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# CONSTITUENTS OF SNEEZEWOOD, *PTAEROXYLON OBLIQUUM*—II[1]

## COUMARINS—THE STRUCTURE OF NIESHOUTOL[2]

R. D. H. MURRAY and M. M. BALLANTYNE
Department of Chemistry, University of Glasgow, Glasgow W.2.

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**Abstract**—Nieshoutol has been shown to possess structure **1** from chemical and spectroscopic evidence. The relationship of the phenolic OH to the dihydrofuran ring was obtained from NMR shielding effects. Demethylation, ester interchange, and cyclic ketal formation showed the OMe to be *ortho* to the OH. Structure **1** was confirmed by observation of a nuclear Overhauser effect.

IN AN earlier communication[1] we reported the isolation of the coumarin nieshoutol, $C_{15}H_{16}O_5$, m.p. 143–144° from sneezewood (Afrikaans: nieshout). This compound, which appears to possess mild sternutatory properties, is the major coumarin constituent of our sample* of *Ptaeroxylon obliquum*,[3] and is now allocated structure **1** on the following spectroscopic and chemical evidence.

The NMR spectrum of nieshoutol disclosed a pair of one proton doublets at $\tau$ 3·81 and 2·13, $J = 9·5$ Hz, the chemical shifts and coupling constant of which are typical of protons in a coumarin nucleus, at C-3 and C-4 respectively. Singlets at $\tau$ 4·83 (1H) and 6·03 (3H) were ascribed to OH and OMe functions, while the remainder of the spectrum (Table 1) could be accounted for by a 2,3,3-trimethyldihydrofuran system attached to an aromatic ring. This evidence led to a partial structure A for nieshoutol.

Chemical confirmation of a phenolic OH group was obtained by the formation of an acetate (**2**), $\gamma_{max}^{CCl_4}$ 1770 cm$^{-1}$, and a methyl ether (**3**). The difference between the UV spectra of nieshoutol in EtOH and in 1% NaOH–EtOH was not that generally ascribed[4–6] to a 7-hydroxycoumarin. Thus the OH function, which is intramolecularly H-bonded, $\gamma_{max}^{CCl_4}$ 3569 cm$^{-1}$, is probably not located at C-7.

Several heavy atom phenolic derivatives of nieshoutol were prepared[7] but these proved unsuitable for X-ray studies. However, it was noted that the NMR spectrum of one of these, the brosylate (**4**) when compared with that of the parent phenol (**1**) showed shielding of both the methine and the secondary Me signals, 0·28 and 0·21 ppm respectively. A similar shielding of the secondary Me system was observed in the spectrum of the corresponding tosylate (**5**). No such effect was observed for the bromobenzoate (**6**) or the mesylate (**7**). It was anticipated that the benzyl ether[8] derivative (**8**) might behave as the arylsulphonates but the observed spectrum was very similar to that of the parent phenol. The specific effects of the C-2′ substituents necessitate a close proximity of the arylsulphonate ring to the dihydrofuran ring, as

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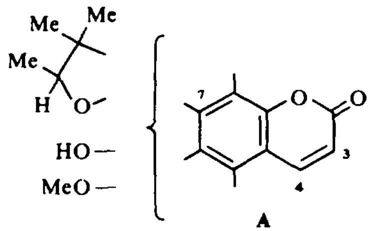
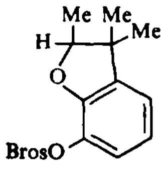
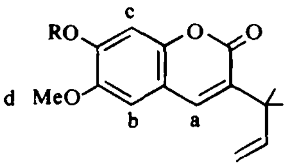
* Obtained from an unknown source in South Africa by Mr. J. H. van Wyk, Forest Research Institute, Pretoria. Nieshoutol has not been detected in the samples of *P. obliquum* examined[3] by Dr. F. M. Dean and Professor D. A. H. Taylor.



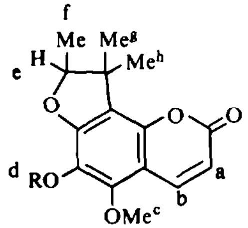
**A**



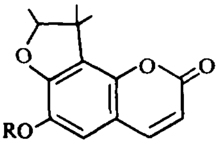
**B**



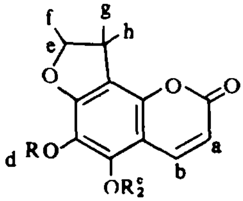
**13**: R = H
**14**: R = Bros
**15**: R = Mes



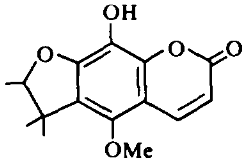
**1**: R = H
**2**: R = Ac
**3**: R = Me
**4**: R = Bros
**5**: R = Tos
**6**. R = $COC_6H_4Br(p)$
**7**: R = Mes
**8**: R = $CH_2Ph$



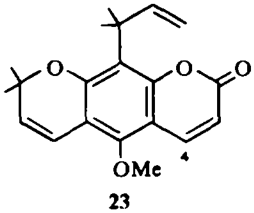
**9**: R = H
**10**: R = Bros
**11**: R = Mes



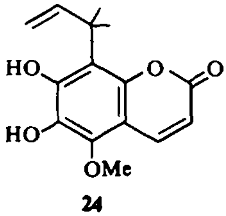
**16**: $R_1$ = Ac, $R_2$ = H
**17**: $R_1$ = $R_2$ = H
**18**: $R_1$ = Ac, $R_2$ = Bros
**19**: $R_1$ = H, $R_2$ = Bros
**20**: $R_1$ = Bros, $R_2$ = H
**21**: $R_1$ = Me, $R_2$ = Bros
**22**: $R_1$ + $R_2$ = $CPh_2$



**12**



**23**

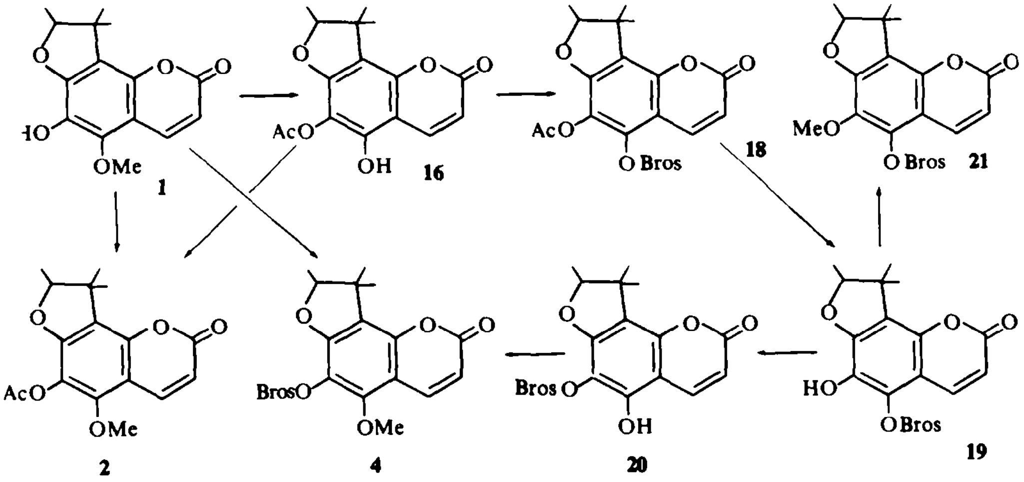


**24**

in partial structure B. To test this hypothesis, the brosylate (**10**) and mesylate (**11**) of the phenol[2] (**9**) were prepared. From comparison of the NMR spectra of **10** and **9**, it can be seen that in the latter there is a marked shielding of the secondary Me system (0·36 and 0·25 ppm for the H and Me respectively). The downfield shift (0·43 ppm) of the aromatic proton in **10** was as expected for a strong electron withdrawing group in the *ortho* position. In the spectrum of the corresponding mesylate (**11**), a similar effect was observed on the position of the signal from the aromatic proton, but unlike the brosylate, the remainder of the spectrum was unaffected.

The above NMR evidence strongly supports the partial structure B and, when taken in conjunction with the deductions from the IR and UV data, suggests that nieshoutol could be represented by either **1** or **12**. The latter structure was initially favoured because nieshoutol and its derivatives all have essentially the same chemical shift for the OMe signal, while the brosylate (**14**) of **13**[9] showed a shielding (0·29 ppm) of the *ortho* OMe.

Since the OH and OMe functions of nieshoutol must be either *ortho* or *para* orientated, it was realized that conclusive information might be gained if nieshoutol could be converted to the corresponding diol. Treatment of **1** with freshly prepared 45% HBr–HOAc at gentle reflux gave, apart from recovered starting material (22%) and its acetate (5%), a hydroxyacetate (22%) which can be more efficiently prepared by demethylation of **2**, and a diol (40%). The two new compounds on methylation with diazomethane gave nieshoutol acetate (**2**) and nieshoutol methyl ether (**3**) respectively, showing that no skeletal rearrangement had accompanied demethylation. Thus the intramolecularly H-bonded OH, $\gamma_{max}^{CCl_4}$ 3570 cm$^{-1}$, present in the hydroxyacetate (**16**) has been derived from the OMe group of nieshoutol (see Fig). Moreover, it can be placed at C-5 because the NMR of the derived brosylate (**18**) shows a significant shielding (0·35 ppm) of the C-4 proton. A similar shielding (0·25 ppm) of a C-4 proton by a tosylate at C-5 has been reported[10] by Joshi *et al.*



FIG

The *ortho* relationship of the OH and OAc functions in **16** was strongly indicated by the upfield shift (0·33 ppm) of the acetate signal in **18**. No such effect would have been expected should the relationship be *para*. The hydroxybrosylate (**19**) which was isolated during the preparation of **18** was shown to arise from hydrolysis of the latter, and on methylation gave primarily a compound isomeric with nieshoutol brosylate (**4**). However, distillation of the hydroxybrosylate gave rise to a mixture of two compounds, one of which was identified by TLC and NMR as the starting material. Methylation of the mixture gave two isomeric compounds, namely **21** and **4**. The isolation of these products substantiated the NMR evidence that ester interchange[11] had occurred during distillation. This can only be explained by an *ortho* relationship of the functionalities involved. It was found in confirmation that the diol (**17**) when kept with dichlorodiphenylmethane in pyridine afforded a cyclic ketal (**22**).

The *peri* relationship of the OMe group with the C-4 proton in nieshoutol was independently established by using the nuclear Overhauser effect.[13] Saturation of the C-4 proton by double irradiation caused a 12% increase of the integrated intensity of the OMe protons when compared with the intensity on irradiating at approximately 50 Hz upfield from the C-4 proton signal. Conversely an 11% increase of the integrated intensity of the C-4 proton resulted from saturation of the OMe signal. A similar effect has been observed[14] by Tori *et al.* on saturation of the OMe protons of poncitrin (**23**).

Nieshoutol is of interest in that it is the only trioxygenated coumarin yet isolated from sneezewood, the remaining coumarins being 6,7-dioxygenated. The optical inactivity of nieshoutol might imply that it is an artefact, possibly arising from cyclization of **24** during isolation. To date, however, this latter compound has not been detected amongst the sneezewood constituents examined.

TABLE 1. CHEMICAL SHIFTS ($\tau$) AT 60 MHz FOR COUMARIN DERIVATIVES

| | Ha | Hb | Hc | Hd | He | Hf | Hg | Hh[a] |
|---|---|---|---|---|---|---|---|---|
| | 1H, d $J$ = 9·5 Hz | 1H, d $J$ = 9·5 Hz | s | s | 1H, q $J$ = 6·5 Hz | 3H, d $J$ = 6·5 Hz | 3H, s | 3H, s |
| 1 | 3·81 | 2·13 | 6·03, 3H | 4·83[b], 1H | 5·43 | 8·59 | 8·46 | 8·72 |
| 2 | 3·83 | 2·15 | 6·08, 3H | 7·63, 3H | 5·45 | 8·62 | 8·45 | 8·70 |
| 3 | 3·87 | 2·12 | 6·01, 6·06 both 3H | | 5·45 | 8·58 | 8·45 | 8·73 |
| 4 | 3·80 | 2·16 | 6·05, 3H | — | 5·71 | 8·80 | 8·52 | 8·82 |
| 5 | 3·85 | 2·15 | 6·08, 3H | — | 5·73 | 8·82 | 8·52 | 8·82 |
| 6 | 3·82 | 2·10 | 6·07, 3H | — | 5·44 | 8·62 | 8·41 | 8·66 |
| 7 | 3·80 | 2·13 | 5·98, 3H | — | 5·36 | 8·57 | 8·43 | 8·67 |
| 8 | 3·86 | 2·15 | 6·05, 3H | — | 5·51 | 8·61 | 8·47 | 8·75 |
| 9 | 3·80 | 2·47 | 3·18, 1H | 4·50[b], 1H, br | 5·44 | 8·59 | 8·43 | 8·71 |
| 10 | 3·75 | 2·43 | 2·75, 1H | — | 5·80 | 8·84 | 8·52 | 8·84 |
| 11 | 3·75 | 2·43 | 2·75, 1H | — | 5·36 | 8·56 | 8·42 | 8·67 |
| 16 | 3·85 | 2·02 | 3·93[b], 1H, br | 7·60, 3H | 5·45 | 8·62 | 8·48 | 8·73 |
| 17 | 3·85 | 2·02 | 4·0[b], 2H, br | | 5·47 | 8·62 | 8·48 | 8·76 |
| 18 | 3·78 | 2·41 | — | 7·93, 3H | 5·39 | 8·60 | 8·42 | 8·67 |
| 19 | 3·82 | 2·35 | — | 4·67[b], 1H, br | 5·40 | 8·58 | 8·44 | 8·70 |
| 20[c] | 3·83 | 2·03 | — | — | 5·89 | 8·88 | 8·58 | 8·92 |
| 21 | 3·77 | 2·30 | — | 6·31, 3H | 5·44 | 8·59 | 8·44 | 8·71 |
| | 1H, s | 1H, s | 1H, s | 3H, s | | | | |
| 13 | 2·53 | 3·16 | 3·17 | 6·07 | | | | |
| 14 | 2·53 | 3·14 | 2·91 | 6·36 | | | | |
| 15 | 2·49 | 3·00 | 2·75 | 6·07 | | | | |

[a] The high field methyl may be that which is *cis* to the C-$2^1$ methyl.[12]

[b] Disappears on addition of $D_2O$.

[c] These values are those obtained after subtraction of the signals attributed to **19** from the NMR spectrum of a mixture of **19** and **20**.

## EXPERIMENTAL

M.ps were determined with a Kofler hot stage apparatus. IR spectra of $CCl_4$ solns were recorded by Mrs. F. Lawrie on Unicam SP 100 Mark II and Perkin–Elmer 225 spectrophotomers; IR spectra of $CHCl_3$ solns were recorded on a Perkin–Elmer 257 spectrophotometer. NMR spectra of solns in $CDCl_3$ with

TMS as internal standard were recorded by Mrs. S. Hamilton with a Varian T-60 spectrometer. Measurement of the Nuclear Overhauser Effect was made by Mr. J. Gall on a Varian HA-100 spectrometer. Mass spectra were recorded by Mr. A. Ritchie with an AEI-GEC MS12 mass spectrometer. Microanalyses were performed by Mr. J. M. L. Cameron and his staff. Specific rotations refer to solns in $CHCl_3$. UV spectra were recorded for EtOH solns on a Unicam SP 800 spectrophotomer. $\lambda$ (in base) refers to solns in 1% NaOH–EtOH. Kieselgel G (Merck) was used for preparative TLC plates which were developed with $CHCl_3$ unless otherwise stated. Light petroleum refers to the fraction b.p. 60–80°.

*Nieshoutol and its derivatives*

*Nieshoutol* (**1**), pale yellow plates, m.p. 143–144°, from $CCl_4$ occurred as 0·1% of dried heartwood of *P. obliquum*. (Found: C, 64·95; H, 5·85. $C_{15}H_{16}O_5$ requires: C, 65·2; H, 5·85%); $\gamma_{max}^{CCl_4}$ 3569, 1736, 1620 and 1578 $cm^{-1}$; $\lambda_{max}$ 230, 251, 258 and 340 nm (log $\varepsilon$ 4·18, 3·64, 3·55 and 4·08), $\lambda_{max}$ (in base) 255, 340 and 400 nm (log $\varepsilon$ 4·26, 3·98and 3·79); mass spectral peaks at $m/e$ 276 ($M^+$), 261, 247, 246, 243, 233, 229, 220 and 205 (relative abundance 98, 100, 9, 15, 7, 32, 56, 12 and 10%); $[\alpha]_D 0°$.

*Methyl ether* (**3**) obtained by diazomethylation (65 hr) of an ethereal soln of nieshoutol (100 mg), *nieshoutol methyl ether* (85 mg; 81%) was eluted from alumina (Woelm, grade I, neutral, 7 g) with EtOAc–light petroleum as a colourless viscous oil, which distilled at 120°/0·05 mm. On standing, the distillate solidified to give colourless needles, m.p. 99–100°. (Found: C, 65·95; H, 6·2. $C_{16}H_{18}O_5$ requires: C, 66·2; H, 6·25%); $\gamma_{max}^{CCl_4}$ 1740 $cm^{-1}$ ($\varepsilon$ 1140); $\lambda_{max}$ 212, 230, 251, 259 and 334 nm (log $\varepsilon$ 4·43, 4·16, 3·75, 3·70 and 4·01); $[\alpha]_D 0°$.

*Acetate* (**2**). $Ac_2O$ (0·15 ml) was added to a soln of nieshoutol (300 mg) in anhydrous pyridine (1 ml) and the mixture kept for 1 hr. Work up and crystallization from ether–light petroleum gave *nieshoutol acetate* as colourless plates (316 mg; 93%), m.p. 126–128°. (Found: C, 64·4; H, 5·85. $C_{17}H_{18}O_6$ requires: C, 64·15; H, 5·7%); $\gamma_{max}^{CHCl_3}$ 1775–1765, 1730, 1613 and 1580 $cm^{-1}$; $\lambda_{max}$ 223, 249, 259 and 328 nm (log $\varepsilon$ 4·19, 3·78, 3·80 and 4·16).

p-*Bromobenzoate* (**6**). Nieshoutol (110 mg) was heated at 65° for 18 hr with *p*-bromobenzoyl chloride in pyridine (12 ml). On cooling, ice was added and the mixture was extracted with EtOAc, the organic layer then washed with $NaHCO_3$ aq, with water till neutral, and dried. The crude reaction product was separated by TLC to give *nieshoutol* p-*bromobenzoate* (83 mg; 45%) as needles, m.p. 213–215° (from $CHCl_3$–light petroleum). (Found: C, 57·3; H, 3·95. $C_{22}H_{19}O_6Br$ requires: C, 57·5; H, 4·2%); $[\alpha]_D 0°$.

p-*Bromobenzenesulphonate* (**4**). Nieshoutol (140 mg) was heated at 80° for 16 hr with *p*-bromobenzenesulphonyl chloride (145 mg) in pyridine (15 ml). Isolated from the reaction mixture as above, *nieshoutol brosylate* was purified by TLC and crystallized from $CHCl_3$–light petroleum as needles (115 mg; 46%) m.p. 175–176°. (Found: C, 51·0; H, 4·3. $C_{21}H_{19}O_7SBr$ requires: C, 50·9; H, 3·9%); $[\alpha]_D 0°$.

*Methanesulphonate* (**7**). Methanesulphonyl chloride (65 mg) was added to a soln of nieshoutol (27 mg) in pyridine (1 ml) and the mixture kept for 3 hr. Work up gave a dark oil which after purification by TLC was distilled at 160°/0·05 mm. The distillate solidified on standing to give *nieshoutol mesylate* as colourless needles (28 mg; 81%), m.p. 140–142°. (Found: C, 54·0; H, 5·15. $C_{16}H_{18}O_7S$ requires: C, 54·25; H, 5·1%).

p-*Toluenesulphonate* (**5**). *p*-Toluenesulphonyl chloride (20 mg) was added to a soln of nieshoutol (27 mg) in pyridine (1 ml). After 20 hr at room temp, TLC indicated that the reaction was not complete. More *p*-toluenesulphonyl chloride (20 mg) was added and the temp raised to 75° for 3 hr. Work-up followed by purification by TLC gave *nieshoutol tosylate* as colourless plates (38 mg; 90%) m.p. 153–155° (from $CHCl_3$–light petroleum). (Found: C, 60·9; H, 5·05. $C_{22}H_{22}O_7S$ requires: C, 61·4; H, 5·15%).

*Benzyl ether* (**8**). $K_2CO_3$ (20 mg) was added to a soln of nieshoutol (20 mg) in acetone (5 ml) and the mixture stirred at room temp for ½ hr. Benzyl bromide (40 mg) was added and the mixture refluxed for 6 hr. Work-up gave a yellow solid which was heated at 35°/0·05 mm for 4 hr to remove excess benzyl bromide. Crystallization from ether–light petroleum yielded *nieshoutol benzyl ether* as colourless plates (25 mg; 91%), m.p. 119–121·5°. (Found: C, 72·05; H, 6·1. $C_{22}H_{22}O_5$ requires: C, 72·1; H, 6·05%).

*Derivatives of 6-demethylnieshoutin* (**9**)

p-*Bromobenzenesulphonate* (**10**. *p*-Bromobenzenesulphonyl chloride (45 mg) was added to a soln of 6-demethylnieshoutin (18 mg) in pyridine (1 ml) and the soln stirred at 84° for 18 hr. Work-up, then purification by TLC gave an oil which was distilled at 150°/0·02 mm. On standing, the distillate solidified to give the *brosylate* as colourless needles (27 mg; 79%), m.p. 128–129·5°. (Found: C, 51·4; H, 3·75. $C_{20}H_{17}O_6SBr$ requires: C, 51·6; H, 3·7%).

*Methanesulphonate* (**11**). Methanesulphonyl chloride (65 mg) was added to a soln of 6-demethylnieshoutin (20 mg) in pyridine (1 ml) and the mixture kept for 2 hr. Work-up, then purification by TLC gave the *mesylate* as colourless plates (23 mg; 87%), m.p. 128–130° (from ether–light petroleum). (Found: C, 55·5; H, 5·05. $C_{15}H_{16}O_6S$ requires: C, 55·55; H, 4·95%).

### *Derivatives of* 3-(1,1-*dimethylallyl*)*scopoletin* (**13**)

p-*Bromobenzenesulphonate* (**14**). *p*-Bromobenzenesulphonyl chloride (124 mg) was added to **13** (50 mg) in pyridine (2 ml), and the soln stirred at 80° for 18 hr. Work-up gave the *brosylate* as pale yellow needles (76 mg; 81%), m.p. 203·5–205°, from $CCl_4$. (Found: C, 52·7; H, 4·0. $C_{21}H_{19}O_6S$ Br requires: C, 52·6; H, 3·95%).

*Methanesulphonate* (**15**). Methanesulphonyl chloride (75 mg) was added to a soln of **13** (26 mg) in pyridine (1 ml), and the mixture kept for 2½ hr. Work up and purification by TLC gave the *mesylate* as colourless needles (27 mg; 80%), m.p. 118–120°, from ether. (Found: C, 56·8; H, 5·5. $C_{16}H_{18}O_6S$ requires: C, 56·8; H, 5·35%).

### *Demethylations*

(i) *Nieshoutol.* Freshly prepared HBr in HOAc (45% w/v; 8 ml) was added to a soln of nieshoutol (100 mg) in HOAc (8 ml) and the mixture heated for 6 hr on a steam bath. On cooling, the soln was poured into iced water (100 ml) and extracted with EtOAc. The organic layer was washed with brine to neutrality, dried and evaporated. The resulting dark oil, after separation on TLC afforded **2** (6 mg; 5%) identified by m.p., m.m.p., IR, NMR and TLC; nieshoutol (22 mg; 22%); the hydroxyacetate **16** (24 mg; 22%), m.p. 176–178·5°, as pale yellow needles, from ether. (Found: C, 62·65; H, 5·2. $C_{16}H_{16}O_6$ requires: C, 63·1; H, 5·3%), $\gamma_{max}^{CHCl_3}$ 3550, 1775–1770, 1730–1720, 1625 and 1580 cm$^{-1}$; $\gamma_{max}^{CCl_4}$ 3570, ~3310, 1786 and 1740 cm$^{-1}$ (ε 130, 40, 245 and 1060); $\lambda_{max}$ 226, 252, 260 and 335 nm (log ε 4·03, 3·67, 3·70 and 3·95) which on methylation (MeI, $K_2CO_3$, acetone) gave nieshoutol acetate (86%), m.p. 126–128°; and **17** (38 mg; 40%) as a pale yellow solid, m.p. 121–126°, from ether–light petroleum, $\gamma_{max}^{CHCl_3}$ 3540, 1730–1720, 1630 and 1585 cm$^{-1}$; mass spectral peaks at *m/e* 262 ($M^+$), 247, 234, 229 and 219 (relative abundance 92, 98, 74, 57 and 100%). After treatment of **17** in MeOH with excess ethereal diazomethane for 18 hr, removal of solvent gave an oil which after purification afforded a dimethyl ether (89%) whose physical properties were identical to those of **3**.

(ii) *Nieshoutol acetate.* Nieshoutol acetate (230 mg) was dissolved in HBr–HOAc (40% w/v; 20 ml) and the soln heated on a steam bath for 3 hr. Using the same work up procedure, the reaction yielded nieshoutol acetate (30 mg; 13%), nieshoutol (29 mg; 15%), the hydroxyacetate **16** (81 mg; 37%) and **17** (39 mg; 20%).

### *Reaction of the hydroxyacetate* (**16**) *with brosyl chloride*

*p*-Bromobenzenesulphonyl chloride (100 mg) was added to the hydroxyacetate (40 mg) in pyridine (2 ml) and the soln stirred at 85° for 18 hr. Work-up followed by preparative TLC gave the *acetoxybrosylate* **18** (28 mg; 41%) as colourless plates, m.p. 209–211·5°, from $CHCl_3$–MeOH. (Found: C, 50·35; H, 3·60. $C_{22}H_{19}O_8S$ Br requires: C, 50·5; H, 3·65%); $\gamma_{max}^{CHCl_3}$ 1785, 1740, 1627 and 1580 cm$^{-1}$ and the *hydroxybrosylate* **19** (22 mg; 35%) as pale yellow plates, m.p. 209° (dec) from $CHCl_3$–$CCl_4$; $\gamma_{max}^{CHCl_3}$ 3555, 1730, 1625 and 1585 cm$^{-1}$; mass spectral peaks at *m/e* 482 and 480 (both $M^+$). The latter compound (20 mg) was also obtained by dissolving **18** (25 mg) in conc $H_2SO_4$ (1 ml) at 0° then immediately adding iced water (25 ml) followed by extraction into EtOAc.

*Methylation.* MeI (0·2 ml) and $K_2CO_3$ (50 mg) were added to a soln of **19** (50 mg) in acetone (10 ml) and the mixture refluxed with stirring for 18 hr. Work-up gave an oil which was resolved by TLC [ether–light petroleum (2:3)] into the *methoxybrosylate* (**21**), pale yellow plates (38 mg; 73%), m.p. 103–104°, from $CHCl_3$–light petroleum. (Found: C, 50·85; H, 3·95. $C_{21}H_{19}O_7S$ Br requires: C, 50·9; H, 3·9%) and **4** (3 mg; 6%), m.p. 175–176°, identified by m.p., m.m.p., IR and TLC.

*Brosylate interconversion.* An attempted sublimation of **19** (20 mg) at 190°/0·05 mm gave a yellowish oil which was shown to be a mixture of **19** and **20** by analytical TLC. Treatment of the crude oil in MeOH (1 ml) with excess ethereal diazomethane for 5 hr gave a mixture which was resolved by TLC into the isomeric **21** (8 mg; 40%) and **4** (6 mg; 30%).

*Benzophenone ketal of 5-demethylnieshoutol* (**17**). Dichlorodiphenylmethane (200 mg) was added to a soln of **17** (81 mg) in pyridine (1 ml) and the mixture kept for 15 hr. Work-up gave a solid which was separated by TLC [EtOAc–light petroleum (1:3)] into benzophenone and the *ketal* **22** as a colourless oil which after distillation at 170°/0·05 mm solidified to crystals, m.p. 194–195° (76 mg; 58%). (Found: C, 76·0; H, 5·1.

$C_{27}H_{22}O_5$ requires: C, 76·05; H, 5·2%), mass spectral peaks at *m/e* 427, 426 ($M^+$), 412, 411, 165 and 105 (relative abundance 23, 81, 27, 95, 53 and 100%).

*Nuclear Overhauser effect.* Measurements were made using a degassed soln of nieshoutol (40 mg) in $CDCl_3$ (~0·4 ml). Integrations were recorded at a sweep rate of 1 Hz sec.

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