Pungent Compounds. Part I. An Improved Synthesis of the Paradols (Alkyl 4-Hydroxy-3-methoxyphenethyl Ketones) and an Assessment of their Pungency

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Eleven members of the homologous series of paradols, of which one, [6]paradol (n-heptyl 4-hydroxy-3-methoxyphenethyl ketone), occurs naturally in the seeds of *Amomum melegueta* Roscoe (Zingiberaceae) (otherwise known as Grains of Paradise, Guinea pepper, or Melegueta pepper), have been synthesised by an improved method. Physical characteristics, including g.l.c. behaviour, and pungency evaluation experiments are described for the series.

THE paradols [1,2] are a series of phenolic ketones of general formula (1), structurally related to the gingerols (2) and the shogaols (6).[3] Representatives of all three types of molecule have been identified [1,3] as pungent principles in the oleoresin of commercial extracts of ginger, prepared from the rhizomes of the tropical plant *Zingiber officinale* Roscoe (Zingiberaceae); [6]gingerol (3) and [6]paradol (13) † have been found [1] in the seeds of *Amomum melegueta* Roscoe (Zingiberaceae), variously known as Grains of Paradise, Guinea pepper, or Melegueta pepper.[4]

As part of a more general programme aimed at correlating pungency with structure, we have prepared all members of the paradol series from [0]paradol (zingerone) (7) to [10]paradol (17).‡ Though [6]paradol (13) is the only naturally occurring member of the series to have been isolated so far, there are strong indications [1] that others probably also exist in nature, in common with the gingerols (2), at least three homologues of which, [6]-, [8]-, and [10]-gingerols [(3), (4), and (5), respectively] are known to be present in ginger oleoresin.[1,3]

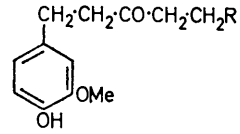
For the preparation of the paradols (7)—(17), we employed initially the classical methods of Nomura and

† The number bracketed before the name designates the number of carbon atoms in the aldehyde which would be produced by a retro-aldol reaction on the gingerol (2). Thus each gingerol (2) is identified by the length of this potentially aldehydic portion of the side chain. To ensure consistency, the same nomenclature has been adopted [1] to cover the shogaols (6) and the paradols (1), though it is recognised that the latter cannot undergo retro-aldol fission.

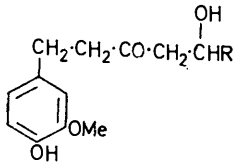
‡ B. P. Appl. 45379/1972.

[1] D. W. Connell, *Austral. J. Chem.*, 1970, **23**, 369.
[2] D. W. Connell, *Food. Technol. Austral.*, 1969, **21**, 570; *Flavour Industry*, 1970, 677.
[3] D. W. Connell and M. D. Sutherland, *Austral. J. Chem.*, 1969, **22**, 1033.
[4] F. Rosengarten, 'The Book of Spices,' Livingston Publishing Co., Wynnewood, Pennsylvania, 1969, pp. 54, 353.

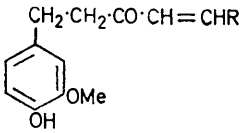
Tsurumi [5] and Berlin and Sherlin,[6] who condensed vanillin (18) with a series of alkyl methyl ketones (19) in the presence of aqueous ethanolic potassium hydroxide at 100° to obtain the didehydroparadols (20)—(28).



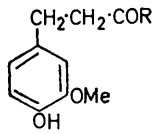
(1) R = alkyl

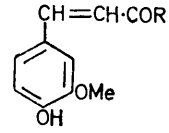


(2) R = alkyl
(3) R = $CH_3 \cdot [CH_2]_4$ [6]gingerol
(4) R = $CH_3 \cdot [CH_2]_6$ [8] ,,
(5) R = $CH_3 \cdot [CH_2]_8$ [10] ,,



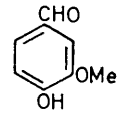
(6) R = alkyl





[0]paradol		(7)	R = CH_3	(20)	didehydro[0]paradol		
[1]	,,	(8)	R = $CH_3 \cdot CH_2$	(21)	,,	[1]	,,
[2]	,,	(9)	R = $CH_3 \cdot [CH_2]_2$	(22)	,,	[2]	,,
[3]	,,	(10)	R = $CH_3 \cdot [CH_2]_3$	(23)	,,	[3]	,,
[4]	,,	(11)	R = $CH_3 \cdot [CH_2]_4$	(24)	,,	[4]	,,
[5]	,,	(12)	R = $CH_3 \cdot [CH_2]_5$	(25)	,,	[5]	,,
[6]	,,	(13)	R = $CH_3 \cdot [CH_2]_6$	(26)	,,	[6]	,,
[7]	,,	(14)	R = $CH_3 \cdot [CH_2]_7$	(27)	,,	[7]	,,
[8]	,,	(15)	R = $CH_3 \cdot [CH_2]_8$	(28)	,,	[8]	,,
[9]	,,	(16)	R = $CH_3 \cdot [CH_2]_9$	(29)	,,	[9]	,,
10]	,,	(17)	R = $CH_3 \cdot [CH_2]_{10}$	(30)	,,	[10]	,,

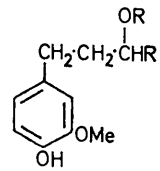
In our hands, however, these reactions gave tarry products and t.l.c. of the reaction mixtures showed that many undesired by-products were present. Furthermore, the yield of didehydroparadol declined rapidly to an unsatisfactory level once the length of the alkyl group in the methyl ketone (19) exceeded four carbon atoms, a trend also noted by Nomura and Tsurumi.[5] To overcome these problems, we investigated milder methods of condensing vanillin (18) with the alkyl methyl ketones (19). We examined the crude mixture of products resulting from each reaction by t.l.c. in order to achieve a synthesis of the didehydroparadols (20)—(30) in maximum yield and purity. In meeting these criteria, condensations under acidic conditions (*e.g.* toluene-*p*-sulphonic acid in toluene under reflux) proved generally unsatisfactory since many by-products were formed. Mild basic conditions {*e.g.* diazabicyclo-[2,2,2]octane (DABCO) in benzene under reflux} were superior to the acidic ones, but the yield of didehydroparadol was still poor. High yields of the didehydroparadols (20)—(30), almost completely devoid of by-products, were obtained using the weak base–weak acid combination favoured by Cope [7] for Knoevenagel reactions, and subsequently used by Stork [8] and by Woodward [9] and their co-workers in other related



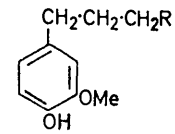
(18)

MeCOR

(19) R = CH_3 to $CH_3 \cdot [CH_2]_{10}$



(31) R = alkyl
(32) R = CH_3
(33) R = $CH_3 \cdot CH_2$
(34) R = $CH_3 \cdot [CH_2]_2$
(35) R = $CH_3 \cdot [CH_2]_5$



(36) R = alkyl
(37) R = CH_3

carbanion reactions. Thus equimolar quantities of pyrrolidine and acetic acid in benzene–ether consistently gave yields of didehydroparadols (20)—(30) in the region of 80—90% (see Table 1), the chain length of the alkyl group in the alkyl methyl ketone (19) having no significant influence over the yield. T.l.c. of the crude mixtures obtained from these condensations showed that the didehydroparadols were free of by-products: any unchanged vanillin (18) was easily removed by treatment with saturated sodium hydrogen sulphite solution.

Physical data and analytical results for the full series of didehydroparadols (20)—(30) are given in Table 1. The i.r. spectra (Nujol) showed prominent bands, varying between the limits indicated, in the following regions: 3400—3460 (phenolic OH), 1642—1680 (αβ-unsaturated ketone carbonyl), 1600—1650 (conjugated olefinic bond), and 1270—1290 cm^{-1} (methoxy-group). The n.m.r. spectra of the first three members (20)—(22) of the series are predictably different from those of the remainder; thereafter, similar features are observed for the rest of the series. For this reason Table 2 summarises the n.m.r. data for the first three members of the series only, together with that for didehydro[6]-paradol (26), which holds special interest as it is a precursor in the synthesis of the naturally occurring

[5] H. Nomura and S. Tsurumi, *Sci. Reports Tohoku Univ.*, 1927, **16**, 565.

[6] A. Ya. Berlin and S. M. Sherlin, *Zhur. obshchei Khim.*, 1948, **18**, 1386 (*Chem. Abs.*, 1949, **43**, 2185c).

[7] A. C. Cope, *J. Amer. Chem. Soc.*, 1937, **59**, 2327; A. C. Cope, C. M. Hofmann, C. Wyckoff, and E. Hardenbergh, *ibid.*, 1941, **63**, 3452. For other references to this type of Knoevenagel catalyst see R. L. Reeves in 'The Chemistry of the Carbonyl Group,' ed. S. Patai, Interscience, London, 1966, p. 567; C. A. Buehler and D. E. Pearson, 'Survey of Organic Syntheses,' Wiley-Interscience, New York, 1970, pp. 841—843.

[8] G. Stork, E. E. van Tamelen, L. J. Friedman, and A. W. Burgstahler, *J. Amer. Chem. Soc.*, 1953, **75**, 384.

[9] R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.

[6]paradol (13). The pattern of mass spectral fragmentation for the series of didehydroparadols (20)—(30) is determined by the length of the alkyl side chain (R)

TABLE 1

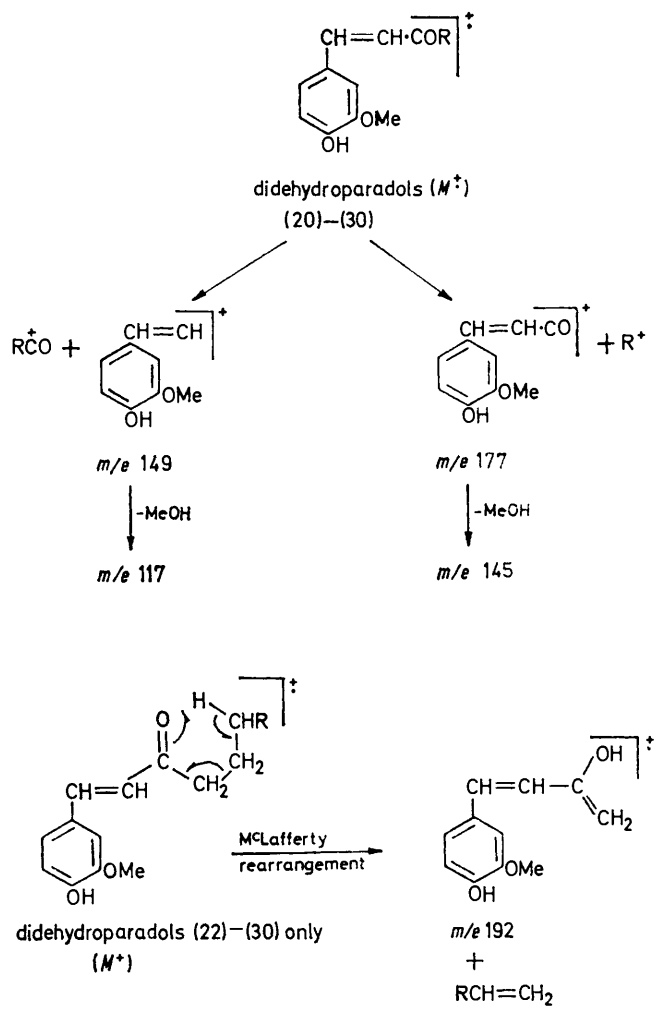
Physical and analytical data for didehydroparadols (20)—(30)

Didehydroparadol	Yield (%)	M.p. (°C)	Lit.[5,6] m.p. (°C)	Microanalysis or accurate mass determination
(20) [a,c]	70	132—133	128—129	Found: *M*, 192·0785 Calc.: *M*, 192·0786
(21) [c]	83	96·5—97·5	91—92	Found: *M*, 206·0950 Calc.: *M*, 206·0943
(22) [d]	89	86—87	82—83	Found: *M*, 220·1096 Calc.: *M*, 220·1100
(23) [b,c]	86	65·5—66·5	39—40	Found: *M*, 234·1256 Calc.: *M*, 234·1263
(24) [b,d]	90·5	51—52	50—50·5	Found: *M*, 248·1413 Calc.: *M*, 248·1412
(25) [c]	87	52—53	48—49	Found: *M*, 262·1566 Calc.: *M*, 262·1568
(26) [e]	94	44—45	42—43	Found: C, 73·5; H, 8·8% Calc.: C, 73·9; H, 8·8%
(27) [e]	85	45—46	45·5—46	Found: C, 74·3; H, 9·1% Calc.: C, 74·45; H, 9·0%
(28) [e]	92·5	57—58	55·5—56	Found: C, 75·2; H, 9·5% Calc.: C, 75·0; H, 9·3%
(29) [d]	84	53—54	52	Found: 318·2202 Calc.: 318·2195
(30) [d]	93·5	76—77		Found: C, 75·6; H, 10·1% Calc.: C, 75·9; H, 9·7%

[a] Prepared by using dilute aqueous alkali. [b] Crude product purified by distillation under reduced pressure followed by crystallisation. [c] Pale yellow crystals. [d] White crystals. [e] Cream needles. All didehydroparadols were recrystallised from benzene–light petroleum (b.p. 60—80°) in the presence of charcoal.

bonded to the carbonyl group: only when this contains at least three carbon atoms does the McLafferty rearrangement (Scheme 1) become possible. Other major fragmentation processes are also indicated in Scheme 1.

The reduction of the didehydroparadols (20)—(30) to the corresponding paradols (7)—(17) was subjected to the same kind of scrutiny by t.l.c. as the condensation



SCHEME 1 Pattern of mass spectral fragmentation for didehydroparadols (20)—(30). The McLafferty rearrangement is only observed for didehydroparadols (22)—(30)

The relative abundance of the molecular ion and fragment ions shows some variation through the didehydroparadol series (20)—(30). However, for brevity, only those values for didehydro[6]paradol (26) are listed:

m/e	(M+·)	276	192	177	149	145	117	89
Relative abundance (%)		20	49	100	24	49	33	42

A metastable peak for the fragmentation *m/e* 177 ⟶ *m/e* 145 is observed in the spectrum of didehydro[6]paradol (26), *m** 118·9 (calc. 118·8), as well as in the spectra of other members of the didehydroparadol series, (20)—(25) and (27)—(30).

TABLE 2

N.m.r. data for didehydroparadols (20)—(22) and (26) (τ values; *J* in Hz)

Didehydroparadol	ArH	ArOH [a]	ArCH=CH	ArCH=CH·CO	ArO·CH3	CO·CH2	CO·CH2[CH2]n	[CH2]n·CH3
(20) [b]	2·85 (3H, m)	3·35br (1H, s)	2·39 (1H, d) *J* 16	3·34 (1H, d) *J* 16	6·07 (3H, s)			7·70 (3H, s)
(21) [c]	2·90 (3H, m)	3·75br (1H, s)	2·40 (1H, d) *J* 17	3·43 (1H, d) *J* 17	6·04 (3H, s)	7·34 (2H, q) *J* 7		8·83 (3H, t) *J* 7
(22) [c]	3·0 (3H, m)	4·17br (1H, s)	2·53 (1H, d) *J* 17	3·34 (1H, d) *J* 17	6·04 (3H, s)	7·45 (2H, q) *J* 7	8·33 (2H, quin) *J* 7	9·05 (3H, t) *J* 7
(26) [c]	2·92 (3H, m)	3·8br (1H, s)	2·40 (1H, d) *J* 17	3·40 (1H, d) *J* 17	6·09 (3H, s)	7·33 (2H, t)	8·87br (10H)	9·12br (3H, t)

[a] Signal disappeared on addition of deuterium oxide. [b] Spectrum recorded in [$^2H_6$]acetone. [c] Spectrum recorded in [^2H]-chloroform–carbon tetrachloride. All spectra recorded at 60 MHz with tetramethylsilane as internal standard.

stage. Variation of the catalyst and of the conditions of hydrogenation (see Experimental section) failed to eliminate the formation of the unwanted by-products (31) and (36). A typical hydrogenation carried out under the most favourable conditions (5% palladium–carbon in ethyl acetate at 5 atm) gave the paradol (1), the alcohol (31), and the alkylguaiacol (36) in the approximate proportions 70 : 25 : 5 (w/w). Isolation of the pure paradol (1) was not difficult, column chromatography proving superior for this purpose to distillation under reduced pressure. A total separation of all three reduction products, (7), (32), and (37), was attempted only in the case of didehydro[0]paradol (didehydrozingerone) (20). From the reduction products of didehydroparadols (21), (22), and (25), the paradols (8), (9), and (12), and their corresponding alcohols (33), (34), and (35), respectively, were isolated. In all other reductions, only the paradol was isolated.

The physical and analytical data for the series of paradols are given in Table 3. In general, the paradols

TABLE 3

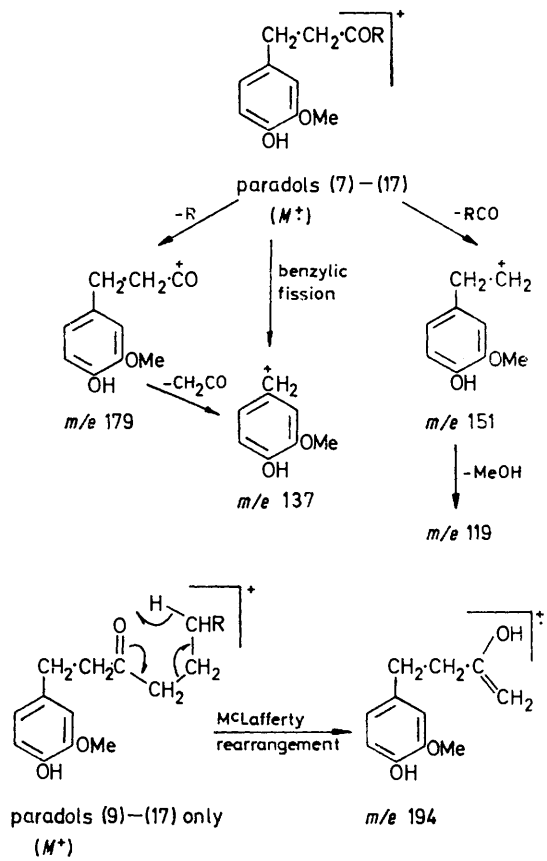
Physical and analytical data for paradols (7)—(17)

Paradol	M.p. (°C)	Lit.,[5,6] m.p.	Microanalysis or accurate mass determination
(7) [a-c,e,f]	41—42	41—42	Found: *M*, 194·0944 Calc.: *M*, 194·0943
(8) [a,c,e]	44·5—45·5	36—37	Found: C, 69·25; H, 7·8 Calc.: C, 69·2; H, 7·7%
(9)	44·5—45·5	44·5—45·5	Found: C, 70·5; H, 8·1 Calc.: C, 70·3; H, 8·2%
(10)	47·5—48	47·5—48·5	Found: C, 71·0; H, 8·5 Calc.: C, 71·15; H, 8·8%
(11)	38	37·5—38	Found: C, 71·7; H, 8·5 Calc.: C, 72·0; H, 8·9%
(12) [a,c,e]	Oil	Oil	Found: *M*, 264·1727 Calc.: *M*, 264·1725
(13)	31—32	30—31	Found: C, 73·15; H, 9·1 Calc.: C, 73·4; H, 9·4%
(14)	35·5—36·5	35·5—36·5	Found: *M*, 292·2038 Calc. *M*, 292·2037
(15)	42—43	42·5—43·5	Found: C, 75·0; H, 10·1 Calc.: C, 74·5; H, 9·9%
(16) [d]	48—49	48—49	Found: C, 75·35; H, 10·35 Calc.: C, 74·9; H, 10·1%
(17)	50—51		Found: C, 75·5; H, 10·4 Calc.: C, 75·4; H, 10·25%

[a] Ethanol used in place of ethyl acetate as hydrogenation solvent. [b] Hydrogenation at atmospheric pressure. [c] Raney nickel used as catalyst in place of palladium–charcoal. [d] Platinum oxide used as catalyst in place of palladium–charcoal. [e] Alcohol (31) isolated. [f] Alkane (36) isolated. All hydrogenations other than those bearing notes *a*—*d* were performed at 5 atm pressure in ethyl acetate with 5% palladium–charcoal as catalyst. All paradols (7)—(17) were crystalline solids with the exception of (12) which was an oil at room temperature.

(7)—(17) have low m.p.s {[5]paradol (12) is an oil at room temperature}, which makes the m.p. a poor criterion of purity. However, notwithstanding the obvious difficulties of purification which must have attended Nomura and Tsumari's preparation [5] of the paradols (7)—(15), the m.p.s reported by them agree closely with those found by ourselves.

The i.r. spectra (Nujol mulls or as films) for the paradols (7)—(17) show bands, varying between the limits indicated, in the regions: 3400—3520 (phenolic OH), 1705—1720 (aliphatic ketone carbonyl), and 1250—1285 cm^{-1} (methoxy-group). The n.m.r. spectra of the first three members and that for [6]paradol (13),



SCHEME 2 Pattern of mass spectral fragmentation for paradols (7)—(17). The McLafferty rearrangement is only observed for paradols (9)—(17)

The relative abundance of the molecular ion and fragment ions shows some variation through the paradol series (7)—(17). However, for brevity, only those for [6]paradol (13) are listed:

m/e	(*M*+·)	278	179	151	137	127	119	99	91	57	43
Relative abundance (%)		54	18	22	100	2	10		7	15	11

Metastable peaks for the following fragmentation processes are observed in the mass spectrum of [6]paradol (13) (recorded on an A.E.I. MS902 double-focusing instrument at 70 eV).

M+· (*m/e* 278) ⟶ *m/e* 137 (base peak).	Found: *m** 67·5. Calc. 67·5
M+· (*m/e* 278) ⟶ *m/e* 151	Found: *m** 82·0. Calc. 82·0
M+· (*m/e* 278) ⟶ *m/e* 179	Found: *m** 115·4. Calc. 115·3
m/e 151 ⟶ *m/e* 119	Found: *m** 93·8. Calc. 93·8

Metastable peaks in the mass spectra of the remaining members of the paradol series, (7)—(12) and (14)—(17), confirm that fragmentations of a similar nature occur in these compounds.

the naturally occurring member, are summarised in Table 4. The n.m.r. spectrum of the last is representative of the remainder of the paradol series, the integral

for the broad methylene signal at τ 8·7 being the only feature undergoing variation. The pattern of fragmentation of the paradols (7)—(17) under electron bombardment was again found to change once the length of the side chain (R) attached to the carbonyl group exceeded the minimum of three carbons necessary to permit the McLafferty rearrangement. Full details are shown in Scheme 2.

Analysis of the g.l.c. data for the paradols (7)—(17) shows that a linear relationship exists between the log of the retention time and the paradol carbon number.

TABLE 4

N.m.r. data for paradols (7)—(9) and (13) (τ values; J in Hz)

Paradol	Ar*H*	Ar*OH* [a]	Ar*O*·C*H*$_3$	Ar*CH*$_2$·*CH*$_2$·CO	CO·*CH*$_2$	[*CH*$_2$]$_n$·*CH*$_3$	[*CH*$_2$]$_n$·*CH*$_3$
(7)	3·33 (3H, m)	4·5 (1H, s)	6·18 (3H, s)	7·31 (4H, t)			7·97 (sH, s)
(8)	3·33 (3H, m)	4·17br (1H, s)	6·22 (3H, s)	7·33 (4H, t)	7·75 (2H, q) J 7		9·05 (3H, t) J 7
(9)	3·33 (3H, m)	3·96br (1H, s)	6·21 (3H, s)	7·32 (4H, t)	7·73 (2H, t) J 7	8·46 (2H, sex) J 7	9·15 (3H, t) J 7
(13)	3·33 (3H, m)	4·45br (1H, s)	6·17 (3H, s)	7·31 (4H, t)	7·6br (2H, t)	8·75br (10H, s)	9·1br (3H, t)

[a] Signal disappeared on addition of deuterium oxide. All spectra were recorded at 60 MHz for solutions in carbon tetrachloride with tetramethylsilane as internal standard.

TABLE 5

G.l.c. retention times for the homologous series of paradols (7)—(17) (stationary phase 5% Apiezon L on 100—120 mesh Chromosorb G; column 9 ft × ¼ in o.d.; column conditions, isothermal at 200°)

Paradol	[0]	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]
t_R/min	2·25	3·60	5·50	10·2	12·15	17·9	28·45	42·5	63·1	95·5	207·0
t_R(paradol)/t_R($C_{16}H_{34}$)	0·11	0·175	0·314	0·500	0·562	0·873	1·384	2·075	3·078	4·660	10·100

This result confirms that found by Connell.[1] Full details of these results are given in Table 5.

The results of taste evaluation experiments (see Table 6) show that [5]-, [6]-, and [7]-paradols [(12)—(14)] possess the most desirable pungency characteristics of the series. These results are broadly in agreement with those reported earlier.[5,10]

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 257 grating spectrometer, n.m.r. spectra with a Varian A60 instrument, and mass spectra with A.E.I. MS12 (single-focusing) and MS902 (double-focusing) instruments. Microanalytical results were obtained by J. Jordan of this Department using a Perkin-Elmer 240 microanalyser. G.l.c. data were obtained with a Pye 104 instrument. For analytical t.l.c. we used Kieselgel G nach Stahl (Merck) and for column chromatography Hopkin and Williams silica gel MFC. Spots on t.l.c. plates were located by spraying with either alkaline potassium permanganate or Brady's reagent.

(a) *Didehydroparadols* (20)—(30).—Experimental details for a typical preparation are given. Any significant departure from this procedure is noted in Table 1.

Didehydro[1]*paradol* [1-(4-*Hydroxy*-3-*methoxyphenyl*)*pent*-1-*en*-3-*one*] (21).—Acetic acid (12·0 g, 0·2 mol) was added slowly to pyrrolidine (14·2 g, 0·2 mol) and the mixture was cooled in an ice-bath. Ethyl methyl ketone (14·4 g, 0·2 mol) was added to the stirred mixture followed, at room temperature, by vanillin (30·4 g, 0·2 mol) in benzene (100 ml) and ether (50 ml) during 1 h. The mixture was stirred for 48 h, during which time regular t.l.c. checks were made. When t.l.c. showed that almost no vanillin remained, the mixture was poured into water and the pH of the aqueous layer tested to ensure that it was slightly acidic (2N-hydrochloric acid was added if required). The organic layer was removed, washed with water, and then stirred for 4 h over saturated sodium hydrogen sulphite solution to remove unchanged vanillin. After separation, the organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. The product, a deep-red viscous oil, was cooled to 0° and on addition of ether (1—2 ml) it crystallised (36·1 g, 83%). Two recrystallisations from benzene–light petroleum (b.p. 60—80°) (charcoal used for the second) gave fine pale-yellow needles of didehydro[1]paradol (21), m.p. 96·5—97·5° (lit.,[5] 91—92°).

(b) *Paradols* (7)—(17).—One example is described in detail. Important deviations from this method are recorded in Table 3.

Didehydro[4]paradol (24) (12·2 g) in ethyl acetate (250 ml) containing palladium–charcoal (5%; 0·2 g) was shaken under hydrogen at 5 atm pressure. After uptake had ceased (2—3 h), the mixture was examined by t.l.c.; no starting material remained. Two other products, assumed to be compounds (33) and (36; R = Et) accompanied the required [4]paradol (11) in the approximate proportions of 25 : 5 : 70, respectively (total yield 12·4 g).

The crude product was chromatographed on a column of silica gel. Benzene–acetone (95 : 5 v/v) eluted a fraction which gave an oil which slowly solidified. Recrystallisation from ether–light petroleum (b.p. 60—80°) gave [4]paradol [1-(4-hydroxy-3-methoxyphenyl)octan-3-one] (11) as fine needles, m.p. 38° (lit.,[5] 37·5—38°).

Other catalysts [Raney nickel, platinum oxide, and tris(triphenylphosphine)chlororhodium(I)] did not significantly alter the composition of the crude hydrogenation mixture.

(c) *Isolation of By-products from Hydrogenation of Didehydroparadols.*—Distillation under reduced pressure failed to effect a complete separation of the two main constituents of the mixture of paradol (1), alcohol (31), and alkylguaiacol (36), resulting from the hydrogenation of didehydroparadols (20)—(30), but column chromatography

[10] N. Pravataroff, *Manuf. Chemist and Aerosol News*, 1967, **38**, 40.

as described in (b) was successful. In general, initial elution of the column containing the crude hydrogenation mixture with benzene enabled the alkylguaiacol (36) to be isolated. Continued elution with benzene–acetone (95 : 5, v/v) gave first the paradol (1) and then the alcohol (31) in pure form, the eluted fractions being monitored by t.l.c. to establish the point of transition. Physical data for the alcohols (32)—(35) are as follows: 4-(3-hydroxybutyl)-2-methoxyphenol (32), pale yellow oil, $\nu_{max.}$ 3360—3440 (OH) and 1275 cm^{-1} (OMe) (Found: M^+, 196·1099 Calc. for $C_{11}H_{16}O_3$: M, 196·1101); 4-(3-*hydroxypentyl*)-2-*methoxyphenol* (33), needles, m.p. 47—48°, $\nu_{max.}$ 3250—3550 (OH) and 1268 cm^{-1} (OMe) (Found: M^+, 210·1254. $C_{12}H_{18}O_3$ requires M, 210·1256); 4-(3-*hydroxyhexyl*)-2-*methoxyphenol* (34), solid, m.p. 47·5—48°, $\nu_{max.}$ 3420 (OH) and 1275 cm^{-1} (OMe) (Found: C, 69·6; H, 8·6%; M^+, 224. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%; M, 224); 4-(3-*hydroxynonyl*)-2-*methoxyphenol* (35), solid, m.p. 53—54°, $\nu_{max.}$ 3400 (OH) and 1250 (OMe) (Found: M^+, 266·1874. $C_{16}H_{26}O_3$ requires M, 266·1881), τ (CCl_4; 60 MHz) 3·35 (3H, m, aromatic), 4·65 (1H, s, phenolic OH), 6·15 (3H, s, OMe), 7·35br (2H, t, J 9 Hz, $ArCH_2$), 8·3br (2H, t, $ArCH_2{\cdot}CH_2$), 6·3—6·6br [1H, $CH_2{\cdot}CH(OH){\cdot}CH_2$], 8·65 (1H, s, $CH{\cdot}OH$), 8·65br {10H, s, $-CH(OH){\cdot}[CH_2]_5{\cdot}CH_3$}, and 9·1br (3H, t, $CH_2{\cdot}CH_3$) (signals at τ 4·65 and 8·65 disappeared on addition of deuterium oxide).

Organoleptic Evaluation.—A panel of ten experienced tasters was used to assess the pungency of the paradols (7)—(17). A 0·1% (w/v) solution of each paradol in ethanol was prepared. The ethanolic solutions were then diluted to 1 part in 50 (v/v), and 1 part in 100 (v/v), respectively, with aqueous 5% (w/v) sucrose solution. These concentrations were chosen after preliminary tests had shown that the threshold at which pungency could be detected for one member of the series, [0]paradol (zingerone) (7), lay within these values.

Samples (5 ml) of each solution were presented to the panel. After swallowing the sample at once, each taster was asked to observe any warming effect on the throat. The results are given in Table 6: the approximate pungency

TABLE 6

Pungency threshold concentrations for paradols (7)—(17)

Paradol			Pugency threshold
[0]paradol		(7)	1 : 50,000
[1]	,,	(8)	1 : 20,000
[2]	,,	(9)	1 : 30,000
[3]	,,	(10)	1 : 50,000
[4]	,,	(11)	1 : 50,000
[5]	,,	(12)	1 : 100,000
[6]	,,	(13)	1 : 100,000
[7]	,,	(14)	1 : 100,000
[8]	,,	(15)	1 : 50,000
[9]	,,	(16)	1 : 25,000
[10]	,,	(17)	1 : 12,500

threshold (*i.e.* the minimum concentration at which pungency can be detected) for each paradol is recorded in the second column.

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