2] originally developed as an acaricide, are of interest for the control of powdery mildews, *e.g.*, apple mildew caused by *Podosphaera leucotricha*. An early suggestion [3] that the aryl portion of this compound was responsible for tenacity and phytotoxicity whilst the crotonoyl portion acted as toxophore, was not substantiated by Kirby and Frick,[4] who found that the free phenol was just as effective against apple and barley mildew as the crotonic ester. More recently [5] certain dinitrophenyl methacrylates and related esters have been claimed to be particularly effective against *P. leucotricha*. In view of the known influence of 6-alkyl substitution in 2,4-dinitrophenols on the inhibition of oxygen uptake by fungal spores,[6] certain 2-alkyl-4,6-dinitrophenyl esters were prepared for testing against the mycelium and spores of *P. leucotricha*.

For the n-alkyl compounds the route consisted of a Fries reaction with the appropriate phenyl ester, Clemmensen reduction of the resultant hydroxy-ketone, dinitration, and esterification. The synthesis of 1-methylheptyl and 1-propylpentyl derivatives followed a similar route, chain-branching being achieved by the reaction of the hydroxyphenyl ketone with the appropriate alkylmagnesium halide, followed by catalytic reduction of the

[1] Part IX, Byrde, Clifford, and Woodcock, *Ann. Appl. Biol.*, 1961, **49**, 225.
[2] Hester and Craig, U.S.P. 2,526,660/1950.
[3] Rich and Horsfall, *Phytopathology*, 1949, **39**, 19.
[4] Kirby and Frick, *Nature*, 1958, **182**, 1445.
[5] Cf. Emmel and Czech, *Anz. Schädlingskunde*, 1960, **10**, 145; Rohm & Haas Co., G.P. 1,053,859/1959; Hartel, 13th Internat. Symp. on Crop Protection, Ghent, 1961.
[6] Shirk and Byrne, *Proc. Soc. Exp. Biol. Med.*, 1951, **77**, 628.

resultant olefin. In the reduction of *o*-(1-methylhept-1-enyl)phenol, some 15% of 2-1′-methylheptylcyclohexanone was also produced (cf. Whitaker [7]).

Details of the biological testing by Dr. R. J. W. Byrde will be published elsewhere.

Experimental

The infrared absorption spectra were determined by using a Perkin-Elmer Infracord spectrophotometer.

2-(1-*Methylhept*-1-*enyl*)*phenol*.—Freshly distilled 2-hydroxyacetophenone (27 g.) in dry ether (75 ml.) was added dropwise to a cooled and stirred ethereal solution of n-hexylmagnesium bromide, prepared from magnesium (14·4 g.) and hexyl bromide (84 ml.), the mixture was refluxed for 2 hr., cooled, and treated with saturated aqueous ammonium chloride, and the product extracted with ether. After being washed with aqueous sodium hydrogen sulphite and sodium hydrogen carbonate, the extract was dried (Na_2SO_4) and the solvent removed. The residual liquid (23·3 g.) was heated with fused potassium hydrogen sulphate (24 g.) at 160° for 1 hr., cooled, and extracted with ether. Removal of the solvent gave the *phenol*, b. p. 130—140°/15 mm., n_D^{15} 1·522 (Found: C, 81·9; H, 10·0. $C_{14}H_{20}O$ requires C, 82·35; H, 9·8%). The 3,5-*dinitrobenzoate* was liquid (Found: N, 6·8. $C_{21}H_{22}N_2O_6$ requires N, 7·0%).

2-1′-*Methylheptylphenol*.—The above alkenylphenol was shaken in ethanol with palladised charcoal and hydrogen at 500—600 lb./sq. in. and 100—110° for 6 hr. After filtration the solvent was removed and the product distilled (b. p. 140—144°/5 mm.). The infrared spectrum showed a strong peak at 1700 cm.$^{-1}$ which was attributed to a ketonic impurity (cf. Whitaker [7]). Treatment with Girard P reagent [8] resulted in the isolation of 2-1′-*methylheptylcyclohexanone*, b. p. 120—126°/20 mm. (Found: C, 79·95; H, 12·2. $C_{14}H_{26}O$ requires C, 80·3; H, 12·0%). 2-1′-*Methylheptylphenol* had b. p. 146—150°/15 mm., $n_D^{14\cdot9}$ 1·509 (Found: C, 81·3; H, 10·8. $C_{14}H_{22}O$ requires C, 81·55; H, 10·7%).

2-1′-*Methylheptyl*-4,6-*dinitrophenyl Butyrate and Crotonate*.—The parent phenol was nitrated in glacial acetic acid as described by Dutton *et al.*[9] The viscous product was esterified without prior distillation, by using the appropriate acid chloride, the esters being freed from unchanged phenol by elution from activated alumina with " AnalaR " benzene. When the infrared spectrum showed no hydroxyl peak in the 3500 cm.$^{-1}$ region, the benzene was evaporated and the samples heated at 80—90° *in vacuo* before analysis. Details are given in the Table.

2-Alkyl-4,6-dinitrophenyl esters.

Alkyl	M. p. or b. p./mm.	Solvent for crystn.*	Found (%) C	H	N	Formula	Required (%) C	H	N
			Crotonates						
(H)	79—79·5°	Aq.MeOH	47·8	3·1	11·3	$C_{10}H_8N_2O_6$	47·6	3·2	11·1
Me	72—73	Aq.EtOH	49·6	4·25	10·5	$C_{11}H_{10}N_2O_6$	49·6	3·75	10·5
Et	55—55·5	Pet	51·5	4·3	10·0	$C_{12}H_{12}N_2O_6$	51·1	4·4	10·2
Pr^n	66·5—67·5	Aq.EtOH	53·0	5·1	9·4	$C_{13}H_{14}N_2O_6$	53·0	4·8	9·5
Bu^n	44·5—45	Aq.MeOH	54·3	5·5	9·0	$C_{14}H_{16}N_2O_6$	54·5	5·2	9·1
n-C_5H_{11}	182—202°/1	—	55·8	5·6	8·7	$C_{15}H_{18}N_2O_6$	55·9	5·6	8·7
n-C_6H_{13}	210—216°/2	—	56·9	6·1	8·5	$C_{16}H_{20}N_2O_6$	57·1	5·95	8·3
n-C_7H_{15}	215—230°/3	—	58·0	6·2	8·1	$C_{17}H_{22}N_2O_6$	58·3	6·3	8·0
C_6H_{13}·CHMe	134—138°/0·01	—	59·3	6·9	7·5	$C_{18}H_{24}N_2O_6$	59·35	6·6	7·7
CHBu^{n}Pr^n ...	180—190°/0·02	—	59·6	6·6	7·8	$C_{18}H_{24}N_2O_6$	59·35	6·6	7·7
			Butyrates						
(H)	35—35·5	Aq.MeOH	47·27	3·95	10·7	$C_{10}H_{10}N_2O_6$	47·25	3·95	11·0
Me	49—50	Pet	49·5	4·4	10·4	$C_{11}H_{12}N_2O_6$	49·3	4·5	10·45
C_6H_{13}·CHMe	168—172°/0·005	—	59·2	6·7	8·0	$C_{18}H_{26}N_2O_6$	59·0	7·1	7·65
CHBu^{n}Pr^n ...	—	—	59·1	7·0	7·8	$C_{18}H_{26}N_2O_6$	59·0	7·1	7·65

* Pet = light petroleum, b. p. 40—60°.

2-(1-*Propylpent*-1-*enyl*)*phenol*.—This was obtained from 2-hydroxybutyrophenone (65 g.) and n-butylmagnesium chloride [from magnesium (24 g.) and n-butyl chloride (92 g.)] as described for the 1-methylhept-1-enyl isomer. Distillation gave the *alkenylphenol* in a fraction, b. p. 136—144°/17 mm., n_D^{14} 1·513 (Found: C, 81·4; H, 9·8. $C_{14}H_{20}O$ requires C, 82·35; H, 9·8%), and a glassy undistilled residue (probably polymeric).

[7] Whitaker, *J. Amer. Chem. Soc.*, 1947, **69**, 2414.
[8] Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1095.
[9] Dutton, Briggs, Brown, and Hillman, *Canad. J. Chem.*, 1953, **31**, 685.

2-1′-*Propylpentylphenol*.—The pentenylphenol was hydrogenated in the presence of palladium charcoal, as described for the isomer. The *product* had b. p. 110—114°/1 mm., n_D^{14} 1·512 (Found: C, 80·6; H, 10·2. $C_{14}H_{22}O$ requires C, 81·5; H, 10·7%). The 3,5-*dinitrobenzoate* was also a liquid, b. p. 130—140°/1·5 mm. (Found: C, 62·8; H, 6·2; N, 6·9. $C_{21}H_{24}N_2O_6$ requires C, 62·8; H, 6·2; N, 7·0%).

2,4-*Dinitro*-6-1′-*propylpentylphenyl Esters*.—These were prepared and purified as described above for the isomers (see Table).

2-*n*-*Alkyl*-4,6-*dinitrophenyl Esters*.—The required phenols were obtained by the method of Dutton *et al.*,[9] though the intermediate *o*-hydroxy-ketones were more satisfactorily prepared by using the conditions of Cullinane and Edwards.[10] Esterification was carried out by refluxing the phenol in dry benzene with acid chloride (1·1 mol.) and pyridine (4 mol.) for 1 hr.

The pentyl and higher members were liquids and initially failed to give satisfactory microanalyses after distillation. This was probably due to traces of the parent phenols formed by thermal decomposition, and the difficulty was overcome by a final percolation through activated alumina before analysis (see Table).

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[10] Cullinane and Edwards, *J.*, 1958, 2926.