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# TRITERPENOID AND OTHER CONSTITUENTS FROM *SANDORICUM INDICUM*

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**Key Word Index**—*Sandoricum indicum*; Meliaceae; bryononic acid; bryonolic acid; pentacyclic triterpenes; mesoinositol; mucic acid.

**Abstract**—Bryononic and bryonolic acids, mesoinositol and mucic acid were identified in the fruits of *Sandoricum indicum*.

*Sandoricum indicum* Cav. (Meliaceae) is a large Malaysian fruit tree. King and Morgan[1] isolated two triterpenoid acids, katonic acid and indicic acid, from the heartwood of this plant and established the structure of katonic acid as 3α-hydroxyolean-12-en-29-oic acid. We have recently investigated the constituents of the fruit hulls of this plant collected from the Bukit Timah campus of the University of Singapore.

The light petrol. extract of the dried powdered fruit hulls yielded a mixture which consisted mainly of a triterpenoid keto-acid, $C_{30}H_{46}O_3$, and a trace amount of a related hydroxy-acid, $C_{30}H_{48}O_3$, which could be separated by silica gel column chromatography with great difficulty. The hydroxy-acid could be readily transformed into the keto-acid by oxidation with Jones reagent[2] whereas the keto-acid could be easily converted into the hydroxy-acid by $NaBH_4$ reduction. These chemical transformations provided easy methods for obtaining pure samples of the two acids from the extracted mixture. The hydroxy-acid has been found to be identical to the bryonolic acid isolated from the roots of *Bryonia dioica* by Biglino *et al.*,[3] who established its structure as (I). Hence, the keto-acid, called bryononic acid, has the structure (II). Some new transformation products, (III) and (IV), and their derivatives, and some additional spectroscopic data, which support the structures assigned to the two acids, are presented in the Experimental. Recently, Tunmann and Kadry[4] reported that examination of the roots of *B. dioica* has resulted in the isolation of, besides bryonolic acid, a very small amount of bryononic acid. Their adopted structure for bryononic acid, based on the previous proposed structure[5] for bryonolic acid, is inconsistent with the results of Biglino *et al.*[3] and those of the present investigation.

The methanol extract of the fruit hulls yielded mesoinositol and dimethyl mucate. As far as we are aware, the latter compound has not been reported to occur naturally although

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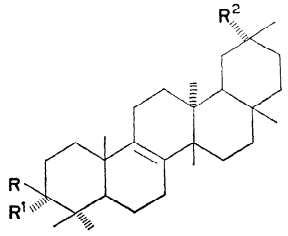
[3] G. BIGLINO, L. CATTEL, O. CAPUTO and G. NOBILI, *Gazz. Chim. Ital.* **99**, 830 (1969); *Chem. Abs.* **72**, 430 (1970).
[4] P. TUNMANN and H. A. KADRY, *Z. Naturforsch.* **26b**, 620 (1971).
[5] G. BIGLINO, (a) Communicazione all' VIII Congresso National di Chimica tenuto congiuntamente con la Society of Chemical Industry di Londra, Torino, 1958; (b) *Atti Accad. Sci. Torino*, **95**, (1960/61).

mucic acid (D-galactaric acid) has previously been isolated from various fruits.[6–10] The dimethyl ester isolated is probably an artifact since methanol was used in the extraction and the methanolic extract was found to be highly acidic (pH 2).



(I) R = OH; $R^1$ = H; $R^2$ = COOH
(II) RR¹ = O; $R^2$ = COOH
(III) R = $R^1$ = H; $R^2$ = $CH_2OH$
(IV) R = OH; $R^1$ = H; $R^2$ = $CH_2OH$

## EXPERIMENTAL

M.ps. were determined on a Hoover capillary apparatus. IR spectra were recorded in Nujol. NMR spectra were determined in $CDCl_3$ with TMS as an internal standard. MS were taken with an A.E.I. MS-9 instrument at 70 eV using direct insertion. Light petrol. refers to the fraction b.p. 56–70°.

*Isolation of bryonoic acid* (II), *bryonolic acid* (I), *mesoinositol and dimethyl mucate.* Dried powdered fruit hulls of *S. indicum* (1·34 kg) were exhaustively extracted successively with (a) light petrol. for 160 hr, and (b) MeOH for 144 hr.

(a) The light petrol. extract deposited a colourless solid (6·65 g), m.p. 230–240°, which was collected. The filtrate was concentrated and the residue was recrystallised from acetone. The acetone solution deposited a colourless solid (15·1 g). TLC and IR spectrum of this substance were identical to those of the solid obtained above. Recrystallization of a portion of this substance from $Me_2CO$–MeOH gave colourless prisms, m.p. 243–245°. TLC of the crystalline product showed that it contained mainly bryononic acid with a trace amount of bryonolic acid which could not be removed by repeated recrystallization from various solvents. A portion of the crude substance (1·5 g) was chromatographed on silica gel (70 g). Elution of the column with light petrol.–$Et_2O$ (10:1) yielded in the earlier fractions bryononic acid (0·89 g), which on recrystallization from $Me_2CO$–MeOH gave colourless needles, m.p. 244–245° (Biglino *et al.*[3] report its m.p. as 227°); $[\alpha]_D$ +37·6° (*c* 8·03 $CHCl_3$) (Found: C, 79·26; H, 10·20. $C_{30}H_{46}O_3$ requires: C, 79·24; H, 10·20%). $\lambda_{max}$ (EtOH) 209 nm (log $\epsilon$ 3·56); $\nu_{max}$ 1727 and 1678 $cm^{-1}$; $\tau$ 9·15*s* (3H), 9·05*s* (3H), 8·96*s* (6H), 8·94*s* (3H), 8·90*s* (3H), 8·79*s* (3H) and no olefinic proton absorption; MS (fragmentation pattern similar to that of multiflor-8-en-3-one[11]): $M^+$ 454 *m/e* (9%), 218 (12), 235 (96), 245 (95), 257 (100), 439 (14); ORD curve (typical of 4,4-dimethyl-3-one triterpenoids of the isomultiflorenone type[12]) in $CHCl_3$ (*c* 0·33): $[\phi]_{450}$ +415°, $[\phi]_{370}$ +831°, $[\phi]_{330}$ +1218°, $[\phi]_{304}^{peak}$ +2492°, $[\phi]_{275}^{trough}$ +831°, $[\phi]_{265}$ +1218°. Bryonoic acid imparted a yellow colour to tetranitromethane and readily formed a sparingly soluble sodium salt. Further elution of the column with the same solvent system yielded mainly a mixture of bryononic and bryonolic acids (0·19 g). Elution of the column with light petrol.–$Et_2O$ (5:1) afforded bryonolic acid which was recrystallized from ethyl acetate in colourless needles (15 mg), m.p. 300–303°, undepressed on admixture with the bryonolic acid supplied by Biglino and having the same IR spectrum; $[\alpha]_D$ +24° (*c* 2·53 in pyridine) (Found: C, 78·31; H, 10·57. Calc. for $C_{30}H_{48}O_3$: C, 78·89; H, 10·59%). [(Lit.[3] m.p. 302–305°, $[\alpha]_D$ +20° (in $CHCl_3$)]; $\lambda_{max}$ (EtOH) 207 nm (log $\epsilon$ 3·66); $\nu_{max}$ 3484 and 1681 $cm^{-1}$; MS: $M^+$ 456 *m/e* (6%), 202 (20), 220 (6), 235 (54), 229 (61), 247 (30), 241 (60), 259 (41), 441 (13). Bryonolic acid is sparingly soluble in common organic solvents.

(b) The MeOH extract, on cooling, deposited a light brownish crystalline solid which was collected and triturated with $CHCl_3$ to give a colourless solid (5·38 g). Sublimation of a portion of this compound at 180–200°/0·2 mm yielded a crystalline product, m.p. 221–223° (Found: C, 40·12; H, 6·93. Calc. for $C_6H_{12}O_6$: C, 40·00; M, 6·71%), undepressed on admixture with authentic mesoinositol and having the same IR spectrum. Acetylation of the product afforded a hexa-acetate, m.p. 217–218° (Found: C, 50·03; H, 5·43. Calc. for $C_{18}H_{24}O_{12}$: C, 50·00; H, 5·60%), which had the same IR spectrum as authentic mesoinositol hexa-acetate. Concentration of the above MeOH filtrate yielded a pale greenish sticky solid (2·4 g), which was collected. Trituration of the sticky solid with acetone yielded a colourless solid which, on recrystallization from

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MeOH, gave needles, m.p. 202–204° (Found: C, 40·43; H, 6·19. Calc. for $C_8H_{14}O_8$: C, 40·34; H, 5·92%), undepressed on admixture with authentic dimethyl mucate and having the same IR spectrum. The dimethyl ester formed a tetra-acetate, m.p. 195–197° (Found: C, 47·75; H, 5·64. Calc. for $C_{16}H_{22}O_{12}$: C, 47·29; H, 5·46%). $[\alpha]_D$ 0°; $\tau$ 7·95*s* (6H), 7·83*s* (6H), 6·28*s* (6H), 4·80*s* (2H) and 4·33*s* (2H).

*Bryononic acid* 2,4-*dinitrophenylhydrazone*. Bryononic acid formed an orange 2,4-*dinitrophenylhydrazone*, m.p. 190° (decomp.) (Found: C, 67·65; H, 8·23. $C_{36}H_{50}O_6N_4$ requires: C, 68·11; H, 7·94%).

*Methyl bryononate*. A mixture of bryononic acid (0·2 g) and 3% methanolic hydrogen chloride (7 ml) was refluxed for 5 hr. The product, *methyl bryononate*, was recrystallized from MeOH in colourless prisms, m.p. 159–160°; $[\alpha]_D$ +46·6° (*c* 1·30 $CHCl_3$) (Found: C, 79·13; H, 10·33. $C_{31}H_{48}O_3$ requires: C, 79·43; H, 10·32%). $\lambda_{max}$ (EtOH) 207 nm (log $\epsilon$ 3·61); $\nu_{max}$ 1735 and 1700 $cm^{-1}$; $\tau$ 9·25*s* (3H), 9·03*s* (3H), 8·97*s* (3H), 8·96*s* (6H), 8·92*s* (3H), 8·83*s* (3H), 6·39*s* (3H); ORD in $CHCl_3$ (*c* 0·392) $[\phi]_{355}$ +810°, $[\phi]_{320}$ +1430°, $[\phi]_{303}^{peak}$ +2500°, $[\phi]_{273}^{trough}$ +477°, $[\phi]_{260}$ +810°. Methyl bryononate could also be obtained in the needle-form, m.p. 140–141° (Biglino *et al.*[3] obtained this compound by the oxidation of methyl bryonolate and report its m.p. as 132°). It formed an orange 2,4-*dinitrophenylhydrazone*, m.p. 249–251° (Found: C, 68·88; H, 8·24; N, 7·90. $C_{38}H_{52}O_6N_4$ requires: C, 69·06; H, 7·93; N, 8·48%). Saponification of methyl bryononate with ethanolic KOH yielded bryononic acid.

*Methyl* 3-*deoxybrononate and* 3-*deoxybryononic acid*. A mixture of methyl bryononate (0·6 g) in absolute EtOH (25 ml), hydrazine hydrate (6·0 ml) and ethylene glycol (60 ml) was refluxed for 1·5 hr. After cooling, KOH (3·6 g) was added to the mixture and the EtOH and excess hydrazine were distilled off. The mixture was then refluxed for another 2 hr at 220° and then poured into $H_2O$, acidified with conc. HCl and extracted with $CHCl_3$. The $CHCl_3$ solution was washed, dried and evaporated to give a mixture of 3-deoxybryononic acid and methyl 3-deoxybryononate. The mixture was refluxed with 4% methanolic HCl for 5 hr. The ester was recrystallized from $Me_2CO$–MeOH in colourless needles, m.p. 165–166°, $[\alpha]_D$ +17·5° (*c* 3·15 $CHCl_3$). (Found: C, 82·33; H, 11·49. $C_{31}H_{50}O_2$ requires: C, 81·88; H, 11·08%). $\tau$ 9·24*s* (3H), 9·18*s* (3H), 9·14*s* (3H), 9·06*s* (6H), 8·98*s* (3H), 8·84*s* (3H) and 6·40*s* (3H). Saponification of the ester with methanolic KOH yielded 3-*deoxybryononic acid*, m.p. 244–247° (Biglino *et al.*[3] report its m.p. as 220°) (Found: C, 81·11; H, 10·90. $C_{30}H_{48}O_2$ requires: C, 81·76; H, 10·98%). $\tau$ 9·18*s* (3H), 9·15*s* (6H), 9·06*s* (6H), 8·98*s* (3H), 8·78*s* (3H) and no olefinic proton absorption.

3-*Deoxybryonolol* (III). A mixture of 3-deoxybryononic acid (0·5 g), $LiAlH_4$ (0·5 g) and anhydrous $Et_2O$ (60 ml) was refluxed for 4 hr. EtOAc was added to decompose the excess $LiAlH_4$ and the mixture was acidified with dil. HCl and extracted with $Et_2O$. Evaporation of the dried $Et_2O$ extract afforded a residue which was recrystallized from $Me_2CO$–MeOH to give colourless *needles* (0·41 g), m.p. 207–210°, $[\alpha]_D$ +45·4° (*c* 1·81 $CHCl_3$) (Found: C, 84·77; H, 11·68. $C_{30}H_{50}O$ requires: C, 84·44; H, 11·81%). $\tau$ 9·18 (3H), 9·13 (3H), 9·05*s* (3H), 9·02*s* (6H), 8·90*s* (3H), 8·88*s* (3H) and 6·68*q* (2H). Acetylation of 3-deoxybryonolol (0·10 g) with $Ac_2O$ (2 ml) and pyridine (2 ml) gave an *acetate* which crystallized from $Me_2CO$–MeOH in colourless needles, m.p. 137–138° (Found: C, 81·62; H, 10·73. $C_{32}H_{52}O_2$ requires: C, 81·99; H, 11·18%). $\tau$ 9·18*s* (3H), 9·13*s* (3H), 9·05*s* (6H), 8·99*s* (3H), 8·91*s* (3H), 8·88*s* (3H), 7·94*s* (3H) and 6·20*s* (2H).

3-Deoxybryonolol formed a *tosylate* which crystallized from acetone in colourless plates, m.p. 189–191° (Found: C, 76·71; H, 9·84; S, 5·33. $C_{37}H_{56}SO_3$ requires: C, 76·51; H, 9·72; S, 5·51%). Prolonged reflux of the tosylate with $LiAlH_4$ gave on work-up mainly 3-deoxybryonolol.

*Bryonolol* (IV). A mixture of bryononic acid (0·38 g), $LiAlH_4$ hydride (0·41 g) in anhydrous $Et_2O$ (100 ml) was refluxed for 3·5 hr. The product recrystallized from EtOAc as colourless *needles* (0·25 g), m.p. 285–288°, $[\alpha]_D$ +33·3° (*c* 1·32 pyridine) (Found: C, 80·69; H, 11·52. $C_{30}H_{50}O_2$ requires: C, 81·39; H, 11·38%). $\nu_{max}$ 3290 $cm^{-1}$; MS: $M^+$ 442 *m/e* (2%), 202 (14), 203 (36), 220 (5), 221 (9), 229 (100), 241 (54), 247 (12), 259 (19), 427 (4). Acetylation of bryonolol with $Ac_2O$ and pyridine yielded a *diacetate* which crystallized from $Me_2CO$–MeOH in solourless plates, m.p. 206–209°, $[\alpha]_D$ +27·8° (*c* 1·25 $CHCl_3$) (Found: C, 77·02; H, 10·33. $C_{34}H_{54}O_4$ requires: C, 77·52; H, 10·33%). $\nu_{max}$ 1727 and 1248 $cm^{-1}$; $\tau$ 9·14*s* (9H), 9·10*s* (3H), 9·02*s* (6H), 8·90*s* (3H), 7·97*s* (3H), 7·94*s* (3H), 6·20*s* (2H) and no olefinic proton absorption: MS: $M^+$ 526 *m/e* (8%), 202 (10), 203 (100), 229 (79), 241 (54), 262 (8), 263 (15), 289 (27), 301 (41), 511 (10). Bryonolol formed a *ditosylate*, m.p. 145–6° (decomp.) (Found: C, 70·43; H, 8·19; S, 8·27. $C_{44}H_{62}S_2O_6$ requires: C, 70·36; H, 8·32; S, 8·54%). $\nu_{max}$ 1175 and 1185 $cm^{-1}$.

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