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FLAVANONES AND XANTHONES FROM *MACLURA POMIFERA*

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Key Word Index—*Maclura pomifera*, Moraceae, root bark, prenylated flavanones, 8-prenyltoxyloxanthone C

Abstract—(±)-Euchrestaflavanones B and C and 8-prenyltoxyloxanthone C have been isolated from the root bark of *Maclura pomifera* A study of the cyclization of alvaxanthone under varying conditions is reported

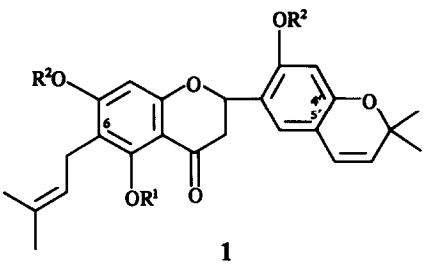
INTRODUCTION

The following phenolics have been reported from *Maclura pomifera* isoflavones (osajin and pomiferin) from the fruits [1], xanthones (macluraxanthone, osajaxanthone, alvaxanthone, 1,3,6,7-tetrahydroxyxanthone, 8-deoxygartanin, 6-deoxyjacarcubin and toxyloxanthones A, B, C and D) from the roots [2–5], flavonols, flavanonols and oxyresveratrol from the heartwood [5–8] We wish now to report the structure elucidation of two flavanones and of a xanthone isolated from a sample collected in Italy

RESULTS AND DISCUSSION

Chromatographic separation of the chloroform extract of the root bark gave two flavanones and a xanthone which were different from any previously reported phenolic The higher R_f compound, $C_{25}H_{26}O_6$ (MW 422), $[\alpha]_D$ 0°, showed spectral data in agreement with a substituted flavanone Since it gave a triacetate, three hydroxyl groups were present, two of which were in the 5- and 7-positions because of the bathochromic shifts in the UV maxima with $AlCl_3$ and NaOAc, respectively The ^{1}H NMR spectrum showed, in addition to three aromatic H singlets, the signals of a chromene ring and a γ,γ-dimethylallyl chain The location of the chromene ring and of the third hydroxyl on ring B, and of the chain on ring A followed from consideration of the mass fragmentation (ions at *m/z* 187 and *m/z* 165) Furthermore, the γ,γ-dimethylallyl chain could be located at C-6 due to the delayed shift of the UV maximum with $AlCl_3$ [9] and a positive Gibbs test

The aromatic ring B protons being uncoupled, only structure **1** ($R^1 = R^2 = H$) with a (2″,3″ 4′,5′) or (2″,3″ 5′,4′) junction of the 6″,6″-dimethyl-2H-pyran ring is possible The structure **1** ($R^1 = R^2 = H$) was definitively assigned to the flavanone after the oxidative cleavage of the dimethyltetrahydro derivative **2** ($R^1 = R^2 = Me$) The reaction gave an acid whose methyl ester **3** was coincident with a compound available in our laboratory (see Experimental) The structure **1** ($R^1 = R^2 = H$) was recently [10] assigned to (−)-euchrestaflavanone C from *Euchresta japonica* (Leguminosae), consequently our



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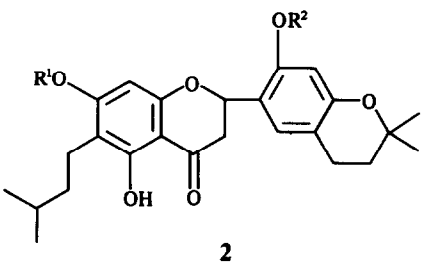

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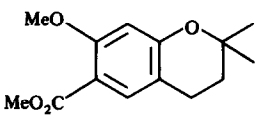

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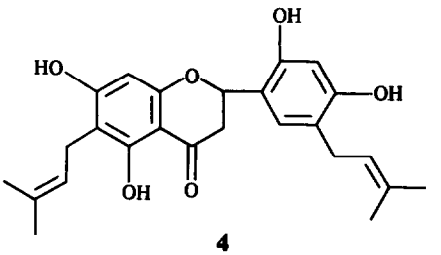

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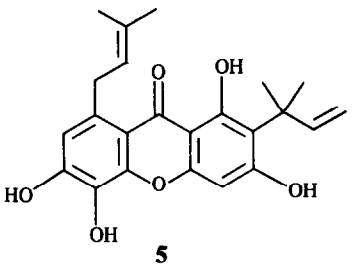
compound from Moraceae is (±)-euchrestaflavanone C To the lower R_f flavanone, $C_{25}H_{28}O_5$ (MW 424), $[\alpha]_D$ 0°, the structure of (±)-euchrestaflavanone B (**4**) was assigned by simple comparison of the spectral data [10]

The third compound, $C_{23}H_{24}O_6$ (MW 396) contained a 1,3,5,6-tetraoxygenated xanthone chromophore similar to that of alvaxanthone (**5**) and macluraxanthone, which were also present in our sample of *M pomifera* In the ^{1}H NMR spectrum (acetone-d_6) the signals of a chelated hydroxyl and two singlet aromatic protons were evident The spectrum also indicated the other substitutents to be a 2,3,3-trimethyl-2,3-dihydrofuran ring and a γ,γ-dimethylallyl chain Noteworthily, the latter exhibited the methylene doublet at a value (δ 3 93) which located the chain on C-8 (as in alvaxanthone, **5** [3]) and, consequently, the trimethyldihydrofuran ring on ring A A positive Gibbs test, a delayed shift of the UV maximum with $AlCl_3$ [9] and the absence of shift of the aromatic ring A proton (H-4) in the ^{1}H NMR spectrum in C_5D_5N permitted us to assign the structure **6** and the name 8-prenyltoxyloxanthone C to our compound

The known xanthones with a trimethyldihydrofuran substituent, e g to xyloxanthone C (**7**) [5] and rheediaxanthone B [11], are optically active The xanthone **6** with $[\alpha]_D$ 0 could be an artefact formed from alvaxanthone, possibly present in the crude extract To confirm the structure **6** we attempted to cyclize the α,α-dimethylallyl chain of alvaxanthone (**5**) The reaction was complicated by the presence of the C-8 chain, which although lacking an adjacent phenolic hydroxyl and cannot cyclize, may add the acid In fact, the usual cyclization method (TFA or HCOOH) gave as the main product the chroman derivatives **8** and **9**, respectively The formation of the chroman ring has been previously observed and discussed [11], the angular cyclization in **8** and **9** was chosen on the basis of a negative Gibbs test, an immediate shift of the UV maximum with $AlCl_3$ and C_5D_5N induced shift (~ +0 4 ppm) in the ring A proton signal (H-2) in the ^{1}H NMR spectrum The desired transformation of **5** to **6** was performed in high yield with HCl (gas) in dry ethanol Under these conditions the isomer **10** was also obtained Anhydrous conditions are necessary to obtain **6**, because in the presence of moisture compound **11** is the main product However, the HCl (gas) method is the most suitable for cyclization of an α,α-dimethylallyl chain onto an adjacent hydroxyl



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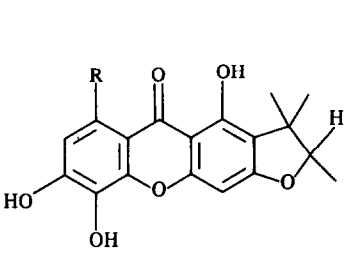
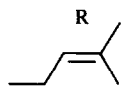
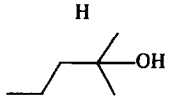
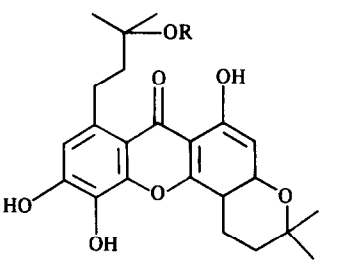


6 R = 

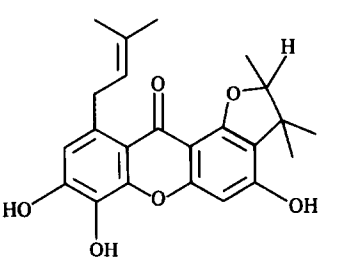
7 R = H

11 R = 



8 R = $COCF_3$

9 R = H



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EXPERIMENTAL

Plant material The roots and the wood of *Maclura pomifera* (Raf) Robinson were collected at Settebagni in the surroundings of Rome and identified by Dr S Pellegrini (Orto Botanico, Rome) A voucher sample is in the Herbarium of Centro Chimica dei Recettori under the cipher MP83

Extraction and fractionation of the roots The ground root bark (500 g) was extracted at room temperature with $CHCl_3$ (× 3) and the pooled extracts evaporated (49 5 g) A portion (31 g) was chromatographed on silica gel to give the following fractions with the indicated solvents MP_1 (10 g), $CHCl_3$, MP_2 (2 g) and MP_3 (3 1 g), $CHCl_3$–MeOH, 95 5, MP_4 (2 45 g) and MP_5 (3 5 g), $CHCl_3$–MeOH, 9 1, MP_6 (1 45 g), $CHCl_3$–MeOH, 4 1 MP_1 (triterpenes and triglycerides) and MP_6 were not further processed Crystallization of MP_2 gave macluraxanthone (850 mg) Silica gel CC (C_6H_6–EtOAc) of MP_3 yielded a mixture of macluraxanthone and osajaxanthone (100 mg, 2% EtOAc), osajaxanthone (150 mg, 5% EtOAc) and a mixture of 8-prenyltoxyloxanthone C and (±)-euchrestaflavanone C (2 1 g, 10% EtOAc), succesively Further CC of the latter gave 8-prenyltoxyloxanthone C (250 mg) and (±)-euchrestaflavanone C (560 mg) Silica gel CC (C_6H_6–EtOAc, 9 1) of MP_4 afforded (±)-euchrestaflavanone C (550 mg) Silica gel CC ($CHCl_3$–MeOH, 9 5) of MP_5 yielded alvaxanthone (1 5 g) and euchrestaflavanone B (1 2 g) The known compounds were identified by comparison of mps and of the spectral data (UV, ^{1}H NMR and MS) with lit data

Extraction and fragmentation of trunk wood The ground trunk wood was extracted with MeOH Crystallization from water of the crude extract gave oxyresveratrol The mother liquor contains morin identified by co-chromatography with an authentic sample Oxyresveratrol (2,4,3',5'-tetrahydrostilbene), mp 195–198°, EIMS (probe) 70 eV, *m/z* (rel int) 244 $[M]^+$ (100), 226 (35), 207 (25), 198 (26), 147 (25), 110 (56) Tetramethyloxyresveratrol, mp 82–84° (heptane), EIMS (probe) 70 eV, *m/z* (rel int) 300 $[M]^+$ (100), 269 (60), 254 (30), 238 (70), 166 (50), 165 (48), 149 (80), 135 (30), 121 (35)

(±)-*Euchrestaflavanone* (**1**, $R^1 = R^2 = H$) Mp 167–170° (CH_2Cl_2–heptane) $[\alpha]_D^{20}$ 0° (*c* 1 2, MeOH) UV λ_{max}^{MeOH} nm 227,

292, λ_{max}^{NaOMe} 326, λ_{max}^{NaOAc} 293, 323, $\lambda_{max}^{AlCl_3}$ 314 after 15 min Gibbs test λ_{max} 680 IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3580, 1620 ^{1}H NMR (60 MHz, $CDCl_3$) δ 12 25 (1H, *s*), 6 90 (*s*, H-6'), 6 30 (*s*, H-8), 6 20 (*d*, *J* = 10 Hz), 6 0 (*s*, H-3'), 5 55 (X part of ABX, H-2), 5 42 (*d*, *J* = 10 Hz), 5 20 (1H, *br t*, *J* = 7 Hz), 3 33 (2H, *br d*, *J* = 7 Hz), 3 0 (AB part of ABX, H_2-3), 1 83 (3H, *s*), 1 76 (3H, *s*), 1 45 (6H, *s*) $\Delta\delta$ (C-6 methylene) = $\delta(C_5D_5N) - \delta(CDCl_3)$ = +0 47 ppm EIMS (probe) 70 eV, *m/z* (rel int) 422 $[M]^+$ (22), 407 $[M-15]^+$ (20), 404 (36), 389 (12), 381 (21), 379 (22), 361 (41), 353 (37), 351 $[M-15-56]^+$ (29), 349 (33), 325 (19), 295 (25), 219 (26), 213 (100), 205 (16), 203 (15), 196 (24), 187 (ring B from *m/z* 351) (100), 177 (34), 165 (RDA from *m/z* 351) (88) Acetylation (pyridine–Ac_2O) gave the oily di- and triacetyl derivatives, **1** (R^1 = H, R^2 = Ac) and **2** (R^1 = R^2 = Ac), respectively Diacetyl derivative, ^{1}H NMR ($CDCl_3$) δ 7 10 (H-6'), 6 50 (H-8), 6 30 (H-3'), 2 25 and 2 23 (3H each) Triacetyl derivative, ^{1}H NMR ($CDCl_3$) δ 7 10 (H-6'), 6 65 (H-8), 6 50 (H-3'), 2 30, 2 25 and 2 20 (3H each)

Hydrogenation and oxidative cleavage of **1** 400 mg of **1** (R^1 = R^2 = H) in EtOH was hydrogenated in the presence of PtO_2 (150 mg) to give tetrahydroeuchrestaflavanone C, **2** (R^1 = R^2 = H), mp 213–215° ($CHCl_3$), $[M]^+$ 426 Methylation with CH_2N_2 gave the monomethyl derivative **2** (R^1 = Me, R^2 = H) and the dimethyl derivative **2** (R^1 = R^2 = Me) Monomethyltetrahydroflavanone, mp 190–192° ($CHCl_3$), ^{1}H NMR ($CDCl_3$) δ 12 15 (1H, *s*), 3 75 (3H, *s*), $[M]^+$ 440 Dimethyltetrahydroflavanone mp 134–136° ($CHCl_3$), ^{1}H NMR ($CDCl_3$) δ 3 77 (3H, *s*), 3 70 (3H, *s*), $[M]^+$ 454

30% H_2O_2 (5 ml) was added dropwise during 30 min to dimethyltetrahydroflavanone (300 mg) in 25% aq KOH (10 ml) with stirring The soln was maintained at 50° for 1 hr, then acidified with HCl 1 1 Purification of the crude extract gave an acid, which by methylation gave 2,2-dimethyl-7-methoxy-6-carbomethoxychromane, **3**, oil, ^{1}H NMR ($CDCl_3$) δ 7 60 (*s*, H-5), 6 33 (*s*, H-8), 3 83 (*s*, 2 × OMe), 2 73 (2H, *t*, *J* = 6 5 Hz), 1 80 (2H, *t*, *J* = 6 5 Hz), 1 35 (6H, *s*), EIMS (probe) 70 eV, *m/z* (rel int) 250 $[M]^+$ (60), 235 (8), 219 (25), 209 (6), 203 (9), 195 $[M-55]^+$ (100), 163 (18) The spectral data were identical to those of **3** prepared by cyclization (H^+) and methylation of 2,4-dihydroxy-5(γ,γ-dimethylallyl)benzoic acid [12]

(±)-*Euchrestaflavanone B* (**4**) Mp 154–156° (CH_2Cl_2–heptane) $[\alpha]_D^{20}$ 0° (*c* 0 9, MeOH) UV λ_{max}^{MeOH} nm 232, 292, 342 sh, λ_{max}^{NaOMe} 329, λ_{max}^{NaOAc} 293, 329, $\lambda_{max}^{AlCl_3}$ 313 after 10 min Gibbs test λ_{max} 680 IR ν_{max}^{KBr} cm^{-1} 3500, 1630 ^{1}H NMR (60 MHz, CD_3COCD_3) δ 12 35 (1H, *s*), 7 10 (*s*, H-6'), 6 43 (*s*, H-8), 6 0 (*s*, H-3'), 5 65 (X part of ABX, H-2), 5 30 (2H, *br*), 3 25 (4H, *br d*, *J* = 7 Hz), 3 0 (AB part of ABX, H_2-3), 1 75–1 60 (12H, *br s*) $\Delta\delta$(C-6 methylene) = $\delta(C_5D_5N) - \delta(CDCl_3)$ = +0 42, $\Delta\delta$(C-5 methylene) = $\delta(C_5D_5N) - \delta(CDCl_3)$ = +0 30 EIMS (probe) 70 eV, *m/z* (rel int) 424 $[M]^+$ (8), 406 (52), 379 $[M-55]^+$ (16), 363 (48), 351 (36), 313 (28), 295 (36), 285 (20), 220 (24), 165 (100), 149 (64)

8-*Prenyltoxyloxanthone C* (**6**) Mp 154–156° (CH_2Cl_2–heptane) $[\alpha]_D^{20}$ 0° (*c* 0 2, $CHCl_3$) UV λ_{max}^{MeOH} nm 256, 279 sh, 328, λ_{max}^{NaOMe} 246, 266 sh, 286 sh, 346, λ_{max}^{NaOAc} 255, 271 sh, 280 sh, 339, $\lambda_{max}^{AlCl_3}$ 338 after 30 min Gibbs test λ_{max} 675 IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3540, 1650, 1610, 1590 ^{1}H NMR (60 MHz, CD_3COCD_3) δ 13 8 (1H, *s*), 6 73 (*s*, H-7), 6 25 (*s*, H-4), 5 37 (1H, *t*, *J* = 7 Hz), 4 47 (1H, *q*, *J* = 6 5 Hz), 3 93 (2H, *d*, *J* = 7 Hz), 1 73 (6H, *br s*), 1 50 (3H, *s*), 1 38 (3H, *d*, *J* = 6 5 Hz), 1 23 (3H, *s*) $\Delta\delta$ = $\delta(C_5D_5N) - \delta(CD_3COCD_3)$ = O(H-4), +0 58 (H-7) EIMS (probe) 70 eV, *m/z* (rel int) 396 $[M]^+$ (42), 381 (34), 367 (11), 353 (100), 341 (13), 325 (35), 276 (32)

Action of acids on alvaxanthone (**5**) (a) Alvaxanthone (100 mg) was refluxed for 45 min in HCOOH Evaporation and CC (SiO_2, C_6H_6–EtOAc, 6 4) gave **9** (75 mg) (b) Alvaxanthone (200 mg) in $CHCl_3$ containing 30% trifluoroacetic acid (TFA) was left at room temperature for 18 hr Evaporation and CC gave **8** (85 mg, C_6H_6–EtOAc, 8 2) and **9** (40 mg, C_6H_6–EtOAc, 6 4), successively (c) Alvaxanthone (250 mg) in dry EtOH was saturated with HCl (gas) and left standing with exclusion of moisture for 6 hr Evaporation and CC (SiO_2, $CHCl_3$–MeOH, 96 4) gave **6** (120 mg) and **10** (80 mg), successively (d) Alvaxanthone (300 mg) was treated as in (c) without exclusion of moisture CC gave **6** (25 mg), **11** (125 mg) and **10** (70 mg), successively

Xanthone **8** Mp 235–238° UV λ_{max}^{MeOH} nm 258, 285 sh, 343 IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3540, 1770 (OTFA), 1650 ^{1}H NMR (CD_3COCD_3) δ 13 1 (1H, *s*) 6 70 (*s*, H-7), 6 0 (*s*, H-2), 3 40–3 00 (2H, *m*), 2 90 (2H, *t*, *J* = 6 Hz), 2 30–1 70 (4H, *m*), 1 63 (3H, *s*), 1 30 (6H, *s*) $\Delta\delta$ = +0 46 (H-2), +0 45 (H-7) EIMS (probe) 70 eV, *m/z* (rel int) 510 $[M]^+$ (not observed), 396 $[M-TFA]^+$ (45), 381 (5), 378 (5), 367 (13), 353 (100), 341 (12), 323 (7), 311 (7), 297 (36), 285 (26)

Xanthone **9** UV λ_{max}^{MeOH} nm 252, 282 sh, 327 Gibbs test negative IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3520, 1640 ^{1}H NMR (CD_3COCD_3) δ 13 20 (1H, *s*), 6 80 (*s*, H-7), 6 10 (*s*, H-2), 3 40–3 00 (2H, *m*), 2 90 (2H, *t*, *J* = 6 Hz), 2 0–1 60 (4H, *m*), 1 35 (6H, *s*), 1 25 (6H, *s*) $\Delta\delta$ = +0 30 (H-2), +0 40 (H-7) EIMS (probe) 70 eV, *m/z* (rel int) 414 $[M]^+$ (2), 396 $[M-H_2O]^+$ (44), 381 (5), 378 (5), 367 (13), 353 (100)

Xanthone **10** UV λ_{max}^{MeOH} nm 251, 280 sh, 312, $\lambda_{max}^{AlCl_3}$ 333, $\lambda_{max}^{AlCl_3+HCl}$ 312 Gibbs test negative ^{1}H NMR (CD_3COCD_3) δ 6 63 (*s*, H-7), 6 45 (*s*, H-4), 5 37 (1H, *t*, *J* = 7 Hz), 4 43 (1H, *q*, *J* = 6 5 Hz), 3 93 (2H, *d*, *J* = 7 Hz), 1 65 (6H, *br s*), 1 43 (3H, *s*), 1 35 (3H, *d*, *J* = 6 5 Hz), 1 20 (3H, *s*) $\Delta\delta$ = +0 15 (H-4), +0 50 (H-7) EIMS (probe) 70 eV, *m/z* (rel int) 396 $[M]^+$ (55), 381 (15), 367 (15), 353 (100), 328 (8), 325 (10), 285 (50)

Xanthone **11** UV λ_{max}^{MeOH} nm 250, 280 sh, 330 Gibbs test λ_{max} 680 ^{1}H NMR (CD_3COCD_3) δ 13 1 (1H, *s*), 6 66 (*s*, H-7), 6 18 (*s*, H-4), 4 43 (1H, *q*, *J* = 6 5 Hz), 3 50–3 10 (2H, *m*), 2 10–1 80 (2H, *m*), 1 65 (6H, *s*), 1 43 (3H, *s*), 1 33 (3H, *d*, *J* = 6 5 Hz), 1 20 (3H, *s*) $\Delta\delta$ = 0 (H-4), +0 44 (H-7) EIMS (probe) 70 eV, *m/z* (rel int) 414 $[M]^+$ (10), 396 (45), 381 (40), 367 (10), 353 (100), 341 (20), 325 (45), 311 (10)

REFERENCES

1 Wolfrom, M L, Harris, W D, Johnson, G F, Mahan, J E, Moffett, S M and Wildi, B (1946) *J Am Chem Soc* **68**, 406
2 Wolfrom, M L, Komitsky, F, Fraenkel, G, Looker, J H, Dickey, E E, McWain, P, Thomson, A, Mundell, P M and Windrath, O M (1964) *J Org Chem* **29**, 692
3 Wolfrom, M L, Komitsky, F and Mundell, P M (1965) *J Org Chem* **30**, 1088
4 Cotterile, P J and Scheinmann, F (1975) *J Chem Soc Chem Commun* 664
5 Deshpande, V H, Rama Rao, A V, Valadan, M and Venkataraman, K (1973) *Indian J Chem* **11**, 518
6 Barnes, R A and Gerber, N N (1955) *J Am Chem Soc* **77**, 3259
7 Laidlow, R A and Smith, G A (1959) *Chem Ind* 1604
8 Drost, K, Olszak, M and Skrzypozak, L (1967) *Planta Med* **15**, 264
9 Alves de Lima, R and Delle Monache, G (1977–8) *Rend Acad Naz dei XL (Rome) (V)* 3, 1088
10 Shirataki, Y, Manaka, A, Yokoe, I and Komatsu, M (1982) *Phytochemistry* **21**, 2959
11 Delle Monache, F, Botta, B, Nicoletti, M, De Barros Côelho, J S and De Andrade Lyra, F D (1981) *J Chem Soc Perkin Trans* 1, 484
12 Delle Monache, F, Delle Monache, G, Marini Bettolo, G B, Fernandes de Albuquerque, M M, De Mello, J F and Goncalves de Lima, O (1976) *Gazz Chim Ital* **106**, 935