Tetrahedron, 1967, Vol. 23, pp. 817 to 824. Pergamon Press Ltd. Printed in Northern Ireland

CHEMICAL EXAMINATION OF *EMBELIA RIBES*—VIII

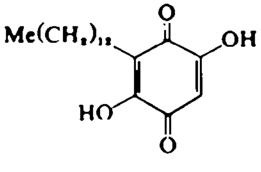
SOME CONDENSATION REACTIONS OF RAPANONE WITH VARIOUS ALDEHYDES AND NITROSO COMPOUNDS

V. K. Murty, T. V. P. Rao and V. Venkateswarlu
Department of Chemistry, Engineering College, Andhra University, Waltair, India

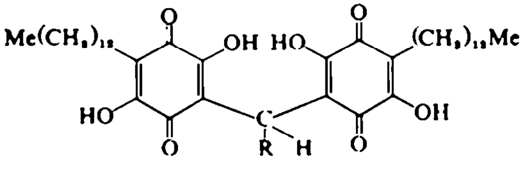
(*Received* 17 *May* 1966; *accepted for publication* 13 *July* 1966)

Abstract—The condensation of rapanone[1] (I) with various aldehydes and nitroso compounds yields the corresponding methylene-bis(2.5-dihydroxy-4-tridecyl-3,6-benzoquinones) (II) or their anhydro derivatives (III). The N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinones) (IV) have been synthesized and their properties recorded.

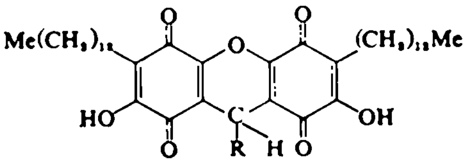
The isolation and synthesis of vilangin[2] has initiated this study of the condensation of various benzoquinones with aldehydes and nitroso compounds. Rapanone[1] (I) condenses readily with formaldehyde to give methylene-bis(2,5-dihydroxy-4-tridecyl-3,6-benzoquinone) (IIa), a higher homologue of vilangin. With acetaldehyde, propionic aldehyde and benzaldehyde, rapanone condenses to give products of both types II and III. In the case of other aromatic aldehydes, only the anhydro (type III) products are obtained. With salicyclic aldehyde a product of type V is also produced. In a similar manner, rapanone condenses with various nitroso compounds giving the corresponding N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone) (IV). These condensation products, (II, III and IV) have been characterized by the preparation of the acetates of their reduction products and our earlier proposals[3] with regard to the nature of these condensations has been substantiated.



I



II



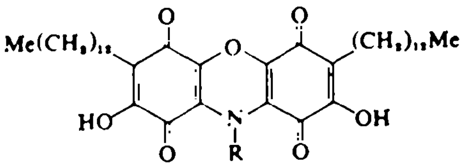
III

---

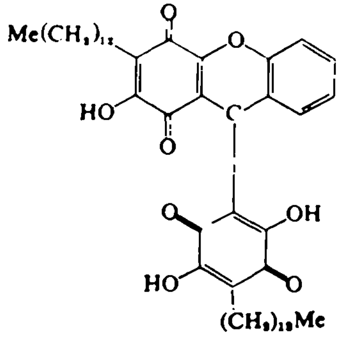
[1] V. Krishna Murty, T. V. Padmanabha Rao and V. Venkateswarlu, *Curr. Sci.* **34**, 16 (1965); *Tetrahedron* **21**, 1445 (1965).

[2] Ch. Bheemasankara Rao and V. Venkateswarlu, *J. Org. Chem.* **26**, 4529 (1962).

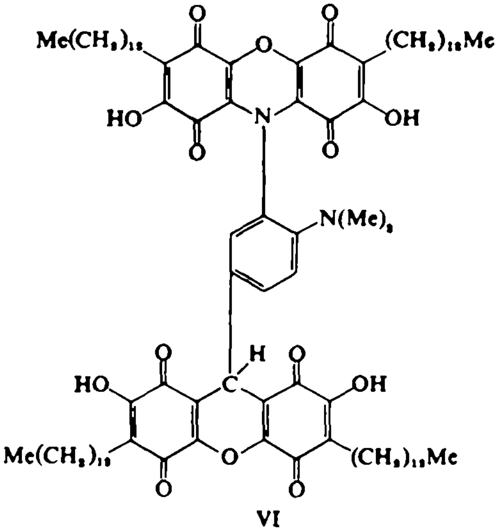
[3] Ch. B. Rao and V. Venkateswarlu, T. V. Padmanabha Rao and V. Venkateswarlu, *Tetrahedron* **18**, 361 (1962); *Ibid.* **20**, 2963 (1964); *Ibid.* **20**, 2967 (1964); *Ibid.* **21**, 381 (1965).



IV



V



VI

EXPERIMENTAL

Methylene-bis(2,5-dihydroxy-4-tridecyl-3,6-benzoquinone), (IIa, R = H)

Rapanone (I; 1 g) in AcOH (30 ml) was gently warmed with 40% formalin (5 ml) on a steam-bath for 10 min. A bright yellow copious ppt was formed and this crystallized as bright yellow prisms, m.p. 245–247°d. (dioxan) and gave a purple ferric reaction. (Found: C, 71·47; H, 9·27; $C_{39}H_{60}O_8$ requires: C, 71·34; H, 9·15%.) The same condensation could also be effected in neutral soln. in 3 hr. Exposure to sunlight was found to accelerate the condensation.

Total synthesis. A suspension of finely powdered methylene-bis(2,5-dihydroxy-3,6-benzoquinone)[4] (2·9 g) and miristoyl peroxide (4·5 g) dissolved in AcOH (100 ml) and dioxan (100 ml) was mechanically stirred and warmed on a steambath for 30 min. Stirring was continued overnight at room temp and the mixture then cooled to 0°. The ppt was then treated with dioxan giving soluble fraction consisting of a 10% yield of IIa, m.p. 245–247°d., a mixed m.p. with the sample prepared earlier being undepressed. (Found: C, 71·52; H, 9·27: $C_{39}H_{60}O_8$ requires: C, 71·34; H, 9·15%.) The dioxan-insoluble portion mainly consisted of the starting methylene-bisbenzoquinone.

Dehydration of IIa in dioxan soln using 3% H_2SO_4 or orthophosphoric acid or HI in Ac_2O or phenol gave IIIa (R = H) as brown prisms, m.p. 150–152° from MeOH, showing a brown ferric reaction. (Found: C, 73·47; H, 9·24: $C_{39}H_{58}O_7$ requires: C, 73·35; H, 9·09%.) The *tetroxime* of IIa was prepared using hydroxylamine hydrochloride in pyridine soln and crystallized as brown yellow prisms, m.p. 126–128° from acetone. (Found: N, 7·94; $C_{39}H_{64}O_8N_4$ requires: N, 7·82%.) The *tetra-2,4-dinitrophenylhydrazone* of IIa crystallized as orange-red rhombs, m.p. 320°d. from excess dioxan. (Found: N, 16·47; $C_{63}H_{76}O_{20}N_{16}$ requires: N, 16·28%.) The *tetraphenylhydrazone of IIa*, crystallized as pale brown prisms, m.p. >320°, from excess acetone. (Found: N, 11·17; $C_{63}H_{84}O_4N_8$ requires: N, 11·03%.) The *tetrasemicarbazone* of IIa, crystallized as pale brown prisms, m.p. 202–204°d. from excess acetone. (Found: N, 19·54; $C_{43}H_{72}O_8N_{12}$ requires: N, 19·00%.) The *tetra-o-benzoyl derivative* of IIa prepared by way of benzoyl chloride and pyridine, crystallized as brown plates and prisms, m.p. 146–148°, from AcOEt pet. ether, giving a negative ferric reaction. (Found: C, 75·12; H, 7·14; $C_{67}H_{76}O_{12}$ requires: C, 75·01; H, 7·09%.)

Acetylation of IIa (1 g) using Ac_2O (15 ml) and pyridine (5 drops) and boiling under reflux for 2 hr, resulted in the formation of a mixture of two acetates which were taken up in AcOH and subsequently separated into 2 fractions using AcOEt: (i) the sparingly soluble as yellowish brown prisms, m.p. 180–182°, which is evidently the normal tetraacetate, methylene-bis(2,5-diacetyloxy-4-tridecyl-3,6-benzoquinone), as this on hydrolysis regenerated IIa. (Found: C, 68·57; H, 8·41; —$COCH_3$, 21·22; $C_{47}H_{68}O_{12}$ requires: C, 68·45; H, 8·25; —$COCH_3$, 20·87%); and (ii) the more easily-soluble which crystallized as yellow plates and prisms, m.p. 134–136°, from excess pet. ether. corresponding to the diacetate of IIIa identical with the acetate obtained direct from IIIa. (Found: C, 71·52; H, 8·64; —$COCH_3$, 12·14; $C_{43}H_{62}O_9$ requires: C, 71·47; H, 8·59; —$COCH_3$, 11·91%.)

Reductive acetylation of IIa in Ac_2O (15 ml) using a trace of Et_3N and Zn dust (3 g; added during 2 hr) yielded a colourless residue, m.p. 202–210°, which was separated into 2 fractions: (i) a sparingly soluble (AcOH) fraction which crystallized as colourless prisms, m.p. 222–224°, and on hydrolysis using cold 8N NaOH followed by acidification and aerial oxidation gave IIIa. Hence this acetate was considered to be the hexaacetate of IIIa. (Found: C, 68·62; H, 8·43; —$COCH_3$, 29·06; $C_{51}H_{74}O_{13}$ requires: C, 68·47; H, 8·28; —$COCH_3$, 28·86%), (ii) a glacial AcOH soluble fraction which crystallized as colourless clusters of short prisms, m.p. 168–170° from MeOH and on hydrolysis using aqueous cold alkali followed by acidification and aerial oxidation gave a small quantity of IIa identical with a sample prepared earlier. This acetate was therefore considered to be the octacetate of IIa. (Found: C, 66·40; H, 8·14; —$COCH_3$, 34·67; $C_{55}H_{80}O_{16}$ requires: C, 66·25; H, 8·03; —$COCH_3$, 34·53%.)

Synthesis of some new methylene-bis-, and N-bisanhydro-benzoquinones from rapanone

Method of preparation. Rapanone (2 moles) was condensed with (1 mole) of aldehyde using (a) AcOH or 25% ethanolic AcOH by boiling under reflux for 3 hr (b) using 10% alcoholic H_2SO_4 or saturating with HCl while boiling under reflux for 2 hr (c) using piperidine in the cold during 24–36 hr. The products obtained were purified by crystallization or short column chromatography.

The following Table gives a summary of the condensation reactions effected and the properties of the products obtained.

TABLE 1

Product	Method of prepn.	Appearance and M.p.	Ferric colour	Formula	Analysis (Theoretical in brackets
Ethylidine-bis(2,5-dihydroxy-4-tridecyl-3,6-benzoquinone) (IIb, R = Me)	a	Shining orange yellow prisms, 131–132° (MeOH)	Red	$C_{40}H_{62}O_8$	C, 71·82(71·63) H, 9·62(9·25)

[4] Ch. B. Rao and V. Venkateswarlu, *Tetrahedron* **18**, 951 (1962).

Table 1. (*contd.*)

Product	Method of prepn.	Appearance and M.p.	Ferric colour	Formula	Analysis (Theoretical in brackets)
Methyl ether of IIb, (Ethylidine-bis(2,5-dimethoxy-4-tridecyl-3,6-benzoquinone)	—	Bright orange red prisms, 59–61° (Pet. ether)	nil	$C_{44}H_{70}O_{8}$	C, 72·85(72·73) H, 9·92(9·64)
Ethylidine-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIb, R = Me)	b	Orange brown short prisms, 166–168° (EtOH)	Purple	$C_{40}H_{60}O_{7}$	C, 73·84(73·62) H, 9·40(9·20)
Ethylidine-bis(anhydro-5-O-acetyl-4-tridecyl-3,6-benzoquinone)	—	Pale yellow rhombs, 68–70° (Pet. ether)	—	$C_{44}H_{64}O_{9}$	C, 72·69(72·73 H, 8·92(8·70) $-COCH_3$, 12·02 (11·69)
Hexacetate of reduced IIIb	—	Colourless 156–158° (pet. ether)	—	$C_{52}H_{76}O_{13}$	C, 68·92(68·73) H, 8·52(8·37) $-COCH_3$, 28·67 (28·41)
Propylidine-bis(2,5-dihydroxy-4-tridecyl-3,6-benzoquinone), (IIc, R = Et)	a	Orange yellow rhombs, 127–129° (MeOH)	Red	$C_{41}H_{64}O_{8}$	C, 72·02(71·93) H, 9·52(9·36)
Propylidine-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIc, R = Et)	b	Deep orange yellow needles, 138–139° (MeOH)	Purple	$C_{41}H_{62}O_{7}$	C, 74·02(73·87) H, 9·52(9·31)
Hexacetate of reduced IIIc	—	Colourless rect. plates 120–122° (benzene)	—	$C_{53}H_{78}O_{13}$	C, 68·72(69·00) H, 8·52(8·46) $-COCH_3$, 28·22(27·99)
Benzal-bis(2,5-dihydroxy-4-tridecyl-3,6-benzoquinone), (IId, R = Ph)	a	Light orange yellow prisms, 108–110° (MeOH)	Intense purple	$C_{45}H_{64}O_{8}$	C, 73·92(73·77) H, 9·02(8·74)
Benzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIId, R = Ph)	a	Orange red rhombs, 150–151° (MeOH)	Red brown	$C_{45}H_{62}O_{7}$	C, 75·72(75·63) H, 8·82(8·68)
Hexaacetate of reduced IIId	—	Colourless plates, 94–96° (pet. ether)	—	$C_{57}H_{78}O_{13}$	C, 70·64(70·52) H, 8·32(8·04) $-COCH_3$, 27·00(26·60)

Table 1. (*contd.*)

Product	Method of prepn.	Appearance and M.p.	Ferric colour	Formula	Analysis (Theoretical in brackets)
β-Phenylallyl-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIe, R = β-phenylallyl)	b	Golden yellow rect. prisms, 184–186° (benzene)	Purple	$C_{47}H_{64}O_7$	C, 76·42(76·23) H, 8·72(8·65)
Hexaacetate of reduced IIIe	—	Colourless prisms, (Benzene) 138–140°	—	$C_{59}H_{80}O_{13}$	C, 71·22(71·08) H, 8·12(8·03) —$COCH_3$, 26·14(25·90)
4′-Methoxybenzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIf, R p-methoxyphenyl)	b or c	Orange red prisms, 129–131° (MeOH)	Intense purple	$C_{46}H_{64}O_8$	C, 74·22(74·18) H, 8·82(8·60)
Hexaacetate of reduced IIIf	—	Colourless rect. plates, 92–94° (Pet. ether)	—	$C_{58}H_{80}O_{14}$	C, 69·82(69·60) H, 8·24(8·00) —$COCH_3$, 26·20(25·80)
4′-Dimethylaminobenzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIg, R = *p*-dimethylaminophenyl)	c	Brown red short prisms, 132–134° (Pet. ether)	Red brown	$C_{47}H_{67}O_7N$	C, 74·32(74·50) H, 9·00(8·85)
Hexaacetate of reduced IIIg	—	Colourless rect. plates, 68–70° (Pet. ether)	—	$C_{59}H_{83}O_{13}N$	C, 69·72(69·90) H, 8·42(8·20) —$COCH_3$, 25·83(25·48)
3′-Nitrobenzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIh, R = *m* nitrophenyl)	b	Bright yellow short prisms, 101–102° (MeOH)	Purple	$C_{45}H_{61}O_9N$	C, 71·27(71·15) H, 7·92(8·04)
Hexaacetate of reduced IIIh	—	Colourless prisms, 71–73° (pet. ether)	—	$C_{57}H_{77}O_{15}N$	C, 67·72(67·41) H, 7·82(7·59) —$COCH_3$, 25·64(25·42)
2′,6′-Dimethoxybenzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIi, R = 2,6-dimethoxyphenyl)	b	Violet brown prisms, 204–206° (MeOH)	Purple	$C_{47}H_{66}O_9$	C, 73·04(72·88) H, 8·72(8·53)
Hexaacetate of reduced IIIi	—	Colourless prisms, 140–142° (Pet. ether)	—	$C_{59}H_{82}O_{15}$	C, 68·82(68·74) H, 8·02(7·96) —$COCH_3$, 25·47 (25·05)
3′,4′-Dimethoxybenzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIj, R = 3,4-dimethoxyphenyl)	b	Dull orange red prisms, 134–136° (MeOH)	Red	$C_{47}H_{66}O_9$	C, 72·64(72·88) H, 8·72(8·53)

Table 1. (*contd.*)

Product	Method of prepn.	Appearance and M.p.	Ferric colour	Formula	Analysis (Theoretical in brackets)
Hexaacetate of reduced IIIj	—	Colourless plates and prisms, 102–104° (Benzene)	—	$C_{59}H_{82}O_{15}$	C, 68·52(68·74) H, 7·77(7·96) —$COCH_3$, 25·42(25·05)
3′-Methoxy-4′-hydroxy-benzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIk, R = 3-methoxy-4-hydroxyphenyl)	b	Deep scarlet red square plates and prisms, 234–236° (Pet. ether)	Purple	$C_{46}H_{64}O_9$	C, 72·43(72·63) H, 8·64(8·42)
Heptaacetate of reduced IIIk	—	Colourless prisms 88–90° (pet. ether	—	$C_{60}H_{82}O_{16}$	C, 68·12(68·05) H, 7·62(7·75) —$COCH_3$, 28·64(28·45)
2′-Hydroxy-3′-methoxy-benzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIl, R = 2-hydroxy-3-methoxy-phenyl	b	Scarlet red prisms, 177–179° (MeOH)	Purple	$C_{46}H_{64}O_9$	C, 72·77(72·63) H, 8·64(8·42)
Heptaacetate of reduced IIIl	—	Colourless prisms, 200–202° (benzene)	—	$C_{60}H_{82}O_{16}$	C, 68·24(68·05) H, 7·64(7·75) —$COCH_3$, 28·64(28·45)
2′-Hydroxybenzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIm, R = 2-hydroxyphenyl)	b	Scarlet red rect. plates and prisms, 146–148° (MeOH)	Purple brown	$C_{45}H_{62}O_8$	C, 74·04(73·98) H, 8·62(8·49)
Heptaacetate of reduced IIIm	—	Colourless plates and prisms, 180–181° (benzene)	—	$C_{59}H_{80}O_{15}$	C, 69·04(68·89) H, 8·12(7·78) —$COCH_3$, 29·42(29·29)
Product V	c	yellow prisms, 159–161° (MeOH)	Purple	$C_{45}H_{62}O_8$	C, 74·14(73·98) H, 8·62(8·49)
2′-Methoxybenzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIn, R = 2-methoxyphenyl)	b	Brown yellow prisms, 139–141° (Pet. ether)	Purple	$C_{46}H_{64}O_8$	C, 74·32(74·18) H, 8·72(8·60)
Hexaacetate of reduced IIIn	—	Colourless prisms, 108–110° (pet. ether)	—	$C_{58}H_{80}O_{14}$	C, 69·72(69·60) H, 8·22(8·00) —$COCH_3$, 26·04(25·80)

Table 1. (*contd.*)

Product	Method of prepn.	Appearance and M.p.	Ferric colour	Formula	Analysis (Theoretical in brackets)
3′,4′-Methylenedioxy-benzal-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IIIp, R = 3,4-methyl-lenedioxyphenyl)	b	Orange red rect. plates, 105–107° (pet. ether)	Purple	$C_{46}H_{62}O_9$	C, 73·04(72·81) H, 8·24(8·18)
Hexaacetate of reduced IIIp	—	Colourless plates 98–100° (pet. ether)	—	$C_{58}H_{78}O_{15}$	C, 68·78(68·64) H, 7·82(7·69) —COCH$_3$, 25·12(25·45)
4′-Dimethylaminophenyl-1′-N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IVa, R = *p*-dimethyl-aminophenyl)	b	Brown prisms, 290–292° (AcOEt)	Brown	$C_{46}H_{66}O_7N_2$	C, 73·04(72·81) H, 8·92(8·71) N, 3·76(3·69)
Hexaacetate of reduced IVa	—	Colourless rect. plates 140–141° (benzene)	—	$C_{58}H_{82}O_{13}N_2$	C, 68·42(68·64) H, 8·31(8·09) —COCH$_3$, 25·82(25·45)
4′-Diethylaminophenyl-1′-N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IVb, R = *p*-dimethylamino-phenyl)	b	Violet brown prisms, 320° (EtOH)	Purple brown	$C_{48}H_{70}O_{12}N_2$	C, 73·02(73·28) H, 9·14(8·91) N, 3·71(3·56)
Hexaacetate of reduced IVb	—	Colourless plates, 102–103° (pet. ether)	—	$C_{60}H_{86}O_{13}N_2$	C, 69·23(69·10) H, 8·47(8·25) —COCH$_3$, 25·12(24·77)
4′-Hydroxynaphthyl-1′-N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzo-quinone), (IVc, R = 4-hydroxy-1-naphthyl)	b	Light brown prisms 141–142° (MeOH)	Brown	$C_{48}H_{63}O_8N$	C, 74·03(73·74) H, 8·34(8·07) N, 1·87(1·79)
Heptaacetate of reduced IVc	—	Colourless rect. plates, 106–108° (benzene-pet. ether)	—	$C_{62}H_{81}O_{15}N$	C, 68·82(68·95) H, 7·47(7·51) —COCH$_3$, 28·21(27·89)
1′-Hydroxynaphthyl-2′-N-bis(anhydro-5-hydro-xy-4-tridecyl-3,6-benzo-quinone), (IVd, R = 1-hydroxynaphthyl)	b	Pale brown prisms, 125–127° (pet. ether)	Purple brown	$C_{48}H_{63}O_8N$	C, 73·82(73·74) H, 8·24(8·07) N, 2·02(1·79)
Heptaacetate of reduced IVd	—	Colourless short prisms, 108–110° (benzene)	—	$C_{62}H_{81}O_{15}N$	C, 69·04(68·95) H, 7·62(7·51) —COCH$_3$, 28·04(27·89)

Table 1. (*contd.*)

Product	Method of prepn.	Appearance and M.p.	Ferric colour	Formula	Analysis (Theoretical in brackets)
2′-Hydroxynaphthyl-1′-N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IVe, R = 2-hydroxynaphthyl)	b	Dark brown prisms 152–154° (MeOH)	Purple	$C_{48}H_{63}O_{8}N$	C, 73·87(73·74) H, 8·14(8·07) N, 2·07(1·79)
Heptaacetate of reduced IVe	—	Colourless short prisms, 110–112° (benzene-pet. ether)	—	$C_{62}H_{81}O_{15}N$	C, 69·07(68·95) H, 7·84(7·51) —$COCH_3$, 28·02(27·89)
4′-Hydroxyphenyl-1′-N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IVf, R *p*-hydroxyphenyl)	b	Orange brown prisms, 134–136° (AcOEt)	Brown	$C_{44}H_{61}O_{8}N$	C, 72·34(72·23) H, 8·41(8·35) N, 2·04(1·92)
Heptaacetate of reduced IVf	—	Colourless rect. plates 110–112° (benzene)	—	$C_{58}H_{79}O_{15}N$	C, 67·78(67·66) H, 7·84(7·68) —$COCH_3$, 29·47(29·26)
4′-Hydroxy-3′methylphenyl-1′-N-bis(anhydro-5-hydroxy-4-tridecyl-3,6-benzoquinone), (IVg, R 4-hydroxy-3-methylphenyl)	b	Dark violet brown rhombs, 138–139° (MeOH)	Purple brown	$C_{45}H_{63}O_{8}N$	C, 72·72(72·47) H, 8·57(8·46) N, 2·03(1·88)
Heptaacetate of reduced IVg	—	colourless prisms, 85–87° (pet. ether)	—	$C_{59}H_{81}O_{15}N$	C, 68·01(67·89) H, 7·82(7·77) —$COCH_3$, 29·12(28·87)
Product VI	b	Yellow short prisms, 127–129° (pet. ether)	Purple	$C_{85}H_{121}O_{14}N_{2}$	C, 73·34(73·20) H, 9·02(8·69) N, 2·14(2·01)

Acknowledgement—Two of the authors (V.K. M. and T. V. P. R.) convey their thanks to the University Grants Commission and the Council of Scientific and Industrial Research, New Delhi for the award of maintenance grants.