

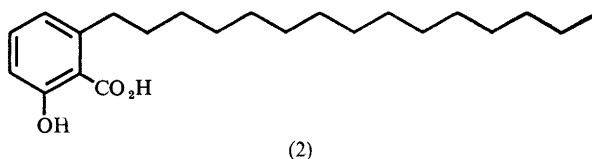
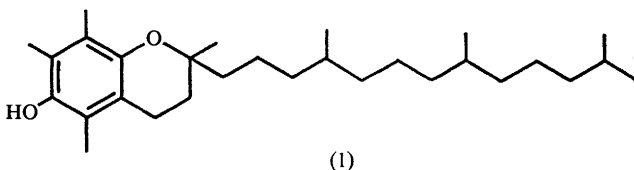
# Non-isoprenoid Long Chain Phenols

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## 1 Origin

Although the lipids are generally thought of as long chain materials of glyceride wax, or steroidal origin, the structural similarity of the methylenic chains of the long chain phenols and of the fatty acid suggest the inclusion of the former within the general term as a subgroup. There are essentially two types of phenolic lipid, or long chain phenol, those in which the side-chain is isoprenoid, as in  $\alpha$ -tocopherol (1), having been derived biogenetically from 'mevalonate' and those which are non-isoprenoid and of 'polyketide' origin,<sup>1</sup> having no branched chains, as in the saturated compound, anacardic acid (2), 6-pentadecyl salicylic acid. This review is concerned with the second group.



Mixed types, not considered in this review, are also known such as grifolin from *Grifolia confluens*, 5-methyl-2-farnesylresorcinol<sup>2</sup> where the ring is of 'polyketide' origin and the side chain is derived from mevalonate.

The chemistry<sup>3</sup> and technology<sup>4</sup> of certain phenolic lipids have not been re-

<sup>1</sup> A. J. Birch, *Proc. Chem. Soc.*, 1962, 3.

<sup>2</sup> Y. Hirata and K. Nakanishi, *J. Biol. Chem.*, 1949, **184**, 135; M. Isobe and T. Goto, *Tetrahedron*, 1968, **24**, 945; J. H. P. Tyman, W. A. Baldwin and C. J. Strawson, *Chem. and Ind.*, 1975, 41.

<sup>3</sup> (a) C. R. Dawson, *Trans. New York Acad. Sci.*, 1956, **18**, 427; (b) D. Jacquemain, Oléagineux, 1959, **14**, 528.

<sup>4</sup> (a) E. M. Evans, *Rubber and Plastic Age*, 1955, 228; (b) J. S. Aggarwal and B. G. K. Murthy, *J. Colour Sci.*, 1972, **11**, 2.

viewed recently and it is appropriate to now summarise the developments which have taken place with these industrially important materials.

## 2 Nomenclature

As with most groups of natural products both trivial and systematic names are used. A useful concise system, somewhat similar to that for the fatty acids, which takes account of the chain length and the number of double bonds and can denote the position and configuration of double bonds is exemplified with  $C_{15}$  anacardic acid *cis-cis*-diene, which becomes (15:2) 8'(Z),11'(Z)-anacardic acid. It is considered that the systematic name, 6-[8'(Z),11'(Z)-pentadecadienyl] salicylic acid is best used for this compound and the former only has the merit of conciseness. Systematic names have been used for the phenolic lipids discussed in the Tables, p. 502. The fatty acid system cannot be applied exactly since the saturated, monoene, diene, and triene substances constituting anacardic acid do not bear separate trivial names as with their fatty acid analogues, stearic, oleic, linoleic, and linolenic acids.\* Nothing probably displaces the value of the systematic name although the first mentioned method does take account of all materials of a given chain length and the configuration can be omitted. Since a trivial name usually refers to one substance only, the  $C_{17}$  homologue of cardanol could be named bis-homocardanol,† a  $C_{14}$  member, norcardanol, and a  $C_{13}$ , bis-norcardanol, a slight improvement on the system referred to in the footnote.\* Inevitably, it is believed, synthetic compounds may well be given systematic names and the natural products trivial ones. For brevity the trivial names with the appropriate ( $n=0$ ), ( $n=1$ ), ( $n=2$ ), or ( $n=3$ ) prefix have been used in this review. A further useful convention for distinguishing the class of phenol from its unsaturated members is to use the terms component phenol and constituent respectively.

## 3 Types of Phenolic Lipid

The phenolic lipids are a comparatively little known group of materials which for convenience may be considered as fatty acids with a phenolic ring instead of a carboxyl as the polar group. Certain of them have had an applied artistic use<sup>5</sup> for centuries and others have a vital role in certain modern technical uses.<sup>4</sup> The general lack of knowledge concerning them may lie in their dual aromatic and aliphatic character. To aromatic chemists they may have appeared as aliphatic entities, and *vice versa*.

The non-isoprenoid phenolic lipids exist in plants from a number of different families notably the *Anacardiaceae*, and are widespread in tropical and temperate climates in tree, shrub (sumac), many small plant, and certain bacterial sources. It is convenient to classify the long chain phenols into groups of phenolic acids,

\*A proposal that cardanol (saturated), ocardanol monoene, cardanol diene, and cardanol triene, should be designated cardanol, cardenol, cardadienol, and cardatrienol respectively would probably be more confusing than useful when also applied to cardol and anacardic acid.

†Generally only  $C_{17}$  homologues are present and the use of bis-homo therefore suffices.

<sup>5</sup> A. S. Dyer, *Interchem. Rev.*, 1945, 4, 35.

dihydric, and monohydric phenols a scheme which has the basis of a chemical taxonomy. Table 1 summarises the naturally occurring phenolic acids, Table 2 the dihydric phenols, and Table 3 the monohydric phenols and in each the botanical classification, common name, main component, systematic name, chemical formulae, and country or source of origin have been given. Certain species contain all three phenolic types, others only two and certain sources uniquely a single material. Although the higher homologues of orsellinic acid fall within the scope of this review, the depsides, in which form the orsellinic acids mostly exist, have been excluded.

*Anacardium occidentale*, the cashew tree, the source of the nut, dominates the phenolic acids on account of its extensive cultivation in a large number of tropical and sub-tropical countries.<sup>6</sup> The nut has edible value while the shell is a source of the technically useful phenolic cashew nut-shell liquid. The nut 2–3 cm in length, is kidney-shaped and attached to the base of the cashew apple (Figure 1). The nut consists of an ivory-coloured kernel covered by a thin brown mem-

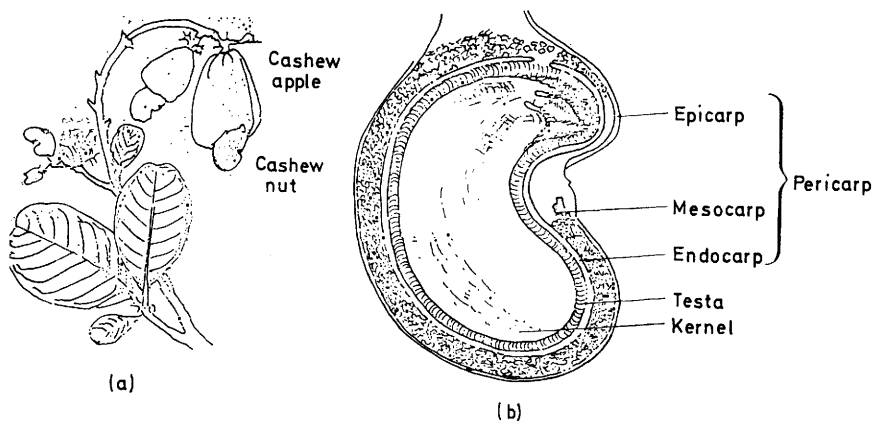


Figure 1

brane (testa) and enclosed by an outer brown porous shell the mesocarp which is about 3 mm thick and contains cashew nut-shell liquid (CNSL) a reddish brown oil. The kernels, freed from the testa, contain 1.6% water, 10% protein<sup>7</sup> (a very rich source), 57.4% fat (substantially derived from saturated glycerides) 5.3% carbohydrate, 2.4% ash, and 0.9% fibre. The shell oil (CNSL) is present to 18–27% of the total raw nut weight, the kernel is approximately 20–25% and the balance is the shell weight and the testa (2%).<sup>8</sup>

The cashew tree was originally native to Brazil where it is still cultivated and, as elsewhere in many countries, found in the wild state. Some 500 million trees

<sup>6</sup> R. J. Wilson, 'The Market for Cashew Nut Kernels and Cashew Nut Shell Liquid', Tropical Products Institute, London, 1975, p. 57.

<sup>7</sup> G. Lossner, *Beitr. Trop. Subtrop. Landwirt. Tropenveterinaermed.*, 1971, 9, 131.

<sup>8</sup> J. H. P. Tyman and S. K. Lam, *Lipids*, 1978, 13, 525.

**Table 1** Long Chain Phenolic Acids (and Derivatives)

<i>Botanical/ Biological origin</i>	<i>Common/ Trivial Name</i>	<i>Main Component (side chain)</i>	<i>Formula</i>	<i>Structure (see p. 508)</i>	<i>Country of Origin</i>
<i>Anacardiaceae</i>					
Anacardium occidentale	Cashew nut, <i>i.e.</i> cashew nut-shell liquid (CNSL)	Anacardic acid (C <sub>15</sub> ) (4 constituents)	6-Pentadecylsalicylic acid 6-[8'(Z)-pentadecenyl]- salicylic acid 6-[8'(Z),11'(Z)-pentadecadienyl]- salicylic acid 6-[8'(Z),11'(Z),14'-pentadecatrienyl]- salicylic acid 6-undecylsalicylic acid	(2) (4) (5) (6) (7)	Brazil, Mozambique, India, Tanzania, Kenya, Nigeria, Sri Lanka, Malaysia, Indonesia <i>etc.</i> Brazil
Anacardium giganteum Hancock	—	Anagigantic acid (C <sub>11</sub> )			
Pentaspadon motleyi Hook	—	Pelandjaic acid (C <sub>17</sub> )	6-[8'(Z)-heptadecenyl] salicylic acid 6-[8'(Z),11'(Z)-heptadecadienyl] salicylic acid	(8) (9)	Australia
Pentaspadon officialis Holmes	—	Pelandjaic acid (C <sub>17</sub> )			

<i>Gymnospermae</i>						
Ginkgoales	Ginkgo biloba (Maidenhair tree)	Ginkgolic acid (C <sub>15</sub> )		(4)	China, Europe, Japan	
		Ginkgolonic acid (C <sub>14</sub> )	(6-tetradecylsalicylic acid)	(9a)		
<i>Compositae</i>						
Chrysanthemum frutescens	Marguerite	Frutescin and relatives (C <sub>8</sub> ) Demethyl- frutescin (C <sub>5</sub> )	Methyl 6-(hexa-2,4-diyanyl) salicylate <i>O</i> -methylether Methyl 6-(penta-2,4-diyanyl) salicylate <i>O</i> -methylether	(10) (11)	Europe, N. America	
<i>Lichens</i>						
Sphaerophorin cetraria	Depsides	Microphyllinic acid		(11a)	World wide	

504 Table 2 Long Chain Dihydric Phenols

Botanical/ Biological origin	Common/ Trivial Name	Main Component (side chain)	Formula	Structure (see pp. 508, 509)	Country of Origin
<i>Anacardiaceae</i>					
Anacardium occidentale	Cashew nut shell liquid (CNSL)	Cardol (R = H) (4 constituents)	5-Pentadecylresorcinol 5-[8'(Z)-pentadecyl]- resorcinol 5-[8'(Z),11'(Z)-pentadecadienyl]- resorcinol 5-[8'(Z),11'(Z),14'-pentadeca- trienyl]resorcinol	(12; R = H) (13; R = H) (14; R = H) (15; R = H)	Brazil, Mozambique, India etc. (as for Anacardium acids)
Rhus vernificera	Japanese lac Chinese lac	2-Methylcardol (R = Me) (4 constituents) Urushiol*	as in (12) to (15) but 2-Methyl before each name 3-pentadecylcatechol 3-[8'(Z)-pentadecenyl]catechol 3-[8'(Z),11'(Z)-pentadecadienyl]- catechol 3-[8'(Z),11'(Z),13'-pentadeca- trienyl]catechol 3-[8'(Z),11'(Z),14'-pentadeca- trienyl]catechol (16), (17), (18), and (20)	(16) (17) (18) (19) (20)	China, Korea, Japan  ditto, N. America
Rhus toxicodendron radicans	poison ivy	Urushiol*			
Rhus toxicodendron diversilobum	poison oak	Urushiol*			

Anacardium semecarpus	Indian marking nut (BNSL)	Bhilawainol	India
Melannorrhœa usitata Wall	Burmese lac	thitsiol	Burma
Gluta renghas	—	glutarenghol	(21)
Semecarpus heterophylla	renghas fruit	renghol	(21a)
Semecarpus vernicifera	Formosan lac	laccol	(21b)
Rhus succedanea	(Indochina lac) Vietnam		(21c)
<i>Proteaceae</i>			Vietnam
Grevilla pyramidalis	—	a cardol monoene	(22)
<i>Gymnospermae</i>			N.W. Australia
Ginkgo biloba		bilobol	(13; R = H)
<i>Triticum</i>			China, Europe, Japan
Triticum vulgare	Wheat bran phenols	5-nonadecylresorcinol 5-heneicosylresorcinol	(23)

\*The name is derived from kiurushi, the Japanese name for sap.

**Table 2 (continued)**

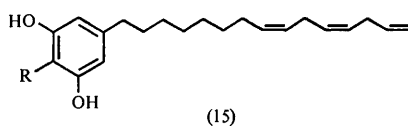
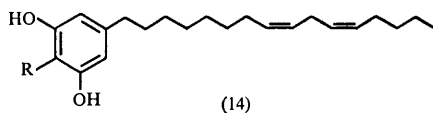
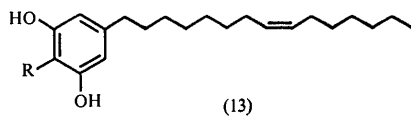
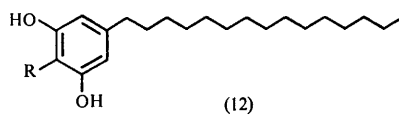
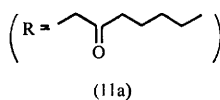
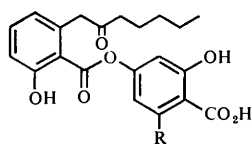
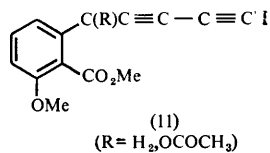
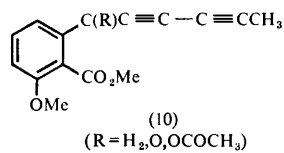
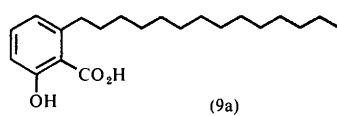
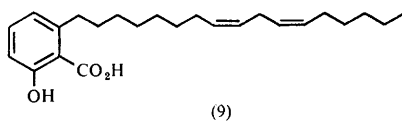
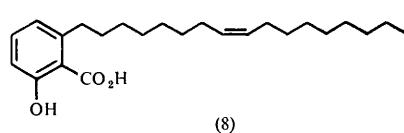
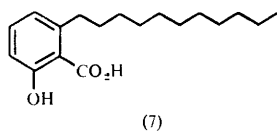
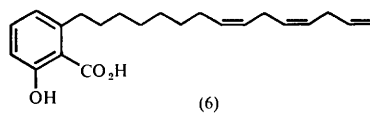
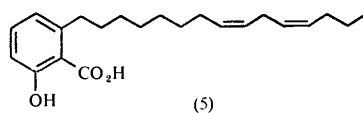
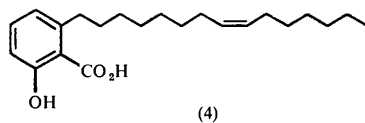
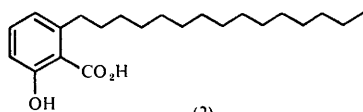
<i>Botanical/</i> <i>Biological origin</i>	<i>Common/</i> <i>Trivial Name</i>	<i>Main Component Formula</i> <i>(side chain)</i>	<i>Structure</i> <i>(see p. 509)</i>	<i>Country of Origin</i>
<i>Bacterial</i> Mycobacterium leprae	$\alpha$ - and $\beta$ - leprosol	5-heptadecyl-4,6-dimethyl- resorcinol monomethyl ether 5-pentadecyl-4,6-dimethyl- resorcinol	(24) (25)	Isolated in Europe
Bacterium pseudomonas sp B-9004	—	2,5-dialkyl resorcinol	(26)	Isolated in Japan

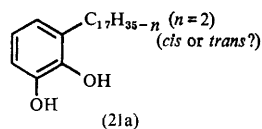
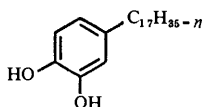
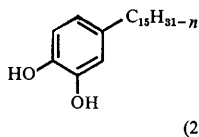
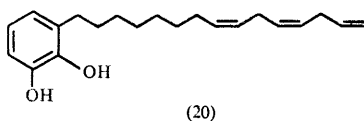
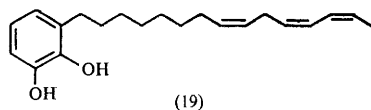
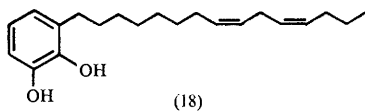
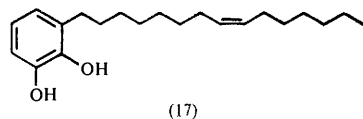
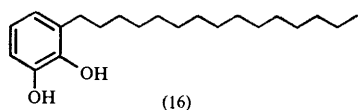


Table 3 Long Chain Monohydric Phenols

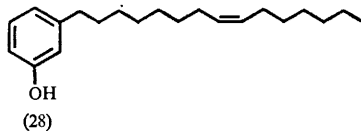
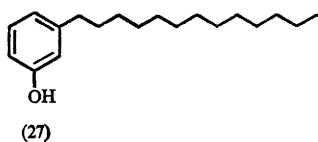
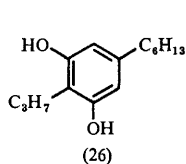
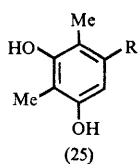
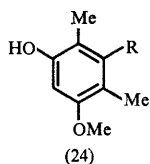
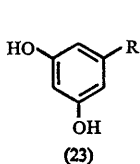
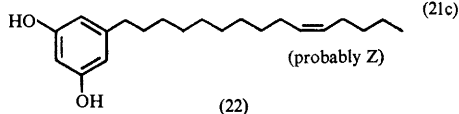
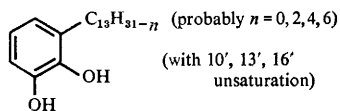
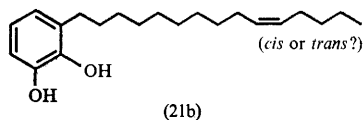
<i>Botanical/ Biological origin</i>	<i>Common/ Trivial Name</i>	<i>Main Component (side chain)</i>	<i>Formula</i>	<i>Structure (see pp. 509, 510)</i>	<i>Country of Origin</i>
<i>Anacardiaceae</i>					
Anacardium occidentale	cashew nut shell liquid	cardanol(C <sub>15</sub> ) (4 constituents)	3-pentadecylphenol 3-[8'(Z)-pentadecenyl]phenol 3-[8'(Z),11'(Z)-pentadecadienyl]- phenol	(27) (28) (29)	As for Anacardic acid, cardol
			3-[8'(Z),11'(Z),14'-pentadeca- trienyl]phenol	(30)	
Camponospermum auriculata		camponosper- manol	3-[2-oxo-9'(Z)-nonadecenyl]phenol	(30a)	Australia, Solomon Islands
<i>Gymnospermae</i>					
Ginkgo biloba		ginkgol			As for ginkgolic acid
<i>Bacterial</i>					
Cytophaga					
Flexibacter elegans	Flexirubin, gliding bacterium	—	2'-n-dodecyl-3'-hydroxy-5'- methylphenyl 1-[3''-methyl-4''-hydroxyphenyl-1''] heptadeca-1(E),3(E),5(E),7(E),9(E),- 11(E),13(E),15(E)-heptaenyl-17-oate	(31)	

*Non-isoprenoid Long Chain Phenols*

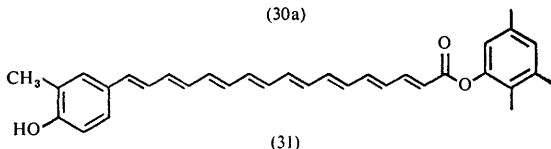
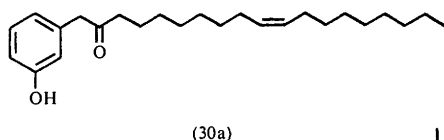
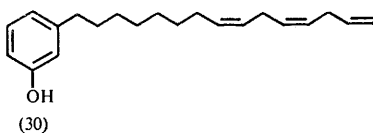
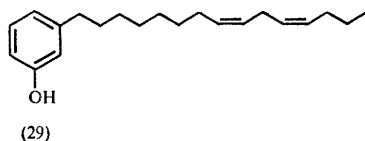




and probably unsaturated members,  
 $n = 0, 2, 4, 6$  (for  $C_{15}$  and  $C_{17}$ )



## Non-isoprenoid Long Chain Phenols



are said to exist in the coastal portion of Brazil. The tree was introduced into Africa through Portuguese influence and from there to India in the seventeenth century. Its development in other non-indigenous countries is comparable with that of the rubber plant. Cashew nut production has increased world wide and it holds a share (20%) almost the same as the almond and the hazel. In recent years Mozambique has become the principal producer as shown in Table 4.\*<sup>6</sup> The phenolic shell liquid (CNSL) could be said to be the most widely distributed and abundant natural phenolic material with potentially an annual availability of nearly 125 000 tons. The cashew nut-shell liquid of *Anacardium occidentale* is unusual in comprising a phenolic acid<sup>9,10</sup> [anacardic acid (3), (4)

**Table 4** Production of cashew nuts for commercial processing and export

	(in tonnes 1000)										
	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973
Brazil	22	16	22	22	26	29	29	26	16	40	25
Mozambique	133	142	119	106	97	189	132	138	156	201	167
Tanzania	43	57	65	75	78	87	94	92	116	127	128
Kenya	5	5	8	6	9	9	10	24	11	16	11
India	66	74	67	59	72	68	68	58	90	77	72
Total	269	294	281	268	282	382	333	338	389	461	403

\*Probably due to political factors, East African production of CNSL since January 1978 has declined and Brazil is now the principal producer with the result that this industrial by-product has quadrupled in value.

<sup>9</sup> Städeler, *Ann. Chim. u Pharm.*, 1847, 63, 137.

<sup>10</sup> (a) H. J. Backer and N. H. Haack, *Rec. Trav. chim.*, 1941, 60, 661; (b) P. T. Izzo and C. R. Dawson, *J. Org. Chem.*, 1949, 14, 1039; (c) V. J. Paul and L. M. Yeddanapalli, *J. Amer. Chem. Soc.*, 1956, 78, 5675; (d) J. H. P. Tyman and N. Jacobs, *J. Chromatog.*, 1971, 54, 83.

(5), and (6)], dihydric phenols, cardol,<sup>9,11</sup> and 2-methylcardol<sup>12</sup> and a monohydric phenol (cardanol).<sup>12a</sup>

**A. Phenolic Acids**—Other *Anacardiaceae* such as *Anacardium giganteum* have a limited exploitation and the same is true of certain *Pentaspadon* types from which oily exudates or latexes have been obtained containing (8), (9).<sup>13</sup> The *Gymnospermae* and *Compositae*\* are sources of the phenolic acid (4)<sup>14</sup> and the methyl ester ethers (10), (11)<sup>15</sup> respectively. The orsellinic acids rarely exist in the free state but they are possibly biogenetic precursors of anacardic acids.

**B. Dihydric Phenols.**—The dihydric phenols are more widely distributed in type than either the phenolic acids or the monohydric phenols. They exist in *Anacardiaceae*, mostly in *Anacardium occidentale*, and in the *Rhus* genus and to a limited extent in the *Proteaceae*, the *Gymnospermae*, and the *Triticum*.

Cardol [(12), (13), (14), (15); R=H]<sup>9,11</sup> and 2-methylcardol<sup>12</sup> (R=Me) are probably the most widely distributed through their presence in natural and technical CNSL. Constituents of urushiol occur in a wide variety of *Anacardium* species mostly in *Rhus vernicifera* [as (16) to (19)]<sup>16</sup> and in *Rhus toxicodendron* [as (16), (17), (18), and (20)],<sup>17</sup> the former being probably the oldest known cultivated source of a phenolic lipid. Originally from China it has been known under cultivation and used as a lacquer† in Japan since the sixth century AD,<sup>5</sup> the latex being collected in the same way as with the rubber plant, *Hevea brasiliensis*. Although the usage of urushiol for Japanese lacquer at the peak period was probably well in excess of 600 tons per annum,<sup>18</sup> technical CNSL has had a much wider application. The compositions of Formosan Lac containing laccol<sup>19</sup> (bis-homourushiol), of Burmese Lac containing thitsiol,<sup>20</sup> (21) (15:1) isourushiol, of *Semecarpus heterophylla*<sup>21</sup> containing renghol, (15:1) urushiol, and

\*The C<sub>5</sub>, C<sub>6</sub> chains in these suggest there may be as yet other undetected materials in the long chain class.

†This is not to be confused with sticklac (or shellac) of Indian origin sometimes called India lac, and based on aleuritic acid.

<sup>11</sup> (a) C. R. Dawson and D. Wasserman, *J. Amer. Chem. Soc.*, 1948, **70**, 3675; (b) W. F. Symes and C. R. Dawson, *Nature*, 1953, **171**, 841.

<sup>12</sup> (a) J. H. P. Tyman and L. J. Morris, *J. Chromatog.*, 1967, **26**, 287; (b) J. H. P. Tyman, *Chem. Comm.*, 1972, 714; (c) J. H. P. Tyman, *J.C.S. Perkin I*, 1973, 1639.

<sup>13</sup> H. J. Backer, A. B. Grevenstuk, and N. H. Haack, *Rec. Trav. chim.*, 1941, **60**, 678; J. A. Lambertson, *Austral. J. Chem.*, 1959, **12**, 234.

<sup>14</sup> (a) S. Furukawa, *Sci. Papers Inst. Phys. Chem. Res. (Tokyo)*, 1934, **24**, 304; (b) F.-Y. Fu, T.-C. Yu, W.-L. Sung, Y. F. Jai, and N. C. Sun, *Hua Hsueh Hsueh Pao*, 1964, **28**, 52 (*Chem. Abs.*, 1964, **60**, 1634).

<sup>15</sup> F. Bohlmann and K. M. Kleine, *Chem. Ber.*, 1962, **95**, 602.

<sup>16</sup> (a) R. Majima, *Chem. Ber.*, 1922, **55B**, 172; (b) S. V. Sunthakar and C. R. Dawson, *J. Amer. Chem. Soc.*, 1954, **76**, 5070; (c) K. H. Markiewitz and C. R. Dawson, *J. Org. Chem.*, 1965, **30**, 1610.

<sup>17</sup> W. F. Symes and C. R. Dawson, *J. Amer. Chem. Soc.*, 1954, **76**, 2959.

<sup>18</sup> R. Majima, *Chem.-Ztg.*, 1911, **35**, 164.

<sup>19</sup> R. Majima, *J. Tokyo Chem. Soc.*, 1919, **40**, 91.

<sup>20</sup> R. Majima and I. Nakamura, *Chem. Ber.*, 1915, **48**, 1597.

<sup>21</sup> H. J. Backer and N. H. Haack, *Rec. Trav. chim.*, 1938, **57**, 225; G. Bertrand, H. J. Backer, and N. H. Haack, *Bull. Soc. chim. France*, 1939, **6**, 1670.

## Non-isoprenoid Long Chain Phenols

*Gluta renghas*<sup>22</sup> containing (17:1) bis-homourushiol are probably more complex than indicated but modern compositional studies are not yet available. The *Proteaceae* family includes *Grevillea pyramidalis*<sup>23</sup> a bushy shrub producing seed pods which in the spring are coated with a red exudate. Amongst the other families the saturated resorcinols (22) and (23) are unusual and it seems probable that unsaturated members may well also be present.\*

The only non-plant sources are *Mycobacterium leprae* which contains  $\alpha$  and  $\beta$ -leprosol (24)<sup>24</sup> and the soil-derived 2,5-dialkylresorcinol (26).<sup>25</sup>

**C. Monohydric Phenols.**—*Anacardium occidentale* contains cardanol<sup>26</sup> [(27), (28), (29), and (30)] a relatively minor component in the natural product but the major one in the derived technical CNSL. Camnospermanol<sup>27</sup> is an unusual lipid containing a keto function in the side chain. The monohydric ginkgo<sup>26a,28</sup> is a chief component of *Ginkgo biloba*. In the non-plant sources flexirubin (31)<sup>29</sup> from *Flexibacter elegans* is similar to the carotenoids in structure.

A characteristic feature of the phenolic lipids is their vesicant action to which some people are acutely sensitive.<sup>3a,30</sup> Probably foremost in this category is urushiol and this aspect has received intensive study. The artistic use to which this material has been put in the Far East does not seem to have been deterred by the physiological action.

## 4 Extraction

This section is concerned with the extraction of two of the phenolic lipids which have been commercially developed, namely *Anacardium occidentale*<sup>4,6,31</sup> and *Rhus vernicifera*.<sup>5</sup> Apart from the edible use of the kernel of the cashew nut, processed shell liquid (technical CNSL) has for more than four decades attracted considerable attention as a source of phenols for formaldehyde polymerisation and use in compounded form as a friction dust for automobile brakes and clutches. Urushiol has had an extensive use in its natural state over many centuries in the art and craft of Japanese lacquering.

\*The co-occurrence of the tocopherols (mevalonate derived) and the C<sub>19</sub> and C<sub>21</sub> phenols (polyketide) is unusual.

<sup>22</sup> H. J. Backer and N. H. Haack, *Rec. Trav. chim.*, 1941, **60**, 656.

<sup>23</sup> J. L. Occolowitz and A. S. Wright, *Austral. J. Chem.*, 1962, **15**, 858.

<sup>24</sup> (a) J. A. Crowder, F. H. Stodola, and R. J. Anderson, *J. Biol. Chem.*, 1936, **114**, 431; (b) J. D. Bu'lock and A. T. Hudson, *J. Chem. Soc.*, (C), 1965, 61.

<sup>25</sup> T. Kitahara and N. Kanda, *J. Antibiotics*, 1975, **28**, 943.

<sup>26</sup> (a) B. Loev and C. R. Dawson, *J. Amer. Chem. Soc.*, 1958, **80**, 643; (b) W. F. Symes and C. R. Dawson, *J. Amer. Chem. Soc.*, 1953, **75**, 4952; (c) P. T. Izzo and C. R. Dawson, *J. Org. Chem.*, 1950, **15**, 707.

<sup>27</sup> J. A. Lambertson, *Austral. J. Chem.*, 1958, **11**, 73.

<sup>28</sup> S. Furukawa, *Sci. Papers Res. Inst. Phys. Chem. Res. (Tokyo)*, 1935, **26**, 178.

<sup>29</sup> (a) H. Reichenbach, H. Kleinig, and H. Achenbach, *Microbiol.*, 1974, **101**, 131; (b) H. Achenbach and J. Witzke, *Angew. Chem. Internat. Edn.*, 1977, **89**, 198.

<sup>30</sup> C. R. Dawson and A. P. Kurtz, *J. Med. Chem.*, 1971, **14**, 729; R. A. Johnson, H. Baer, C. H. Kirkpatrick, C. R. Dawson, and R. G. Khurana, *J. Allergy Clin. Immunol.*, 1972, **49**, 27.

<sup>31</sup> D. C. Russell, 'Cashew Nut Processing', *Agric. Serv. Bull.*, 6, FAO, Rome, 1969; V. Ramanathan and V. Pacheiyappan, *Paintindia*, 1955, **25**, 12.

**A. Cashew Nut-shell Liquid.**—Interest in the cashew nut was centred originally on obtaining the kernel, and the shell liquid was of little interest until its useful properties in formaldehyde polymerisation were appreciated in the years preceding World War II.

Most CNSL is now extracted automatically by the hot 'CNSL bath process' in which raw nuts are heated at 180—190 °C whilst held on a slowly travelling conveyor belt submerged below the liquid level. The natural CNSL is decarboxylated and the cardanol produced from the anacardic acid supplements the technical CNSL in the hot bath. The roasted nuts (after removal of residual CNSL) with the inner shell intact are shelled by either the Sturtevant procedure\* in which the nut is projected on to a hard plate which shatters the shell and centrifugally allows a separation of the intact kernel, or the Oltremare process in which the shell is cut around the middle and the two halves removed leaving the intact kernel. Some natural CNSL is obtained by cold solvent extraction on a very limited scale in Brazil and in East Africa. Since the main demand is for cardanol the natural material has to be subsequently decarboxylated and accordingly most manufacture is directed towards obtaining technical CNSL.

Considerable attention is paid to the prevention of contamination of the kernel by traces of CNSL and appropriate specifications and analytical procedures<sup>32</sup> enable the situation to be safeguarded.

**B. Urushiol.**—The extraction of urushiol from the tree *Rhus vernicifera* has been carried out systematically in Japan since the sixth century and almost certainly was also used in China during the Chou dynasty of 1122—249 BC. The process is completely different from that used for technical CNSL since the natural product occurs in the sap of the tree *Rhus vernicifera* and, unlike technical CNSL, is the objective rather than the by-product of cultivation. The tree is tapped at about the tenth year of cultivation by lateral sloping incisions in the bark. After removal of the bark the fluid sap is collected from the trunk and from branches greater than one inch in diameter during June to September. The tree is killed as a result but the roots give five or six shoots which eventually become available for lacquer production after approximately six years. The sap is white to greyish in colour, of treacly consistency at first, but on exposure to the air turns yellow brown and then black. After removal of impurities and water it is used in its natural state. The crude sap containing approximately 70% urushiol, 4% gum, 2% albuminous materials, and 24% water<sup>33</sup> is stirred to give a uniform consistency, filtered, heated, and stirred to reduce the moisture content and finally stored in air-tight containers. Often about 20% tung oil was added to the final lac. In 1910 some 600 tons was produced at a value then of approximately \$700 per ton. On account of its value it was sometimes adulterated.

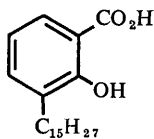
\*A method developed collaboratively with the Tropical Products Institute.

<sup>32</sup> T. W. Hammonds, *Analyst*, 1966, **91**, 401.

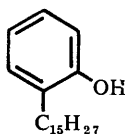
<sup>33</sup> O. Korshelt and H. Yoshida, *Trans. Asiatic Soc. Japan*, 1884, **12**, 182.

## 5 Structure of Phenolic Lipids

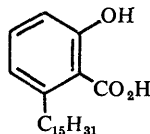
**A. Component Phenols of Anacardium Occidentale.**—In view of the dominant position this material holds amongst the phenolic lipids it is discussed first. Natural cashew nut-shell liquid was first investigated systematically in 1847 by Städeler<sup>9</sup> who separated cardol from anacardic acid and decarboxylated the latter, although the correct formula for the acid,  $C_{22}H_{32}O_3^*$  was not established<sup>34</sup> until forty years later. The presence of a salicylic acid system and a pentadecadienyl side chain were later recognised<sup>35</sup> but the erroneous structures (32) and (33) for anacardic acid and anacardol† were put forward by analogy with work on pelandjauic acid<sup>36</sup> and pelandjauol.



(32)

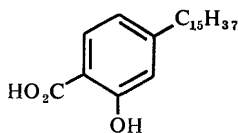


(33)



(3)

Doubts concerning earlier structural work<sup>37</sup> led Gohkle *et al.*<sup>38</sup> to synthesise 2- and 4-pentadecylphenol which however proved to be different from hydrogenated anacardol and suggested that it was 3-pentadecyl phenol (27), a conclusion independently reached by Backer and Haack.<sup>10a</sup> They isolated 3-methoxyphthalic acid and 3-methoxybenzoic acid together with palmitic acid, by oxidative degradation of hydrogenated and methylated anacardic acid and anacardol respectively and synthesised<sup>10a</sup> the latter (discussed later). The formation of 3-methoxyphthalic acid indicated formula (3) for hydrogenated anacardic acid but it could not be synthesised by the Kolbe reaction on hydrogenated anacardol since this gave (34). (15:0)-Anacardic acid has been synthesised by two different methods.<sup>39a</sup>



(34)

\*This is the molecular formula for the diene, which is the average unsaturation. The inhomogeneity was not recognised until more than sixty years later.

†The name anacardol was later changed to cardanol by M. T. Harvey on account of its confusion with another product, isolated by D. S. Naidu, *J. Indian Sci.*, 1925, **8A**, 129.

<sup>34</sup> S. Ruhemann and S. Skinner, *J. Chem. Soc.*, 1887, **51**, 663.

<sup>35</sup> A. J. H. Smit, *Proc. K. Akad. Wetenschappen Amsterdam*, 1931, **34**, 165.

<sup>36</sup> P. von Romburg, *Proc. Akad. Sci. Amsterdam*, 1930, **33**, 589.

<sup>37</sup> P. P. Pillay, *J. Indian Chem. Soc.*, 1935, **12**, 226.

<sup>38</sup> G. Gokhale, M. Patel, and R. Shah, *Current Sci.*, 1940, **9**, 362.

<sup>39</sup> (a) A. A. Durrani and J. H. P. Tyman, *Chem. and Ind.*, 1971, 934, 1972, 762; A. A. Durrani and J. H. P. Tyman, *J.C.S. Perkin I*, 1979, 2069 and 2079; (b) J. H. P. Tyman and A. A. Durrani, *Tetrahedron Letters*, 1973, **73**, 4839.



The structure of cardol from natural CNSL first isolated and examined by Städeler and later, with a more detailed but still erroneous outcome, by Spiegel and Correll<sup>40</sup> was reinvestigated by Backer and Haack<sup>10a</sup> who put forward the molecular formula,  $C_{15}H_{27}C_6H_3(OH)_2$  for what they considered to be penta-decadienylresorcinol. The hydrogenated material was assigned the structure (12; R=H) since oxidation of the methyl ether gave 3,5-dimethoxybenzoic and palmitic acid. The structure was confirmed by synthesis<sup>41</sup> some years later.

Recently the 2-methylhomologues of cardol [(12) to (15); R=CH<sub>3</sub>] were separated by argentation t.l.c., structurally investigated by mass spectrometry and <sup>1</sup>H n.m.r., and the hydrogenated material synthesised.<sup>12a,b,c</sup> Cardanol [(27) to (30)] was found to be present in natural CNSL.

The main component phenolic material in technical CNSL renamed cardanol and thought mistakenly<sup>42</sup> to be a monophenol with a C<sub>14</sub> side chain was re-examined by Dawson and Wasserman<sup>43</sup> and shown to be substantially identical, except for the degree of unsaturation, with the product of solvent extraction of natural CNSL followed by thermal decarboxylation.

In the early structural work it was universally believed that a pentadecadienyl side chain was present in the component phenols. Later, cardanol was shown to consist of a mono- and a di-olefin which formed crystalline glycols separable by fractional crystallisation. Oxidation of the glycol from the mono-olefin with periodic acid furnished heptaldehyde indicating the double bond to be at the 8' position.<sup>44</sup> Similar work with anacardic acid demonstrated its hetero-olefinic nature<sup>10b</sup> and in addition to a diol and a tetraol it appeared likely that a polyol, probably a hexaol, was present.

Subsequently by chromatography of cardanol methyl ether on alumina, resolution into the saturated material, cardanol monoene, cardanol diene, and cardanol triene methyl ethers was effected. The structure of the methyl ether of each unsaturated constituent was found by ozonolytic cleavage.<sup>45</sup> The presence of unsaturation at the 8', 11' positions in the diene was found by the isolation of 8'-(3-methoxyphenyl)octanoic acid, oxalic acid, and n-butyraldehyde. The isolation of the same acid, oxalic acid (2 moles), and formaldehyde indicated unsaturation at the 8', 11', and 14' positions in the triene since the formation of oxalic acid rather than malonic acid had been established earlier in the oxidation of methylene-interrupted polyolefins.<sup>46</sup> The unsaturation constituents of cardanol thus have structures (28) to (30). The monoene, diene, and triene have been synthesised.<sup>47,48</sup>

By low temperature crystallisation (from acetone at -80°C), followed by

<sup>40</sup> L. Spiegel and M. Correll, *Ber. Deut. Pharm. Ges.*, 1913, **23**, 356.

<sup>41</sup> D. Wasserman and C. R. Dawson, *J. Amer. Chem. Soc.*, 1948, **70**, 2675.

<sup>42</sup> M. T. Harvey and S. Caplan, *Ind. and Eng. Chem.*, 1940, **32**, 1306.

<sup>43</sup> D. Wasserman and C. R. Dawson, *Ind. and Eng. Chem.*, 1945, **37**, 396.

<sup>44</sup> M. Slettinger and C. R. Dawson, *J. Amer. Chem. Soc.*, 1946, **68**, 345.

<sup>45</sup> W. F. Symes, *Dissertation Abs.*, 1954, **14**, 1554.

<sup>46</sup> D. T. Mowry, W. R. Brode, and J. D. Brown, *J. Biol. Chem.*, 1952, **142**, 679.

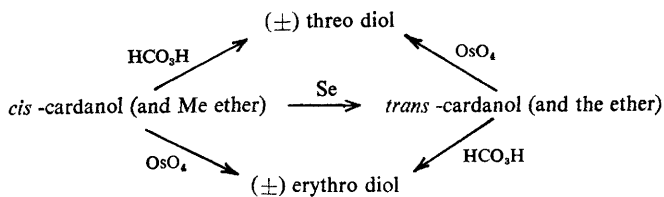
<sup>47</sup> J. H. P. Tyman and J. Caplin, *Chem. and Ind.*, 1973, **40** and 953.

<sup>48</sup> J. H. P. Tyman, unpublished data.

potassium permanganate oxidation, Paul and Yeddanapalli<sup>10c</sup> isolated the monoene, diene, and triene constituents and showed the unsaturation to be present at the 8', 11', and 14' positions giving the structures (4) to (6) respectively for the three constituents.

Cardol dimethyl ether was separated by chromatography on alumina into three unsaturated constituents and the unsaturation shown to be at the 8', 11', and 14' positions as with cardanol and anacardic acid. The monoene, diene, and triene constituents therefore had the structures [(13) and (14); R = H] respectively.<sup>11b</sup> The monoene<sup>49</sup> and the dimethyl ether of the diene have been synthesised.<sup>50a</sup>

In early work the *trans* configuration was assigned to the 8' and 11' unsaturation in the constituents of cardanol, anacardic acid and cardol. The supposed synthetic 3-[8'pentadecenyl]anisole<sup>51</sup> thought to be the *cis* isomer, on account of the final hydrogenation step, was converted to a glycol different in m.p. from that derived from cardanol monoene methyl ether from which it was concluded that the natural monoene had the *trans* configuration. Later, an examination of the natural product revealed a band at 10.4  $\mu\text{m}$  (960  $\text{cm}^{-1}$ ) characteristic of the C—H bond in a *cis*-olefin, also present in the diene and triene.\* Dihydroxylation of natural (*cis*) cardanol monoene methyl ether with osmic acid gave the same glycol as the dihydroxylation with performic acid of *trans*-cardanol monoene methyl ether, itself obtained by the isomerisation of the *cis*-isomer with selenium.<sup>26b</sup> Recently these observations have been extended and applied to the phenol itself as shown in Scheme 1.<sup>52</sup> Examination of the constituents of cardol revealed that they also possessed the *cis* configuration. The existence of the unsaturated constituents of cardanol, cardol, 2-methylcardol, and anacardic acid in the *cis* configuration has been shown in the <sup>1</sup>H n.m.r. spectra by the *J* coupling constant values of the olefinic hydrogens.<sup>10d,48,53</sup>



Scheme 1

\*The reason for this discrepancy in m.p. was attributed to the fact that the synthetic product contained none of the olefin but the corresponding alkane and alkyne, dihydroxylation of which had taken place to give a different product entirely e.g.  $\text{—C}\equiv\text{C—}\rightarrow\text{—CO—CH(OH)—}$ .

<sup>49</sup> J. H. P. Tyman and S. W. D. Odle, *Chem. and Ind.*, 1975, 88.

<sup>50</sup> (a) C. J. Baylis, M. Phil. Thesis, Brunel University, 1977; (b) J. H. P. Tyman, unpublished data.

<sup>51</sup> M. Sletzingner and C. R. Dawson, *J. Org. Chem.*, 1949, 14, 849.

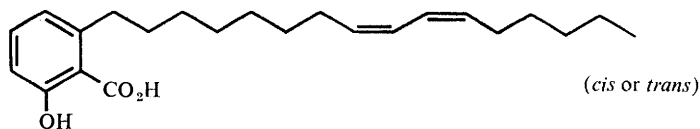
<sup>52</sup> J. H. P. Tyman and A. A. Durrani, unpublished data.

<sup>53</sup> J. H. P. Tyman and R. J. Edwards, unpublished data; P. Gedom, P. Sampathkumaran and M. Sivasamban, *Indian J. Chem.*, 1972, 10, 388.

**B. Phenolic Acids from Other Species.**—The component phenols of *Ginkgo biloba*, ginkgol and bilobol, have been separated and by colour reactions, oxidative degradation and hydrogenation the structure established. Ginkgolic acid was shown to be identical to (15:1) anacardic acid, (4), 6-[8' (Z)-pentadecenyl] salicylic acid by decarboxylation to ginkgol<sup>14a</sup> [identical to (15:1) cardanol] and hydrogenation of the latter to (15:0) cardanol. It has been synthesised.<sup>54</sup> Loev and Dawson<sup>26b</sup> concluded that ginkgol was the 8'-monoene and not a mixture like cardanol. Bilobol<sup>55</sup> was identical with (15:1) cardol, (13; R=H). The isolation of the C<sub>14</sub> side chain compound ginkgolonic acid<sup>14b</sup> (Table 1) has been verified by the identical melting points of *O*-methyl dihydroginkgolonic acid and synthetic 6-*n*-tetradecylsalicylic acid *O*-methyl ether.<sup>39b</sup>

The structure of anagigantic acid (7) followed from the isolation of dodecanoic acid and 3-methoxybenzoic acid upon oxidative degradation of the methylated natural product.<sup>56</sup> 6-*n*-Undecylsalicylic acid has been synthesised<sup>39a</sup> and it appears to be identical with anagigantic acid.

Pelandjauic acid was examined quite early<sup>36</sup> in the study of phenolic lipids but the structure was further partly elucidated by Backer *et al.*<sup>13a</sup> who believed it to be 6-heptadecadienyl salicylic acid (9) through reactions similar to those carried out in the anacardic acid series. Tetrahydropelandjauol by hydrogenation and decarboxylation was identical with synthetic 3-*n*-heptadecylphenol. 6-*n*-Heptadecylsalicylic acid has been synthesised.<sup>39a</sup> It has been shown<sup>13b</sup> that *Pentaspadon motleyi* and *Pentaspadon officinalis* are indistinguishable and consist of mixtures of the monoene and diene\* with unsaturation at the 8' and 8', 11' position. Experiments with alkaline isomerisation unambiguously indicated that the diene possesses structure (9) and that an earlier formulation<sup>57</sup> of the material as a C<sub>16</sub> 8', 10'-conjugated diene (35) was incorrect.



(35)

Certain short chain anacardic acids exist as methyl ethers methyl esters, three having a C<sub>6</sub> (10) and two a C<sub>5</sub> side chain (11).<sup>15</sup> They were separable by chromatography. Complete hydrogenation of the three former gave 6-*n*-hexylsalicylic acid *O*-methyl ether and the two latter gave 6-*n*-pentylsalicylic acid *O*-methyl ether both of which have been synthesised.<sup>39b</sup> Both (10) and (11) gave 3-methoxy-

\*In a sample from Professor Backer's collection evidence was found by the author (argentation t.l.c.) of a saturated and a triene constituent.

<sup>54</sup> J. H. P. Tyman, *J. Org. Chem.*, 1976, **41**, 894.

<sup>55</sup> S. Furukawa, *Sci. Papers Inst. Phys. Chem. Res. (Tokyo)*, 1933, **21**, 273.

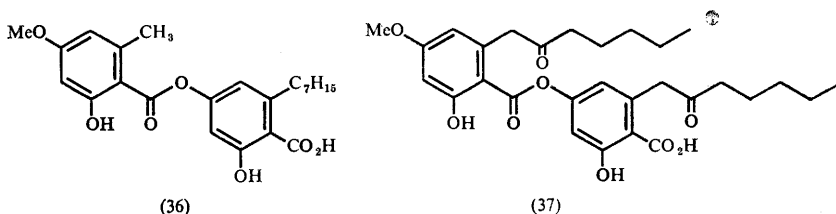
<sup>56</sup> N. K. Sharma and V. N. Sharm, *Indian J. Chem.*, 1966, **4**, 99, 320.

<sup>57</sup> T. G. H. Jones and F. Smith, *Proc. Roy. Soc., Queensland*, 1929, **41**, 73.

## Non-isoprenoid Long Chain Phenols

phthalic acid upon oxidation. The pure compounds were identified as methyl 6-(hexa-2',4'-diynyl), 6-(1'-acetoxyhexa-2',4'-diynyl), 6-(1'-oxohexa-2',4'-diynyl) salicylate *O*-methyl ethers, methyl 6-(penta-2',4'-diynyl), and methyl 6-(1'-acetoxy-penta-2',4'-diynyl) salicylate *O*-methyl ethers.<sup>15</sup>

Discussion of long chain phenolic acids would be incomplete without reference to the higher homologues of orsellinic acid. Their ready decarboxylation accounts for their small distribution in the phenolic lipids and also for the wide occurrence of a number of 5-alkylresorcinols. A C<sub>7</sub> homologous orsellinic acid in combined (depside) form appears in spaerophorin<sup>58</sup> (36) and in the 2'-oxoform in microphyllinic acid<sup>59</sup> (37). The structures of the orsellinic depsides and depsidones have been the subject of extensive classical researches notably by Asahina.<sup>60</sup>



**C. Dihydric Compounds (other than Cardol).—(i) Resorcinol Compounds.** The exudate from *Grevillea pyramidalis* contains more than 60% of 5-[10'-penta-deceny]resorcinol,<sup>23</sup> the dimethyl ether of which gave 3,5-dimethoxybenzoic acid upon oxidation while the dihydro derivative gave n-hexadecanoic acid indicating the presence of a C<sub>15</sub> side chain. Ozonolysis of the dimethyl ether produced valeraldehyde and indicated the 10'-monoene structure (22) (Table 2). The *m*-substitution was proved elegantly by mass spectrometry<sup>61</sup> and has provided a general method for detecting this orientation. The configuration of the double bond was not established, but it seems very likely, by analogy with most phenolic lipids, to be *cis*.

From the non-saponifiable portion of a n-hexane extract of wheat bran five saturated long chain resorcinols have been isolated.<sup>62</sup> Although at first thought to be homogeneous, the C<sub>20</sub> side chain revealed by <sup>1</sup>H n.m.r. and elemental analysis seemed unlikely biogenetically and chromatographic examination of the methylated material showed the presence of 82% of 5-nonadecylresorcinol (23; R=C<sub>19</sub>H<sub>39</sub>) and some 5-heneicosylresorcinol (23; R=C<sub>21</sub>H<sub>43</sub>), the remainder comprising the C<sub>17</sub>, C<sub>23</sub>, and C<sub>25</sub> homologues. The structures were

<sup>58</sup> Y. Asahina and A. Hasimoto, *Chem. Ber.*, 1936, **69B**, 416.

<sup>59</sup> T. Asahina and F. Fuzikawa, *Chem. Ber.*, 1935, **68B**, 80.

<sup>60</sup> Y. Asahina, *Phytochim.*, 1934, **8**, 33.

<sup>61</sup> J. L. Occolowitz, *Analyt. Chem.*, 1964, **36**, 3177.

<sup>62</sup> E. Wenkert, E.-M. Loeser, S. N. Mahapatra, F. Schenker, and E. M. Wilson, *J. Org. Chem.*, 1964, **29**, 435.

deduced by colour reactions and by chromatographic and spectroscopic comparison with the isomeric methylresorcinol dimethyl ethers. The C<sub>19</sub> and C<sub>21</sub> members were synthesised.

Bacterial sources have given rise to long chain dihydric phenols and the first group of these, the  $\alpha$ - and  $\beta$ -leprosols, was isolated some years ago by Stodola, Crowder, and Anderson<sup>24a</sup> from the non-saponifiable fraction of the acetone soluble neutral fatty material of *Mycobacterium leprae*. The leprosols were considered to be 4,5,6-trialkylresorcinols although Asano and Iguti<sup>63</sup> who synthesised several probable compounds were not able to confirm this structural assignment. Bu'lock and Hudson,<sup>24b</sup> reinvestigating the problem\* reached the conclusion that  $\beta$ -leprosol was a mixture of (a minor part) the monomethyl ether of 4,6-dimethyl-n-heptadecyl- and 4,6-dimethyl-n-pentadecyl-resorcinol (a major part) (24; R = C<sub>17</sub>H<sub>35</sub> and C<sub>15</sub>H<sub>31</sub> respectively) and nor- $\beta$ -leprosol was the dihydric phenol. Asano and Iguti's synthetic material had been compared with a mixture. The *m*-substitution was demonstrated by mass spectrometry and the possible alternative structure (25) (Table 2) eliminated from <sup>1</sup>H n.m.r. spectroscopic evidence (in deuterobenzene solution) by the non-equivalence of the methyl groups in comparison with the singlet exhibited by nor- $\beta$ -leprosol. The (17:0) nor- $\beta$ -leprosol was resynthesised<sup>24b</sup> as was (15:0) nor- $\beta$ -leprosol dimethyl ether.<sup>64</sup> It appears possible that  $\alpha$ -leprosol could be related to (25).

Recently, the 2,5-dialkylresorcinol (26) 2-n-propyl-5-n-hexylresorcinol has been isolated and structurally elucidated.<sup>25</sup>

(ii) *Catechol Compounds.* (a) *Urushiol from Rhus species.* The major natural product amongst the dihydric phenols is urushiol notably in *Rhus toxicodendron*<sup>17</sup> and *Rhus vernicifera*†<sup>16</sup> both of which have been studied extensively.

Majima<sup>16</sup> established that urushiol contained a catechol system with a 3-substituted C<sub>15</sub> side chain and was composed of a saturated and several unsaturated constituents. Hydrogenation gave a single material, 3-pentadecylcatechol, which was synthesised.<sup>65</sup> Hill<sup>66</sup> showed that the product of complete hydrogenation of urushiol, 3-pentadecylcatechol, from *Rhus toxicodendron* was identical with that from *Rhus vernicifera*.

From ozonolytic studies‡ on the unseparated constituents of urushiol dimethyl ether Majima considered a monoene (38), a diene (39), and a triene (40) to be probably present.

Although it seemed to have been assumed that the two *Rhus* species were

\*This was carried out with the remaining few mg of  $\beta$ -leprosol. None of the  $\alpha$ -leprosols was available.

†In some literature the name *verniciiflua* is also used.

‡Professor S. Ito of Tohoku University, Sendai, has mentioned to the author that Majima's ozonolytic and structural work carried out at the same University and at Kiel was based on the technique of Willstätter at the latter University.

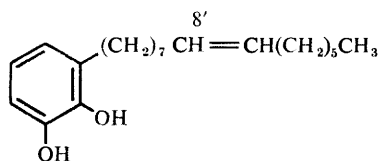
<sup>63</sup> M. Asano and S. Iguti, *J. Pharm. Soc. Japan*, 1951, **71**, 1218.

<sup>64</sup> J. H. P. Tyman and C. A. Barratt, unpublished data.

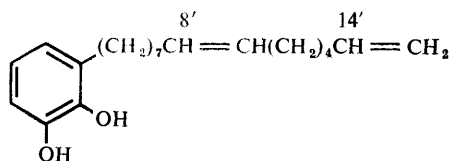
<sup>65</sup> R. Majima, *Chem. Ber.*, 1912, **45**, 2727; R. Majima and J. Tahara, *Chem. Ber.*, 1915, **48**, 1606.

<sup>66</sup> G. A. Hill, V. Mattacotti, and W. D. Graham, *J. Amer. Chem. Soc.*, 1934, **56**, 2736.

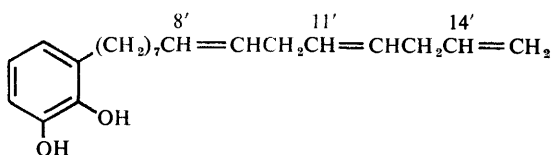
## Non-isoprenoid Long Chain Phenols



(38)



(39)



(40)

structurally identical they were in fact different compositionally and structurally as revealed by the work of Dawson and co-workers.<sup>16b,17</sup> Systematic separation of the four constituents by chromatography of the dimethyl ethers, a technique used for the separation of the constituents of cardanol methyl ether, followed by ozonolysis of the monoene, diene, and triene showed that in *Rhus toxicodendron* the structures of the 8'-monoene, the 8',11'-diene, and the 8',11',14'-triene were (17), (18), and (20) respectively, each being substantially present in the *cis* configuration from the presence of an i.r. band at 10.6  $\mu\text{m}$ . Chromatographic separation, ozonolysis, and u.v. absorption indicated the monoene, diene, and triene constituents of *Rhus vernicifera* to have the structures (17), (18), and (19), all mainly in the *cis*-configuration, the differences from Majima's proposals being with 8',11'-diene and the 8',11',13'-triene. The semi-conjugated structure rested upon u.v. spectral evidence and 8',11',13' rather than 8',10',13' unsaturation from the absence of acetaldehyde in the ozonolysis of the maleic anhydride adduct. The absence of a terminal vinylic group in the triene from lac urushiol and its presence in the triene from *Rhus toxicodendron* can be demonstrated by <sup>1</sup>H n.m.r.<sup>67</sup>

(b) *Catechols from other species.* A number of species of the *Anacardiaceae* family contain one or more urushiol constituents with a C<sub>15</sub> or C<sub>17</sub> side chain. (15:1) Urushiol (bhilawainol) in both the *cis* and *trans*-forms has been identified in *Anacardium semecarpus*. Identification of the configurational isomers followed from the isolation of two different glycols by hydroxylation.<sup>68</sup>

Renghol from *Semecarpus heterophylla*<sup>21</sup> is 3-[10'-pentadecenyl]catechol most probably in the *cis*-configuration.

Laccol from *Semecarpus vernicifera*<sup>19</sup> appears to contain a monoene, 3-[10'-heptadecenyl]catechol, and a triene, 3-[10',13',6'-heptadecatrienyl] catechol, both probably *cis* in configuration.

<sup>67</sup> J. H. P. Tyman and A. J. Matthews, unpublished data.

<sup>68</sup> B. Loev, *Nature*, 1960, **186**, 389.

Glutarenghol from *Gluta rhengas*<sup>22</sup> is probably 3-[10'-heptadecenyl]catechol, in the *cis* configuration.

The only 4-substituted catechol to be isolated, thitsiol<sup>20</sup> (21) (or isourushiol) gave upon hydrogenation 4-heptadecylcatechol which was synthesised. It seems likely that a 10'-monoene may well be present by analogy with related materials.

**D. Monohydric Phenols.**—Apart from cardanol and ginkgol which were discussed in relation to the phenolic acids there are a few monohydric phenols which appear to be unassociated with an acidic precursor. Camnospermanol from Tigaso oil obtained from *Camnospermum auriculata*, a species of the Anacardiaceae family is unusual in apparently arising from a 'tetraketide' by interaction with oleic acid. The structure (Table 3) was confirmed by synthesis.<sup>27</sup>

An exceptional phenolic material is flexirubin (31) the pigment of the 'gliding bacterium', *Flexibacter elegans*. It consists of a mono phenolic polyene acyl (ester) derivative of a dihydric phenol, 2-n-dodecyl-5-methylresorcinol, and has been synthesised in the form of the dimethyl ether.<sup>29</sup>

## 6 Quantitative Compositional Examination of Phenolic Lipids by Various Physical Methods

Progress in the structural elucidation of the constituents of the component phenols in *Anacardium occidentale* (of natural and technical origin) and of various *Rhus* species was possible once chromatographic separation of the methyl ethers had been effected. Apart from the use of column chromatography<sup>45</sup> no other separational methods were employed and only infrared examination<sup>26b</sup> was used in configurational studies.

Many further advances have been made in recent years by the employment of other chromatographic and spectroscopic procedures. For industrial purposes detailed compositional studies are desirable to avoid empirical approaches to the chemical reactions of the component phenols.

Thin layer chromatographic (t.l.c.) separation<sup>12a</sup> of natural and technical CNSL<sup>12a,69</sup> and of urushiol<sup>70,71</sup> with a multiple development technique followed by u.v. spectrophotometry either in an indirect elution method<sup>12a</sup> or by direct densitometry<sup>72</sup> enabled the component phenols to be totally and quantitatively analysed.

The saturated, monoene, diene, and triene constituents of each component phenol have been separated by argentation t.l.c.<sup>12a,69</sup> or on a large scale in argentated dry-packed columns.<sup>73</sup> High performance liquid chromatography with a reverse phase technique effected a direct separation of the component

<sup>69</sup> G. K. Murthy, M. A. Sivasamban, and J. S. Aggarwal, *J. Chromatog.*, 1968, **32**, 519.

<sup>70</sup> J. H. P. Tyman and A. J. Matthews, presented in part at the 26th IUPAC Congress, Tokyo, July 1977.

<sup>71</sup> T. Kato and J. Kumanotani, *J. Polymer Sci., Part A-1, Polymer Chem.*, 1969, **7**, 1455.

<sup>72</sup> J. H. P. Tyman, *J. Chromatog.*, 1978, **166**, 159.

<sup>73</sup> J. H. P. Tyman, S. K. Sood, and A. A. Durrani, unpublished data.

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phenols and their constituents.<sup>74</sup> Adsorption chromatographic separation of natural CNSL after preliminary removal of anacardic acid on alumina followed by separation of remaining component phenols on silicagel,<sup>12</sup> or directly of technical CNSL,<sup>64,69</sup> was valuable both preparatively and analytically.

Gas liquid chromatography of natural and technical CNSL and of urushiol from various *Rhus* sources has been carried out.<sup>70,75</sup> Although the hydrogenated phenols and the unsaturated phenols are sufficiently volatile on non-polar column (such as SE30),<sup>75</sup> tailing peaks due to adsorption made the use of the methyl ethers [of the (15:0) phenols]<sup>76</sup> or the silyl ethers<sup>77</sup> desirable. Quantitative analysis was possible provided corrective response factors were applied.<sup>75,76</sup> By the use of the hydrogenated and methylated component phenols the composition of natural and of technical CNSL from various regional sources was examined.<sup>8,77a</sup> Table 5 shows the composition of natural and technical CNSL

**Table 5** Phenolic composition (%) (C<sub>15</sub>) of natural and technical CNSL

(15:0) Component (or other material)	Natural		Technical	
	Total*	Volatile (g.l.c.)†	Total*	Volatile (g.l.c.)†
Cardanol	1.20	1.59	62.86	82.99
Cardol	11.31	13.78	11.25	14.34
2-Methyl cardol	2.04	2.64	2.08	2.67
Anacardic acid	64.93	81.95	—‡	—‡
Polymer (and minor materials)§ by diff.	20.3	—	23.8	

\*Results expressed as hydrogenated/methylated materials.

†Results expressed as unsaturated phenols.

‡There is approximately up to 1% anacardic acid present in technical CNSL.

§The minor materials are mainly homologous phenols (or the hydrogenated methyl ethers).

of Mozambique origin. With an internal standard in the g.l.c procedure the presence of polymeric material in both natural and technical CNSL was revealed.<sup>77b</sup> It seems most probable from chemical and mass spectroscopic examination that the non-volatile material is dimeric in natural CNSL and rather more polymeric in technical CNSL and arises by way of a Diels-Alder reaction, reminiscent of the formation of 'Kitol' from vitamin A.<sup>78</sup> Although formation of dimeric and polymeric material might be expected in technical CNSL, in the natural product its origin would be necessarily non-thermal and most likely to occur by way of a photochemical or biogenetic route.

<sup>74</sup> R. F. K. Meredith, personal communication; J. H. P. Tyman and K. H. Tam, unpublished data.

<sup>75</sup> J. H. P. Tyman, *J. Chromatog.*, 1975, **111**, 285.

<sup>76</sup> J. H. P. Tyman, *Analyt. Chem.*, 1976, **48**, 30.

<sup>77</sup> (a) J. H. P. Tyman, D. Wilczynski, and M. A. Kashani, *J. Amer. Oil Chem. Soc.*, 1978, **55**, 663; (b) J. H. P. Tyman, *J. Chromatog.*, 1978, **156**, 255.

<sup>78</sup> B. V. Burger, C. F. Gasbers, K. Pachler, R. Bonnett, and B. C. L. Weedon, *Chem. Comm.*, 1965, 588.



The unsaturated constituents of each component phenol were quantitatively analysed by g.l.c.<sup>79,80</sup> and by mass spectrometry.<sup>81a</sup> In the g.l.c. procedure the component phenols were separated by initial adsorption t.l.c., methylated and each component containing the constituents examined on a PEGA column upon which complete resolution occurred. The trimethylsilylated component phenols were also<sup>77a</sup> examined and the total composition of natural and technical CNSL and of urushiol from *Rhus toxicodendron*<sup>82</sup> and *Rhus vernicifera* was found.<sup>70</sup> By this method, combined with mass spectrometry, the presence of the non-conjugated 8',11',14'-triene constituent as well as the major constituent, the semi-conjugated 8',11',13'-triene, was established,<sup>70</sup> although by column chromatography and ozonolysis it had eluded detection. Mass spectrometry has proved of great value as an extremely rapid and reliable method for the quantitative analysis of the saturated monoene, diene, and triene constituents all of which have a comparable volatility and differ conveniently by two mass units. Following isotopic corrections and allowance for the different relative response factors of each constituent, excellent agreement (Table 6) was found between the g.l.c. and m.s. methods of analysis.<sup>81b</sup>

**Table 6** Comparison of the results of g.l.c. and t.l.c.-m.s. methods of analysis of natural CNSL

Component phenol	g.l.c.				t.l.c.-m.s.			
	corrected results using RRF† values				corrected results			
	15:0	15:1	15:2	15:3	15:0	15:1	15:2	15:3
Cardanol	1.42	31.83	14.54	52.21	1.98	31.31	15.23	51.47
Methyl anacardate	4.05	38.3	17.30	40.4	3.65	38.19	16.50	41.65
Cardol	0.001	9.10	22.44	68.36	0.24	10.74	20.64	68.39
2-Methyl cardol*	1.63	18.08	19.55	60.74	3.9	18.43	20.15	57.50

\*These results (g.c. and m.s.) have not been corrected with respect to RRF in either set although the m.s. figures have been corrected for the P+2 peak contribution.

†RRF, Relative response factor.

Mass spectroscopy could be conducted with a preparatory t.l.c. separation or by the g.l.c./m.s. technique in which the component phenols could be analysed from the g.l.c. results and their constituents from m.s., provided a dual correction procedure and a concentration adjustment were incorporated.

U.v. spectrophotometry<sup>12a,72</sup> and <sup>1</sup>H n.m.r. spectroscopy<sup>12,53</sup> have been useful both for structural and quantitative work while i.r. has been employed in the detection of the terminal vinyl group (890—910 cm<sup>-1</sup>). The chemical shifts of various structural features were readily distinguishable and, in the case of anacardic acid, provided a method of analysis<sup>10d</sup> for the saturated monoene,

<sup>76</sup> J. H. P. Tyman, *J. Chromatog.*, 1975, **111**, 277.

<sup>80</sup> J. L. Gellerman and H. Schlenk, *Analyt. Chem.*, 1968, **40**, 739.

<sup>81</sup> J. H. P. Tyman, *J. Chromatog.*, (a) 1977, **136**, 289; (b) 1977, **138**, 97.

<sup>82</sup> J. H. P. Tyman and C. H. Khor, *Chem. and Ind.*, 1974, 526.

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diene, and triene constituents. The method was extended to the analysis of the constituents of cardol, 2-methylcardol, and cardanol.<sup>53</sup> The structural features  $-\text{CH}=\text{CH}_2$  and  $-\text{CH}=\text{CH}-\text{CH}_3$  in *Rhus toxicodendron* and *Rhus vernicifera* respectively were readily distinguished.<sup>70,82</sup> <sup>13</sup>C n.m.r. spectroscopy of the constituents of the component phenols confirmed the previously assigned structural features.

The polymeric material found by g.l.c. can also be determined by t.l.c. or by molecular distillation.<sup>77</sup> Conventional distillation of technical CNSL can be effected only at 0.1 mm, a pressure attainable by the use of wide bore pathways in the equipment, since polymerisation commences at temperatures in the region of 220 °C. The relative merits of batch and continuous distillation and the influence of residence times have been considered.<sup>83</sup>

### 7 Biosynthesis of Non-isoprenoid Phenolic Lipids

The biosynthesis of long chain phenols has not been described although experimental work is currently being conducted by the <sup>13</sup>C labelling technique to establish the pathway in *Ginkgo biloba*.<sup>84</sup> There is probably little doubt that the sequences involved resemble those for 6-methylsalicylic acid (in *Penicillium griseofulvum*).<sup>1</sup> The biosynthesis has to account for the occurrence of 'Claisen condensation' of the polyketide precursor to the exclusion of the 'aldol' (phloroacetophenone) pathway, and for the simultaneous formation of cardol, 2-methylcardol, and cardanol and probably follows the pathway shown in Scheme 2. The similarity of the unsaturation in the constituents of anacardic acid and cardanol on the one hand and of cardol and 2-methylcardol on the other<sup>79</sup> has to be considered and desaturation mechanisms parallel to those for the polyethenoid fatty acids would also be expected to occur.

In the urushiol series, occurrence of oxidative decarboxylation of anacardic acid<sup>85</sup> has been postulated but this could not be effected *in vitro*.<sup>86</sup> Equally, reduction of (41) to anacardic aldehyde (42) followed by a natural enzymatic Dakin pathway or hydroxylation of cardanol formed from anacardic acid seem valid alternatives. Many other possibilities appear to exist for polyketide cyclisation, and the specificity of reactions in individual cases has to be explained.

### 8 Synthesis of Phenolic Lipids

The value of synthesis in the field of phenolic lipids has been in the confirmation of structures and in enabling structure/property correlation to be made through providing generally applicable synthetic procedures for different isomers.

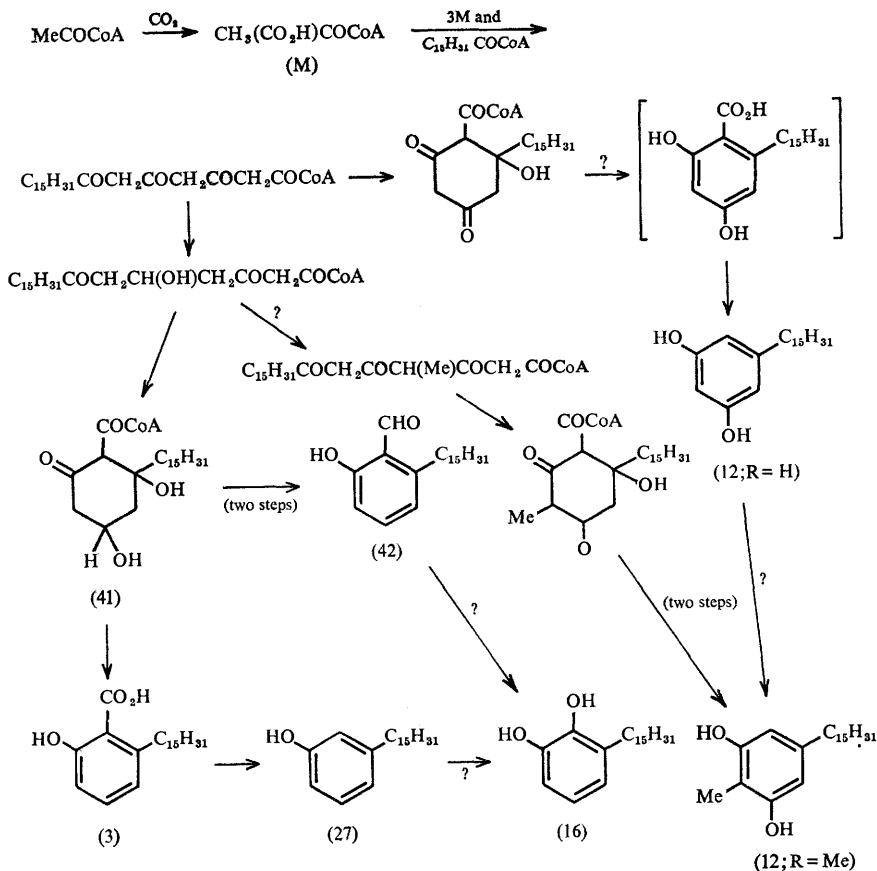
**A. Saturated Mono and Dihydric Phenols.**—For the typical saturated (15:0) and (17:0) *m*-substituted phenolic lipids, the standard approach has been interaction

<sup>83</sup> A. K. Mitra and G. N. Panday, *Chem. Age. India*, 1976, 27, 944.

<sup>84</sup> J. H. P. Tyman, unpublished data.

<sup>85</sup> A. J. Birch and F. W. Donovan, *Austral. J. Chem.*, 1953, 6, 360.

<sup>86</sup> S. K. Lam, M.Phil. Thesis, Brunel University, 1976; presented in part at the 11th IUPAC Symp. on Chem. Nat. Prod., Varna, Sept. 1978.



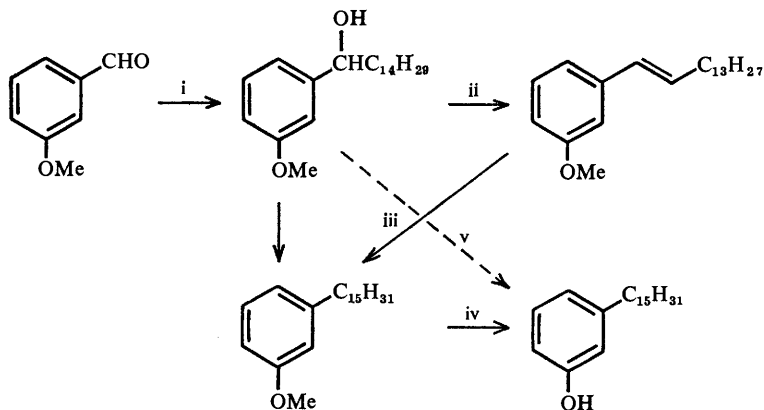
Scheme 2

of the appropriate substituted benzaldehyde with the required *n*-alkylmagnesium bromide followed by reduction and demethylation. With minor variations this has been used for 3-pentadecylphenol,<sup>10a</sup> 3-pentadecylcatechol,<sup>87</sup> 4-pentadecylcatechol,<sup>12c, 88</sup> 5-pentadecylresorcinol,<sup>41</sup> 5-nonodecylresorcinol,<sup>62</sup> 5-heneicosylresorcinol,<sup>62</sup> 3-heptadecylcatechol, 5-pentadecyl-2-methylresorcinol,<sup>12c</sup> 5-pentadecyl-4-methylresorcinol<sup>12c</sup> and certain non-naturally occurring materials.<sup>88</sup> The process is shown in Scheme 3 for (15:0) cardanol.

<sup>87</sup> C. R. Dawson, D. Wasserman, and H. Keil, *J. Amer. Chem. Soc.*, 1946, **68**, 534.

<sup>88</sup> C. R. Dawson and B. Loev, *J. Amer. Chem. Soc.*, 1956, **78**, 4083.

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Reagents: i,  $C_{14}H_{29}Br, Mg$ ; ii,  $KHSO_4$ ; iii,  $H_2, Pd/C$  (or direct with  $H^+$  addn.); iv,  $Pyr.HCl$ ; v,  $HI/P$

Scheme 3

Although the methyl group has been the generally employed protective group, benzyl has also been used since it is simultaneously removed in the direct hydrogenolysis.\*<sup>48</sup> Attempts to use the phenolic aldehyde have met with varying success.<sup>88</sup> The Grignard method of synthesis suffers from two defects,<sup>12c</sup> the formation of Wurtz coupling products which interfere with the purification of the secondary alcohol and the tendency of the alkylmagnesium bromide to oxidise and eventually form the alcohol, a troublesome impurity unless the reaction is conducted in an inert atmosphere. The two reactions can be



avoided by the use of the corresponding alkyl lithium (generated *in situ*). Direct hydrogenolysis proceeds smoothly with the addition of an acidic catalyst.<sup>48</sup> Demethylation of phenolic methyl ethers having C—Me groups by means of pyridine hydrochloride can result in C-methyl group migration.<sup>89</sup> Boron tribromide at low temperature is an alternative highly effective reagent.<sup>48</sup> Since the starting aldehydes are not always readily available, acids, esters, and acid derivatives are alternatives. Conversion of esters to  $\beta$ -ketoesters and alkylation of the latter is less satisfactory than formation of the 'ylid' with dimethylsulphoxide<sup>50</sup> followed by alkylation with the ( $C_{13}$ ) alkyl iodide. Interaction of the methoxybenzoylchloride with a ( $C_{14}$ ) dialkyl lithium cuprate followed by Wolff-Kishner reduction was quite successful.<sup>50</sup> Direct reaction of 2,3-dimethoxyphenyllithium with n-pentadecylbromide has been described as effective<sup>90</sup> but not confirmed.<sup>91</sup>

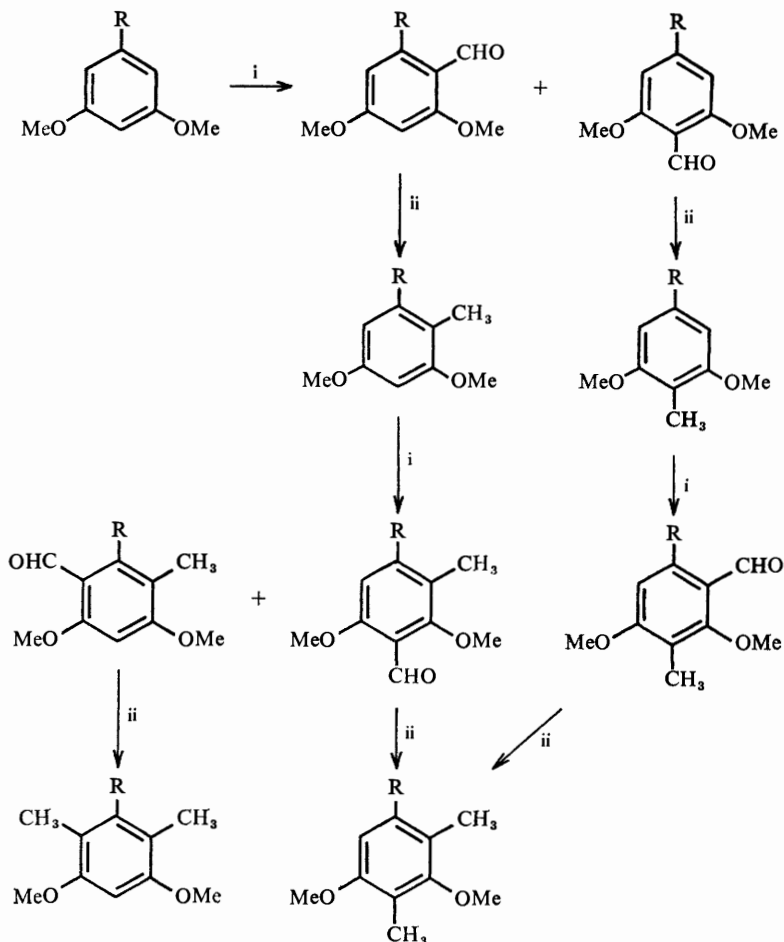
\*If in the urushiol series 2-benzyloxy-3-methoxybenzaldehyde is used some 2-phenyl-7-methoxybenzofuran is formed.

<sup>88</sup> J. H. P. Tyman, *Chem. Comm.*, 1972, 914.

<sup>90</sup> T. Hanafusa and Y. Yukawa, *Chem. and Ind.*, 1961, 23.

<sup>91</sup> J. S. Byck and C. R. Dawson, *J. Org. Chem.*, 1968, 33, 2451.

For the polymethyl phenolic lipids, the commencing aldehydes were not readily available and a different approach (Scheme 4) involving the use of a preformed alkyl chain and the Vilsmeier-Haack reaction was adopted ( $R = C_{15}$  or  $C_{17}$ ),<sup>24b,64</sup>



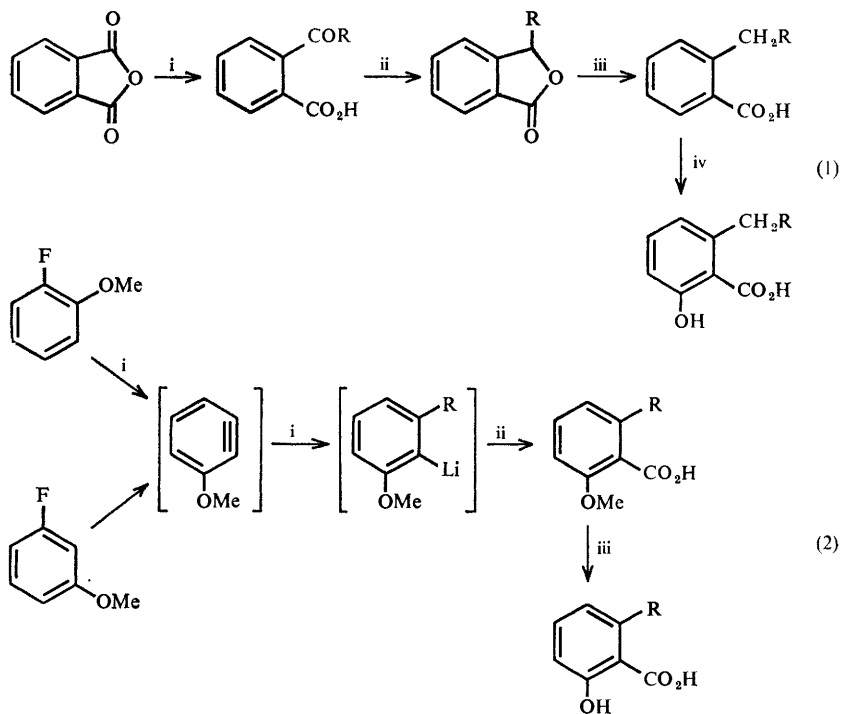
Reagents: i,  $HCONMe_2$ ,  $POCl_3$ ; ii,  $N_2H_4$ ,  $KOH$ , digol

Scheme 4

**B. Saturated Phenolic Acids.**—Two routes<sup>39a</sup> (Scheme 5) to phenolic acids have proved useful. In the first a 2-ketobenzoic acid (tautomeric with a 3-hydroxyphthalide) was reduced to a phthalide and thence to a 2-alkylbenzoic acid, the basic copper salt of which upon thermolysis gave a 6-alkyl salicylic acid. In the

## Non-isoprenoid Long Chain Phenols

second method, *o*-fluoroanisole or *m*-fluoroanisole was reacted with an *n*-alkyllithium and the product carbonated followed by demethylation. A similar approach has enabled, by reaction of 3,5-dimethoxyfluorobenzene, the homologous orsellinic acid dimethylethers to be derived.<sup>39b</sup>



Reagents: (1) i,  $(R)_2Cd$ ; ii,  $NaBH_4$ ; iii,  $HI/P$ ; iv,  $CuSO_4$ , basic salt,  $\Delta$ .  
 (2) i,  $RLi$ ; ii,  $CO_2$ ; iii,  $HI/P$  or  $BCl_3$ .

### Scheme 5

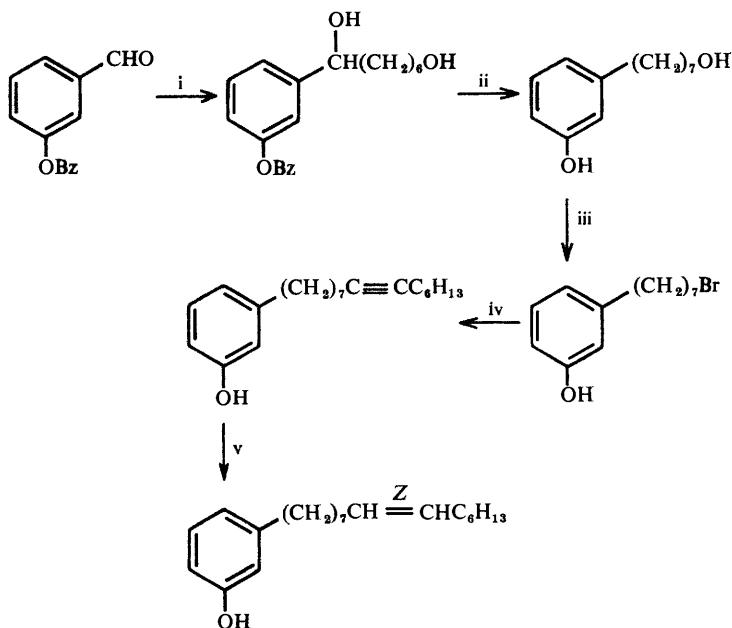
**C. Unsaturated Mono- and Dihydric Phenols, and Phenolic Acids.**—(i) *Monoenes*. In early work the synthesis of certain monoene methyl ethers<sup>51,92</sup> and of 'urusheol'<sup>93</sup> were described but it seems doubtful whether the materials obtained were authentic, and in all cases the products were not able to be characterised spectroscopically and chromatographically (g.l.c. and argentation t.l.c.). The procedures initiated nevertheless do undoubtedly represent a progressive step. Difficulties arose in the syntheses<sup>48</sup> from the problem of protective group removal without affecting the unsaturation, in obtaining specificity in the reduction of

<sup>92</sup> D. Wasserman and C. R. Dawson, *J. Org. Chem.*, 1943, **8**, 73.

<sup>93</sup> B. Loev and C. R. Dawson, *J. Org. Chem.*, 1959, **24**, 900.

the alkyne precursor of the product and, as far as Wittig reaction procedures are concerned, in steric control.

The acetylenic route<sup>48</sup> for 3-[8'(Z)-pentadecenyl]phenol was as shown in Scheme 6.



Reagents: i, Mg, Cl(CH<sub>2</sub>)<sub>6</sub>OCH(CH<sub>3</sub>)OC<sub>2</sub>H<sub>5</sub>; ii, H<sub>2</sub>, Pd/H<sup>+</sup>; iii, PBr<sub>3</sub> or HBr, H<sub>2</sub>SO<sub>4</sub>; iv, -C≡CC<sub>6</sub>H<sub>13</sub>, THF, HMPT; v, H<sub>2</sub>, Pd/BaSO<sub>4</sub>.

**Scheme 6**

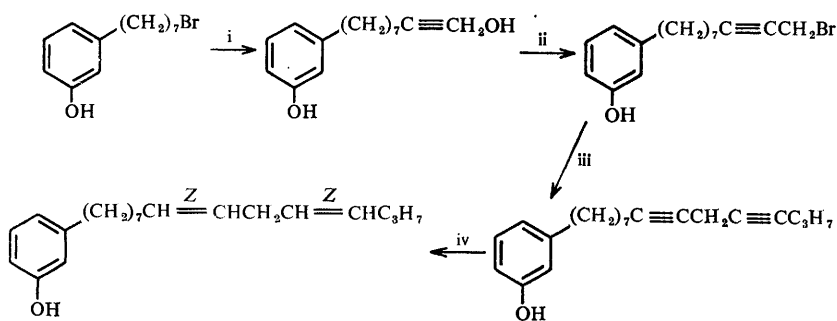
The use of lithium with the ethyl 6-chlorohexyl acetal of acetaldehyde, Cl(CH<sub>2</sub>)<sub>6</sub>OCH(CH<sub>3</sub>)OC<sub>2</sub>H<sub>5</sub>, was highly effective and completely avoided Wurtz type products. By the same general procedure, 2,3-dimethoxybenzaldehyde gave 7-(2',3'-dimethoxyphenyl)heptan-1-ol, which with boron tribromide gave 7-(2',3'-dihydroxyphenyl)heptyl bromide and hence by two steps, 3-[8'(Z)-pentadecenyl] catechol identical with (15:1) urushiol.<sup>85</sup> The synthetic urushiol dimethyl ether<sup>92</sup> and 'urushenol', (15:1) urushiol,<sup>93</sup> previously reported, were not spectroscopically or chromatographically characterised and evidence of probable Wurtz impurities in the latter was subsequently indicated. For (15:1) cardol,<sup>49</sup> the use of 3,5-dibenzyloxybenzaldehyde in a lithium type procedure or the demethylation of 7-(3',5'-dimethoxyphenyl) heptan-1-ol proceeded less effectively but by demethylation of 5-[8'(Z)-pentadecenyl]resorcinol dimethyl ether with lithium iodide/collidine, the dihydric phenol was obtained. (15:1) Anacardic acid (ginkgolic acid) was synthesised<sup>54</sup> from methyl 6-(7'-hydroxyheptyl)

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salicylate, obtained by the aryne route from *m*-fluoranisole, by the boron tri-bromide and alkylation procedures of earlier syntheses.

Generally the alternative approach to introduction of the unsaturation by the Wittig procedure has been less specific as for example in the reactions of 8'-(3'-methoxyphenyl)octan-1-ol with *n*-heptylphosphoran when the formation of 12% of the *trans* and 88% *cis* products was observed.<sup>94</sup>

(ii) *Dienes and Trienes*. The synthesis of the phenolic dienes and more particularly the trienes have met with greater difficulty. Diene syntheses were based on the use of methoxyphenyldecyn-2-1-ols rather than methoxyphenylnonyn-1 because of an observed isomerisation in the latter case.<sup>95</sup> (15:2) Cardanol, 3-[8'(Z), 11'(Z)]-pentadecadienyl phenol was prepared by the route shown in Scheme 7.<sup>48</sup>



Reagents: i,  $\text{HC}\equiv\text{CCH}_2\text{OThp}$ , Bu Li, HMPT; ii,  $\text{PBr}_3$ , pyr.;  
 iii,  $\text{EtMgBr}$ ,  $\text{HC}\equiv\text{CC}_3\text{H}_7$ ; iv,  $\text{H}_2$ , Pd/BaSO<sub>4</sub>, quinoline.

**Scheme 7**

A similar approach to (15:2) cardol dimethyl ether<sup>50a</sup> and (15:2) urushiol dimethyl ether was successfully applied.<sup>50b</sup> The synthesis of the latter by way of a Wittig procedure using 3-(2',3'-dimethoxyphenyl)octan-1-ol obtained from natural urushiol dimethyl ether as shown in Scheme 8 has been described<sup>96</sup> but with no details or indication of specificity. The use of crotonaldehyde at the last stage gave the 8',11',13'-triene.

Trienes could not be obtained by the preceding synthesis (Scheme 7) with acetylenic Grignard reagents from either pent-1-ene-4-yne or penta-1,4-diyne. The major problem was the great ease of hydrogenation of a terminal alkyne or vinyl group compared with a disubstituted alkyne\* and accordingly the terminal double bond was introduced at the last stage as shown in Scheme 9 which has met with some degree of success, (R = Me or H).

\*The synthesis of phenolic lipids in this respect is more difficult than that of polyethenoid fatty acids.

<sup>94</sup> J. H. P. Tyman and S. T. Foo, unpublished data.

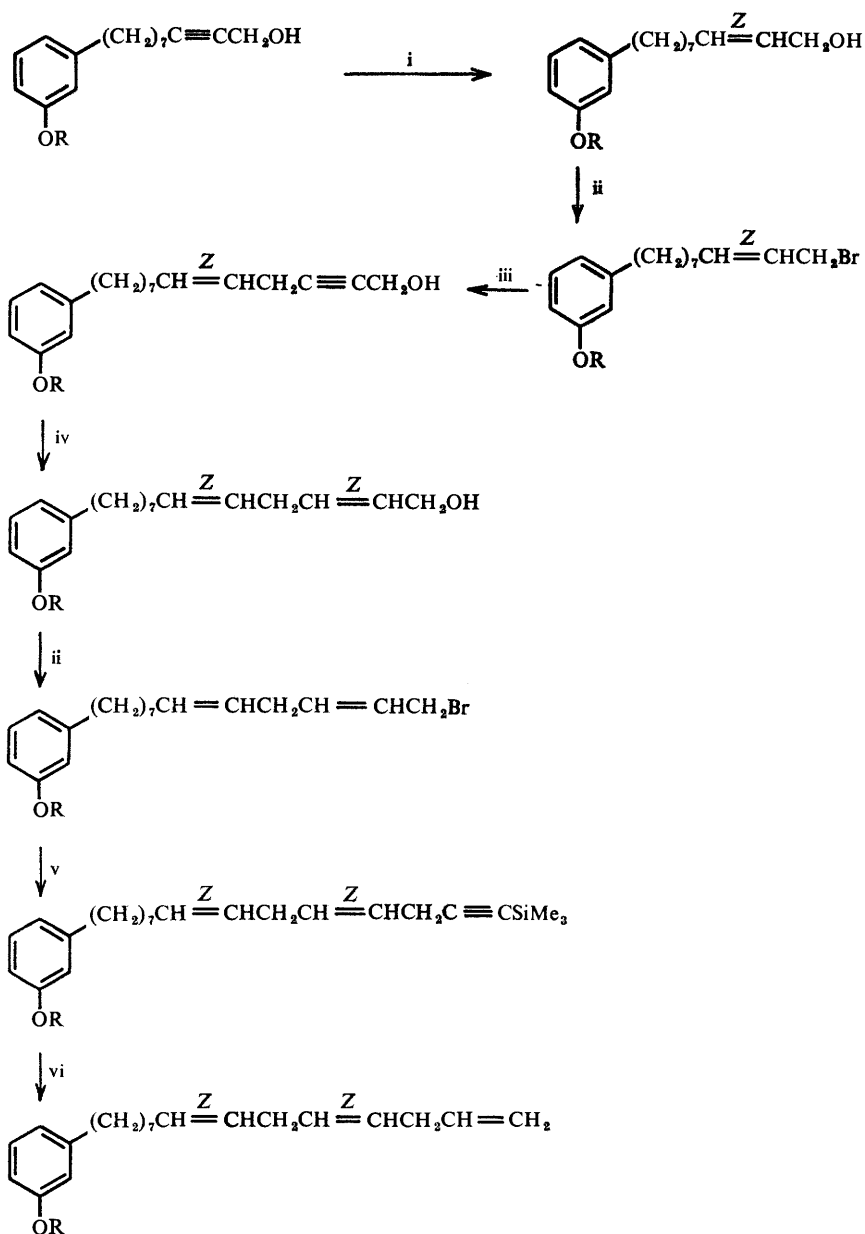
<sup>95</sup> J. H. P. Tyman, *Synth. Comm.*, 1975, **5**, 21.

<sup>96</sup> M. Sato, *Yakugaku*, 1973, **22**, 349; M. Sato, S. Suzuka, and K. Doi, *Nippon Kagaku Zasshi*, 1969, **90**, 1039.



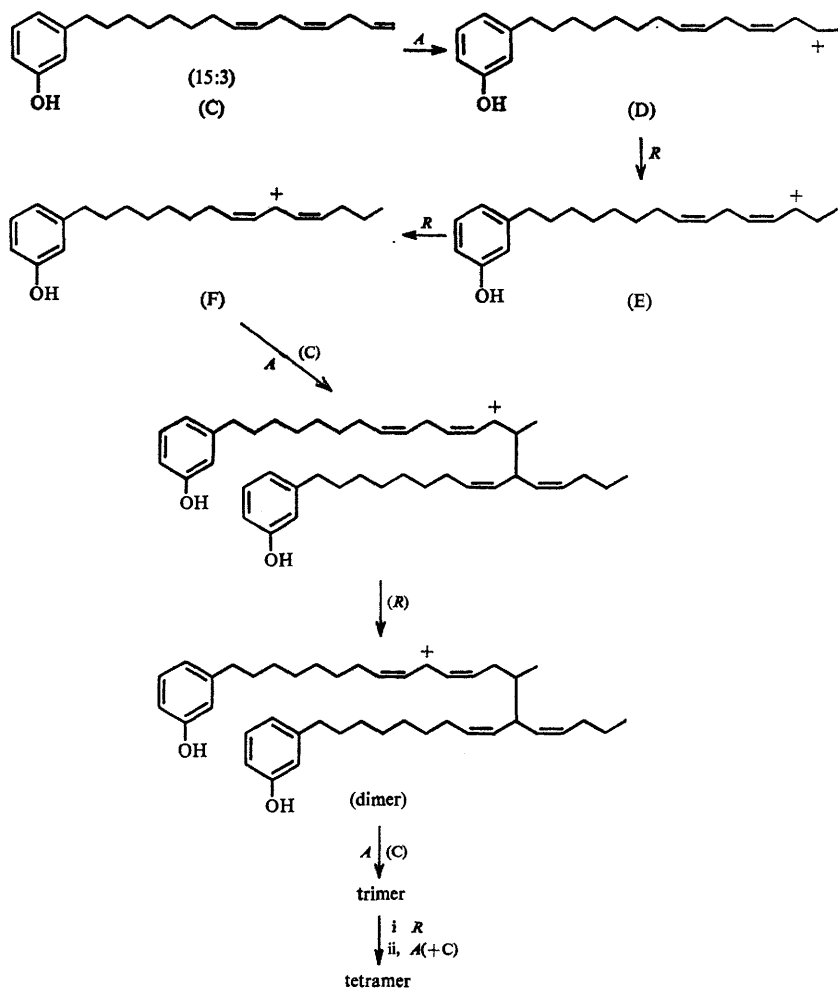


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Reagents: i,  $\text{H}_2$ , Pd/BaSO<sub>4</sub>, quin.; ii, PBr<sub>2</sub>pyr.; iii,  $\text{HC}\equiv\text{CCH}_2\text{OThp}$ , EtMgBr, CuCl, AgNO<sub>3</sub>/TLC; iv,  $\text{H}_2$ , Pd/BaSO<sub>4</sub>, quin.; v,  $\text{HC}\equiv\text{CSiMe}_3$ , EtMgBr, CuCl; vi, AgNO<sub>3</sub>,  $\text{H}_2$ , Pd/BaSO<sub>4</sub>, quin.

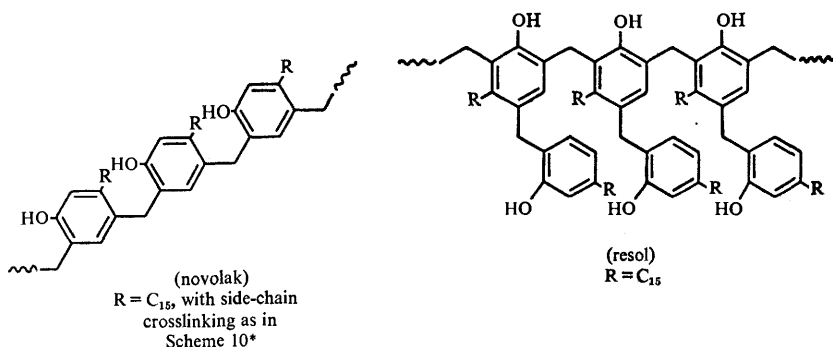
Scheme 9



Scheme 10

use as surface coatings, modified rubbers, foundry mold and core binder compositions, ion exchange resins, water-proofing materials, insulating products, anti-corrosive paints, and in numerous other products. Cation exchangers have

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been produced by the sulphonation of CNSL/formaldehyde resins prepared in the presence of hydrochloric acid<sup>100</sup> and in other ways.<sup>101</sup>

In most of the applications it seems probable that the long chains in CNSL impart flexibility due to internal plasticising, result in the formation of soft resins at elevated temperatures, unlike phenol/formaldehyde resins which are hard, give solubility in a number of solvents, and strong hydrophobic character conferring resistance to acids and alkalis.

Derivatives of CNSL resulting from interaction with formaldehyde and tetramethylenepentamine have been used as weak anion exchangers.<sup>102</sup>

(ii) *Other Chemical Uses.* Derivatives of hydrogenated cardanol, cardol, and anacardic acid have been obtained by synthesis and have found novel applications as dyestuffs, pharmaceuticals, detergents, anti-oxidants, and monomers for polymerisation.

Hydrogenated cardanol has been sulphonated with sulphuric acid<sup>103</sup> and with chloresulphonic acid<sup>104</sup> and the surface active properties of the anionic product (43) extensively studied.<sup>103</sup> The sulphonic acid of the unhydrogenated material has been obtained.<sup>105</sup> By the Mannich reaction between hydrogenated cardanol, formaldehyde, and dimethylamine, followed by quaternisation the cationic surface active material (44) was obtained which also possessed germicidal action.<sup>106</sup> By nitration<sup>107</sup> of hydrogenated cardanol (3-pentadecyl-

\*Only 2- and 4-methylol derivatives of cardanol have been obtained and the formula of the resol is thus more speculative, involving substitution in the 6-position.

<sup>100</sup> N. Krishnaswamy, K. P. Govindan and R. N. Pandya, *Chem. and Ind.*, 1957, 1456; H. M. Bhavnagary and N. Krishnaswamy, *Indian J. Technol.*, 1967, 5, 170.

<sup>101</sup> J. H. P. Tyman and A. A. Durrani, unpublished data.

<sup>102</sup> B. D. Dasare and N. Krishnaswamy, *Indian J. Technol.*, 1965, 3, 170.

<sup>103</sup> S. C. Sethi, B. C. Subba Rao and S. B. Kulkarni, *Indian J. Technol.*, 1963, 1, 348; *Indian P.* 71 754, 1962.

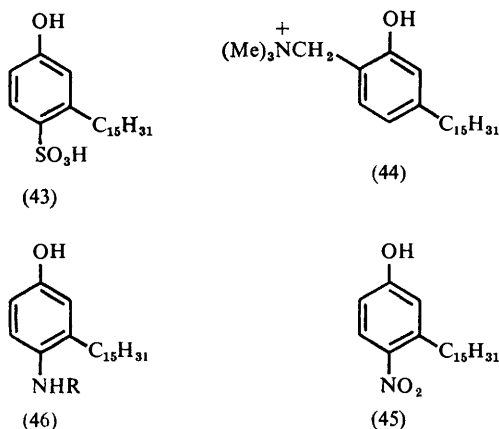
<sup>104</sup> D. Wasserman, U.S.P. 2 586 191, 1952.

<sup>105</sup> J. H. P. Tyman and A. A. Durrani, unpublished data.

<sup>106</sup> A. S. Gulati, V. S. Krishnamachar, and B. C. Subba Rao, *Indian J. Chem.*, 1964, 2, 114.

<sup>107</sup> C. R. Dawson and D. Wasserman, *J. Amer. Chem. Soc.*, 1950, 72, 4994; U.S.P. 2 502 436, 1950; U.S.P. 2 502 708, 1950.

phenol), the 4-nitro compound (45) and the 6-nitro compound were obtained the former of which has been converted to a number of useful products. 4-Aminocardanol (46; R=H) has been oxidised to 2-pentadecylhydroquinone, an anti-



oxidant for gasoline. The  $\beta$ -naphthylamine derivatives (46; R=C<sub>10</sub>H<sub>7</sub>) was found to be a highly efficient anti-oxidant,<sup>108</sup> superior to phenyl  $\beta$ -naphthylamine, for rubber. Hydrogenated cardanol coupled with benzenediazonium chloride to give 2-pentadecyl-4-hydroxyazobenzene,<sup>109</sup> a valuable oil soluble pigment the structure of which was established by reduction to the 4-amino compounds (46; R=H).

The bactericidal action of sodium anacardate has been investigated.<sup>110</sup> A range of drug analogues of warfarin, phenolphthalein, saligenin, salicylamide, and salicylanilide has been prepared from 3-pentadecylphenol and 5-pentadecylresorcinol.<sup>111</sup> Acyl derivations of 6-aminopenicillanic acid emulating the sterically hindered 2,6-dimethoxybenzoyl compound have been prepared with 2-methoxy-6-n-butylbenzoic and 2-methoxy-6-n-pentadecylbenzoic acid.<sup>112</sup>

Apart from the use of saturated materials numerous addition products of the unsaturated side chains have been obtained many of which such as hydroxy compounds were isolated during the structural elucidation of the cashew phenols. Epoxidation has been examined by several different procedures.<sup>113</sup> Processes for achieving structural changes such as conjugative and isomerisation treatments have been studied.<sup>114</sup>

<sup>108</sup> N. D. Ghatge and R. G. Gokhale, *Indian J. Technol.*, 1971, **9**, 391.

<sup>109</sup> V. S. Pansare and A. B. Kulkarni, *J. Indian Chem. Soc.*, 1964, **41**, 251; C. R. Dawson and D. Wasserman (to Harvel Corporation), U.S.P. 2 496 151, 1950.

<sup>110</sup> F. Eichbaum, *Mem. Inst. Butantan*, 1946, **19**, 71; A. Biswas and A. Ray, *Nature*, 1958, **182**, 1299.

<sup>111</sup> A. S. Gulati and B. C. Subba Rao, *Indian J. Chem.*, 1964, **2**, 337.

<sup>112</sup> Beecham Res. Ltd., and J. H. P. Tyman, unpublished data.

<sup>113</sup> J. H. P. Tyman and A. A. Durrani, unpublished data.

<sup>114</sup> J. H. P. Tyman and S. K. Sood, unpublished data.

**B. Urushiol.**—(i) *General Surface Coatings.* Although fewer general chemical reactions have been carried out with urushiol (as Japanese lac) compared with CNSL, a significant amount of utilisation has been achieved relatively recently.

Most of the work on urushiol has been with simple transformation products intended to improve the rate of polymerisation or type of surface coating compared with that from the untreated natural product, or to enable lacquered materials to be baked (cured) rather than processed under ambient conditions. High adhesion, thermal, acid and alkali resistant epoxy resin paints have been based on urushiol and hexamethylenetetramine heated together and added to an epoxy resin followed by dissolution of the mixture in a solvent.<sup>115</sup> Black pigments for printing inks, plastics, and carbon paper have been obtained from urushiol and certain iron salts.<sup>116</sup> Salts of thiophosphate esters of urushiol (and of cardanol) have found use as lubricants and additives.<sup>117</sup>

The mechanism of the oxidative polymerisation and cross linking of Japanese lacquer has been studied<sup>75</sup> and is considered to involve urushiol quinone formed by the enzyme laccase and its dimerisation with the 8,11,13-triolefinic constituent.

Synthetic urushiol analogues have been prepared in attempts to obtain Japanese lacquers with improved properties.<sup>118</sup>

(ii) *Japanese Lacquering.* This summary would be incomplete without reference to the practice of Japanese lacquering. The use of lac existed in most Far Eastern countries although the technique was outstandingly employed in China and Japan. The procedure has been described.<sup>5</sup> In the lacquering process which was applied to a vast range of objects and even to buildings, the base of the work was invariably wood although metals and porcelain were sometimes used. The base object was polished, cracks or joints filled and a final polishing given. The first coating of a clear lacquer dressing was allowed to dry completely before a priming composition was applied consisting of lacquer mixed with burnt clay, quicklime, and pig's blood. After drying, hardening, and polishing of this coating with a whetstone, the next coating of lacquer was used with wheat flour and a cloth strengthener of hempen, linen, paper, or silk pressed and smoothed over the partially dried surface. Succeeding layers were then coated over a period of weeks to produce a surface which was finally decorated. For artistic use Chinese lac was frequently pigmented with indigo, gamboge, orpiment, ochre, cinnabar, safflower, or animal or vegetable charcoal. Gold and silver dusts and foils, mother of pearl, jade, coral, ivory, and other decorative substances were used. Carved lacquer work was a Chinese practice in which multicoloured uniform layers were cut back to reveal the colour required by the design. This artistry reached its peak in the 16th, 17th, and 18th centuries.

Thanks are due to Mr. T. W. Hammonds (Tropical Products Institute, London), Professor S. C. Bevan (School of Chemistry, Brunel University), Dr. G. Patten-

<sup>115</sup> S. Iwahashi, Japan P. 6142, 1957.

<sup>116</sup> K. Ohashi, U.S.P. 2 981 978, 1959; Japan P. 7118, 1957.

<sup>117</sup> J. R. Morris (to Texas Co.) U.S.P. 2 417 562, 1947.

<sup>118</sup> A. Terada, *Osaka Koggo Gijutsu Shikensho Kiko*, 1965, 16, 47.

den (University of Nottingham), Mr. J. F. Vine (Fletcher and Stewart and Co. Ltd.), Mr. W. T. Mercer (Wigglesworth and Co. Ltd.), Mr. A. E. Brett, [TR International (Chemical) Ltd.], Mr. J. L. Keesing (Living Collection Division), and Miss R. Angel (Museum Division, Royal Botanic Gardens, Kew, Surrey) for certain information.