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NITRATION OF DEHYDROABIETIC ACID DERIVATIVES[1)]

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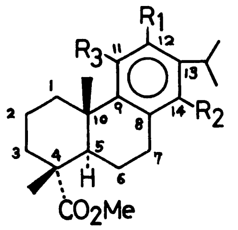
Nitration of various dehydroabietic acid derivatives was examined and it was found that nitration was affected by the structure. An interesting substitution occurred at 11,13 (deisopropylation) and 14 positions.

The nitration of dehydroabietic acid derivatives has been studied by many groups for the introduction of a substituent into their aromatic C-ring. However, some important problems still remain unsolved.

Recently, an interesting reaction was found in that the nitration of 7-oxo ester (II) gave 13-nitro-deisopropyl (III) and 14-nitro esters[3)] (IV). By extending the above study, nitration of various dehydroabietic acid derivatives was examined.

First, the influence of 12- and 14-substituents of 7-oxo ester (II) was examined. Nitration[4)] of 12-nitro-[5)] (V) and 14-nitro-7-oxo esters[9)] (IV) did not proceed but other 12-substituted 7-oxo esters[5)] (12-hydroxy (VI) and 12-bromo compound (VII)) were smoothly nitrated to give not the expected 11-nitro compounds but exclusively the corresponding 13-nitro-deisopropyl esters, (VIII), mp 151~152°, δ 7.12(s; 11-H), 8.78(s; 14-H), and (IX), mp 154~156°, δ 7.78(s; 11-H), 8.43(s; 14-H). 14-Hydroxy-7-oxo ester[5)] (X) was nitrated to give two kinds of product, 13-nitro-[10)] (XI), mp 151~153°, δ 6.96, 8.16(each d, J=8 Hz; 11- and 12-H), and 11,13-dinitro-7-oxo esters[10)] (XII), mp 168~169°, δ 1.36(s; 4-Me), 1.62(s; 10-Me), 8.22(s; 12-H), with deisopropylation. Furthermore, nitration of Δ^5-7-oxo ester[11)] (XVI) was different from that of 7-oxo ester (II) and gave mainly 14-nitro ester[10)] (XVII), mp 198~200°, δ 6.11(s; 6-H), 7.64(s; 11- and 12-H). These results are interes-



I $R_1=R_2=R_3=H$

Methyl Dehydroabietate

XIII $R_1=NO_2$, $R_2=R_3=H$

XIV $R_1=Br$, $R_2=R_3=H$

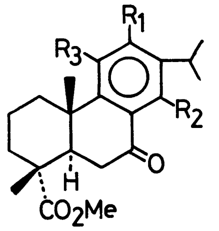
XV $R_1=OAc$, $R_2=R_3=H$

XVIII $R_1=OH$, $R_2=R_3=H$

XX $R_1=Br$, $R_2=NO_2$, $R_3=H$

XXI $R_1=OH$, $R_2=H$, $R_3=NO_2$

XXIII $R_1=OMe$, $R_2=H$, $R_3=NO_2$



II $R_1=R_2=R_3=H$

IV $R_1=R_3=H$, $R_2=NO_2$

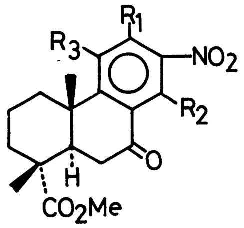
V $R_1=NO_2$, $R_2=R_3=H$

VI $R_1=OH$, $R_2=R_3=H$

VII $R_1=Br$, $R_2=R_3=H$

X $R_1=R_3=H$, $R_2=OH$

XXII $R_1=OMe$, $R_2=H$, $R_3=NO_2$



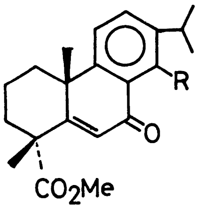
III $R_1=R_2=R_3=H$

VIII $R_1=OH$, $R_2=R_3=H$

IX $R_1=Br$, $R_2=R_3=H$

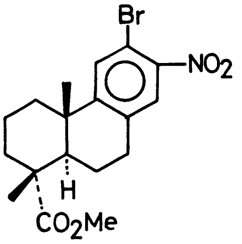
XI $R_1=R_3=H$, $R_2=OH$

XII $R_1=H$, $R_2=OH$, $R_3=NO_2$

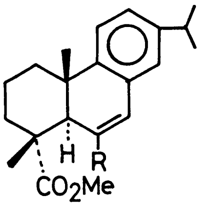


XVI R=H

XVII $R=NO_2$

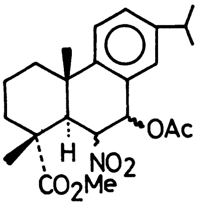


XIX



XXIV R=H

XXVI $R=NO_2$



XXV

ting in contrast to the nitration of 12,14-unsubstituted ester (II→III + IV).

The location of the substituents in the nitration products was clearly elucidated by nmr analysis of the coupling pattern between 14-proton appearing in a lower magnetic field (an effect of 7-oxo group) and other aromatic protons.

The interesting result found from the nitration of 7-oxo derivatives aroused our interest on how a substituent in the C-ring of 7-deoxo compound affected the nitration. With the use of 12-bromo[7] (XIV) and 12-hydroxy esters[8] (XVIII) for the nitration, the behavior of the two esters (XIV and XVIII) to nitration was found to be markedly different. In the same way as in 7-oxo ester series, 12-bromo ester (XIV) was nitrated to give 13-nitro-deisopropyl ester (XIX), mp 131.5~132°, δ 7.58, 7.59(each s, 11- and 14-H), and 14-nitro ester[10] (XX), mp 164.5~167°, δ 1.21, 1.26

(each s; 10- and 4-Me), 7.54(s; 11-H). On the contrary, the nitration of 12-hydroxy ester (XVIII) gave a complex mixture and, therefore, the condition was changed to milder one (c.HNO_3(d=1.38)-Ac_2O). The resulting product was only 11-nitro compound (XXI), mp 167.5~170.5°, δ 1.27(s; 4-Me), 1.48(s; 10-Me), 6.97(s; 14-H), which was different type of series from the usual 13-nitro-deisopropyl products. For the structural determination, these products (XIX and XXI) were converted to the corresponding 7-oxo esters (IX and XXII, mp 132~134°, δ 8.18(s; 14-H), via XXIII, mp 148~149°, δ 7.01(s; 14-H)) and their nmr spectra with respect to aromatic protons were analyzed.

Finally, the influence of 6(7)-double bond on the nitration was examined. Δ^6-Ester$^{12)}$(XXIV) was nitrated as usual and gave an inseparable mixture. However, a mild nitration (c.HNO_3(d=1.38)-Ac_2O) of XXIV gave mainly an addition product of the double bond (XXV), mp 140~141°, δ 2.06(s; 7-OCOMe), 2.90(d, J=12 Hz; 5-H), 5.05 (dd, J=6, 12 Hz; 6-H), 6.55(d, J=6 Hz; 7-H). By treatment on alumina, the ester (XXV) easily gave Δ^6-6-nitro ester (XXVI), bp 150°(bath temp.)/0.001 mm Hg, δ 3.80 (d, J=3 Hz; 5-H), 7.62(d, J=3 Hz; 7-H), with the elimination of acetic acid.

In conclusion, it is possible to effect optional nitration at 11,13 (with deisopropylation) and 14 positions of dehydroabietic acid derivatives by the reaction reported herein. Application of this reaction and detailed examination of this nitration are in progress in this laboratory.

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References

1) New compounds indicated melting points or boiling points gave satisfactorily analytical values. All melting points were measured on a micro-hot stage and are uncorrected. Nmr spectra were measured at 100 MHz in $CDCl_3$ (5~10% solution) vs. Me_4Si as internal reference.

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4) With the exception of the nitration condition shown in parentheses, fuming HNO_3(d=1.47)-c.H_2SO_4 (20:1) (30 min, in ice-salt bath) was used as the reagent.

5) Methyl 12- or 14-substituted 7-oxo-dehydroabietates used for the nitration were

prepared as follows: 12-Nitro- (V), mp 137.5~139.5°, and 12-bromo-7-oxo esters (VII), mp 118.5~121°, were obtained by oxidation of XIII6) and XIV7), respectively. 12-Hydroxy-7-oxo ester (VI), mp 262~263.5°, was obtained from XV8) by oxidation and successive hydrolysis, and 14-hydroxy-7-oxo ester (X), mp 68~70°, from IV9) via the corresponding amine by the usual treatment.

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10) Proof of their structures by nmr analysis and chemical relation will be described later in our detailed report.

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