Phytochemistry, 1974, Vol. 13, pp. 623 to 625. Pergamon Press. Printed in England.

XANTHOXYLONE: A NEW TRITERPENOID KETONE FROM *XANTHOXYLUM RHETSA*

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Key Word Index—*Xanthoxylum rhetsa*; Rutaceae; pentacyclic triterpenoid ketone; xanthoxylone; structure and stereochemistry.

Abstract—Xanthoxylone, a new pentacyclic triterpenoid ketone has been isolated from a rutaceous plant, *Xanthoxylum rhetsa.* From spectral properties and conversion experiments the structure and stereochemistry of the terpenoid have been deduced as **1**.

INTRODUCTION

OCCURRENCE of triterpenoids and tetranortriterpenoids from degraded euphol series in the Rutaceae is well documented.[1-3] During an investigation of alkaloids in *Xanthoxylum* species which are known to produce a number of alkamides, aporphine alkaloids and alkaloids of indoloquinazolone series,[4] a new pentacyclic triterpene, xanthoxylone has been isolated from *X. rhetsa.* Structure and stereochemistry of the terpenoid has been settled and it is shown to be 7-keto-β-amyrene (**1**).

RESULTS AND DISCUSSION

Xanthoxylone (**1**), $C_{30}H_{48}O$ (M^+ 424·3721), m.p. 230° isolated from the petrol extract of the plant was purified by silica gel chromatography. It responded to the Liebermann–Burchardt but not to the Zimmerman test. However, it gave a pale yellow colour with tetranitromethane indicating the presence of unsaturation. The trisubstituted nature of the double bond was apparent from its IR spectrum (825 cm^{-1}) and also from one proton multiplet at δ 5·55 in the 60 MHz NMR spectrum of xanthoxylone. The NMR spectrum also showed the presence of 8 tertiary methyls (δ 0·82–1·12) and a two proton signal at δ 2·45 assigned to the methylene protons attached to a carbonyl function. The occurrence of a carbonyl function as a 6-membered ring ketone was evident from the IR spectrum (1720 cm^{-1}). These spectral measurements in conjunction with the MS of the compound suggest that the latter is a triterpenoid ketone of the oleanene or ursene series.[5]

(**1**) was not amenable to reduction with $NaBH_4$ under mild conditions but when refluxed with this reagent for 36 hr, it gave the β-equatorial alcohol (**2**), m.p. 252–254° (no carbonyl

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[1] HALSALL, T. G. and APLIN, R. T. (1964) *Progress in the Chemistry of Organic Natural Products* (ZECHMEISTER, L., ed.), Vol. 22, p. 153, Springer, New York.

[2] KULSHRESHTHA, M. J., KULSHRESHTHA, D. K. and RASTOGI, R. P. (1972) *Phytochemistry* **11**, 2369.

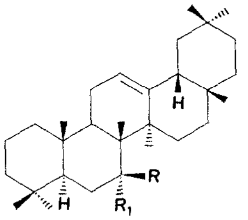
[3] DREYER, D. L. (1968) *Progress in the Chemistry of Organic Natural Products* (ZECHMEISTER, L., ed.), Vol. 26, p. 190, Springer, New York.

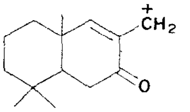
[4] CHATTERJEE, A., BOSE S. and GHOSH, C. (1959) *Tetrahedron* **7**, 257.

[5] BUDZIKIEWICZ, H., WILSON, J. M. and DJERASSI, C. (1963) *J. Am. Chem. Soc.* **85**, 3689.

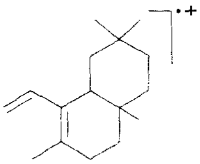
peak at 1720 cm^{-1}) [Acetate (**3**), m.p. 281–283°, ν_{max} 1730 cm^{-1}]. The ketone appears to be sterically hindered.

The β-amyrene skeleton for xanthoxylone was established as follows. The NaBH$_4$ reduction product (**2**) was dehydrated to a diene (**4**). The latter upon catalytic hydrogenation yielded a hydrocarbon, m.p. 159° identical (m.m.p. and co-TLC) with β-amyrene (**5**),[6] prepared from authentic β-amyrin by standard procedures.





m/e 205



m/e 218

(**1**) R, R$_1$ = O; (**2**) R = OH, R$_1$ = H; (**3**) R = OCOMe, R$_1$ = H;
(**4**) 6,7-Dehydro-**5**; (**5**) R = R$_1$ = H.

Only the position of the carbonyl group in the β-amyrene (**5**) skeleton remains to be located. The strong peak at *m/e* 205 in the MS indicates that the keto function could be at either C-1, C-2, C-3, C-6 or C-7. Its location at C-1 was excluded from the NMR spectrum, by the absence[7] of any downfield C-10 methyl proton singlet (around δ 1·30) and also by the lack of peaks at *m/e* 139 and 257 in the MS. The ion fragments corresponding to the above peaks would be expected to be formed as a result of McLafferty rearrangement of C-1 ketone and C-11 hydrogens and subsequent fission.[8] The keto group cannot be placed at C-2 since then two sets of doublets for two protons each ($-C\underline{H}_2COC\underline{H}_2-$) would be expected in the NMR spectrum. The occurrence of carbonyl at C-3 is ruled out because it would lead to a known compound, β-amyrenone,[6] which is different from (**1**). The placement of the oxofunction at C-6 was excluded from the NMR spectrum by the appearance of a two proton multiplet at δ 2·45 and the absence of one proton singlet for the methine proton at C-5. Furthermore, the carbonyl function at C-6 would not affect[5] the principal fragmentation process (i.e. Retro-Diels-Alder cleavage of ring C) which would generate the base peak at *m/e* 218 (species, *b*). Thus the carbonyl group must be at C-7, leading to structure (**1**) for xanthoxylone. This structure is consistent with the mass fragmentation pattern which besides showing the molecular ion peak at *m/e* 424·3721, showed other significant peaks at *m/e* 205·1937 (base peak), 217·1948, 218·2022 and 285·2203. In particular, the fragment *a* at *m/e* 205·1937 is derivable from McLafferty rearrangement of C-7-ketone and C-15 hydrogen and subsequent fission across 9, 11 bond with concommitant loss of two hydrogens.

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[6] *Elsevier's Encyclopaedia of Organic Chemistry*, Vol. 14, p. 526; Vol. 14, Supplement p. 939S, (1940, 1952) Elsevier, New York.

[7] LAVIE, D., GLOTTER, E. and SHVO, Y. (1965) *J. Org. Chem.* **30**, 1774.

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EXPERIMENTAL

M.ps were determined on electrically heated Toshniwal apparatus and are uncorrected. UV spectra were measured in 95% EtOH (aldehyde free), IR spectra were taken on a KBr disc unless otherwise stated. The analytical samples were dried at 80° over P_2O_5 for 24 hr *in vacuo*. Anhyd. Na_2SO_4 was used for drying and silica gel for column chromatography.

Isolation of xanthoxylone. Zanthoxylum rhetsa (bark, 850 g) was soxhletted with petrol. for 24 hr. The concentrated petrol. extract (20 g) was chromatographed over silica gel (360 g). Elution of the column with petrol.–C_6H_6 (3:1) afforded xanthoxylone (**1**), yield 0·004%. It was crystallized from petrol.–C_6H_6 (6:1), m.p. 230° (Found: C, 84·1; H, 10·98; O, 3·7. Calc. for $C_{30}H_{48}O$: C, 84·9; H, 11·32; O, 3·77%).

Reduction of xanthoxylone with sodium borohydride. To a soln of xanthoxylone (45 mg) in MeOH, $NaBH_4$ (100 mg) was added and the mixture was refluxed for 36 hr. MeOH was removed, the resulting mass was decomposed with H_2O, extracted with $CHCl_3$ and dried. Removal of the solvent gave the alcohol (**2**) (30 mg) which crystallized from C_6H_6, m.p. 252–254° (Found: C, 83·95; H, 11·43; O, 3·68. Calc. for $C_{30}H_{50}O$: C, 84·50; H, 11·73; O, 3·75%). The acetate of **2** had m.p. 281–283° (Found: C, 81·68; H, 11·0; O, 6·38. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·1; O, 6·62%).

Dehydration of the alcohol with potassium bisulphate. Alcohol (**2**) (18 mg) was mixed with anhyd. $KHSO_4$ (54 mg), the mixture was fused and sublimed under reduced pressure. A small amount of an oily product was obtained at 245° at 2 mm. pressure. It was then extracted with $CHCl_3$. The $CHCl_3$ extract upon removal of the solvent gave the homogeneous diene which resisted all attempts at crystallization.

Catalytic hydrogenation of the diene. To a soln of the diene (12 mg) in spectral EtOH (40 ml) PtO_2 (10 mg) was added and H_2 gas was passed for 4 hr. PtO_2 was filtered off and removal of alcohol under reduced pressure furnished the hydrocarbon (β-amyrene), m.p. 159° (lit.[6] m.p. 162–163°) (Found: C, 87·0; H, 11·98. Calc. for $C_{30}H_{50}$: C, 87·8; H, 12·19%).

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