[Chem. Pharm. Bull. 22(7)1547—1554(1974)]

UDC 547.597.04 : 542.958.1

Diterpenoids. XXVIII. Nitration of Methyl 7-Oxo-dehydroabietate Derivatives[1]

Akira Tahara, Hiroyuki Akita, and Yasuo Ohtsuka

Rikagaku Kenkyusho (The Institute of Physical and Chemical Research)[2]

(Received December 10, 1973)

The nitration of **11** gave 14-nitro (**12**) and 13-nitro ester (**10**), in *ca.* 1 : 1 ratio. Next, some methyl 7-oxo-derivatives having a substituent in 12 position (**18**, **19**, **21**, and **23**) were smoothly nitrated to give selectively the corresponding 13-nitro-deisopropyl ester, and the nitration of the corresponding 14-substituted ester (**26**) gave a mixture consisting of three compounds. On the contrary, a nitration of **39** gave only 14-nitro product (**40**). Finally, a nitration of **41** gave an addition product (**42**) to the double bond.

For the new utilization of pine rosin, biologically active compounds were synthesized by chemical conversion from *l*-abietic acid (**1**), the main component of rosin. In this project, substitution (nitration in the present case) at the optional position of the aromatic C-ring of dehydroabietic acid derivatives is regarded as one of the important basic problems.

A few studies have been reported on this nitration. These reports showed that methyl dehydroabietate (**2**) and methyl deisopropyl-*allo*-dehydroabietate (**3**) were nitrated to give mixed products (**2**→**4**+**5**;[3] **3**→**6**+**7**+**8**[4]) and the 7-oxo ester (**9**) gave only 13-substituted ester (**10**).[5] However, the selective substitution[3a,6] at 11, 13 (accompanied with deisopropylation), or 14 position of dehydroabietic acid derivatives has not been sufficiently investigated.

For these reasons, nitration of methyl 7-oxo-dehydroabietate (**11**)[7] aroused our interest, because C-11 and C-13 at position *meta* to the polar 7-oxo group are sterically hindered and are substituted by an isopropyl group. The nitration of **11** did not proceed under a mild condition (conc.HNO_3 (d=1.38): Ac_2O=0.03: 1 or conc.HNO_3 (d=1.38): H_2SO_4=20: 1), but gave 14-nitro (**12**) and 13-nitro esters (**10**) in place of the expected 11-nitro ester (**13**), in *ca.* 1: 1 ratio under a drastic condition (fuming HNO_3 (d=1.47): H_2SO_4=20: 1, fuming HNO_3 (d=1.52): H_2SO_4=20: 1, fuming HNO_3 (d=1.52): 70% $HClO_4$aq.=4: 1 and fuming HNO_3 (d=1.52): f.H_2SO_4(60%SO_3)=4: 1). It is notable that the nitration took place preferentially at C-13 (with deisopropylation) and C-14 (position *ortho* to 7-oxo group), in spite of the unoccupied position at C-11 and C-12.

---

1) A part of the work was published as preliminary communication: Y. Ohtsuka, H. Akita, and A. Tahara, *Chem. Pharm. Bull.* (Tokyo), **21**, 2740 (1972); *idem*, *Chemistry Letters*, **1973**, 229. Part XXVII: Y. Ohtsuka and A. Tahara, *Chem. Pharm. Bull.* (Tokyo), **21**, 653 (1973).

All melting points were measured on a micro-hot stage and are uncorrected. NMR spectra were measured (δ) at 100 MHz (*: 60 MHz) in $CDCl_3$ *vs.* Me_4Si as internal reference. IR data (KBr disk) indicated maximum absorption as cm^{-1}. GLC (t_R) was measured under the column condition (2 m×4 mm, 1.5% OV-17 on Shimalite W (80—100 mesh)) and its peak area was calculated by height × width at half height.

2) Location: *Wako-shi*, *Saitama*.

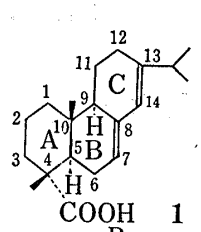
3) *a*) W. Campbell and M. Morgana, *J. Am. Chem. Soc.*, **63**, 1838 (1941); *b*) E. Ochiai and M. Ohta, *Yakugaku Zasshi*, **74**, 203 (1954); *c*) A.S. Levinson, *J. Org. Chem.*, **36**, 3062 (1971).

4) M. Ohta, *Yakugaku Zasshi*, **77**, 924 (1957).

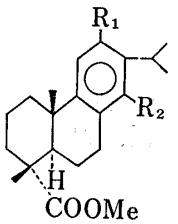
5) *a*) E. Wenkert, R.W.J. Carney, and C. Kaneko, *J. Am. Chem. Soc.*, **83**, 4440 (1961); *b*) A. Tahara and O. Hoshino, *Sci. Papers Inst. Phys. Chem. Res.* (Japan), **56**, 88 (1962).

6) The selective substitutions at 12 position of the series were carried out by a few method. *a*) L.F. Fieser and W.P. Campbell, *J. Am. Chem. Soc.*, **60**, 2631 (1938); *b*) T. Hasselstrom and J.D. McPherson, *ibid.*, **60**, 2340 (1938); *c*) L.F. Fieser and W.P. Campbell, *ibid.*, **61**, 2528 (1939).

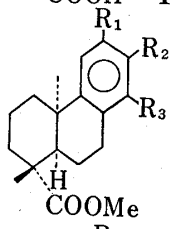
7) E. Wenkert and B.G. Jackson, *J. Am. Chem. Soc.*, **80**, 211 (1958).



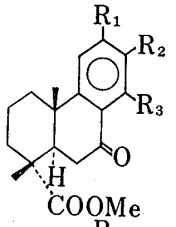
1



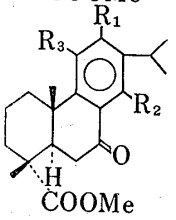
2: $R_1=R_2=H$
4: $R_1=NO_2$, $R_2=H$
5: $R_2=NO_2$, $R_1=H$
14: $R_1=Ac$, $R_2=H$
15: $R_1=R_2=NO_2$
17: $R_1=OAc$, $R_2=H$
20: $R_1=OMe$, $R_2=H$
22: $R_1=Br$, $R_2=H$



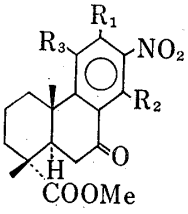
3: $R_1=R_2=R_3=H$
6: $R_1=NO_2$, $R_2=R_3=H$
7: $R_2=NO_2$, $R_1=R_3=H$
8: $R_3=NO_2$, $R_1=R_2=H$



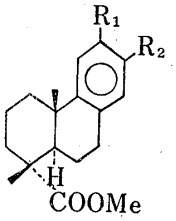
9: $R_1=R_2=R_3=H$
10: $R_2=NO_2$, $R_1=R_3=H$
30: $R_1=OAc$, $R_2=R_3=H$
34: $R_2=NH_2$, $R_1=R_3=H$
38: $R_3=OH$, $R_1=R_2=H$



11: $R_1=R_2=R_3=H$
12: $R_2=NO_2$, $R_1=R_3=H$
13: $R_3=NO_2$, $R_1=R_2=H$
18: $R_1=OH$, $R_2=R_3=H$
19: $R_1=OAc$, $R_2=R_3=H$
21: $R_1=OMe$, $R_2=R_3=H$
23: $R_1=Br$, $R_2=R_3=H$
24: $R_1=NO_2$, $R_2=R_3=H$
25: $R_2=NH_2$, $R_1=R_3=H$
26: $R_2=OH$, $R_1=R_3=H$
35: $R_2=OH$, $R_3=NO_2$, $R_1=H$



27: $R_1=OH$, $R_2=R_3=H$
28: $R_1=OMe$, $R_2=R_3=H$
29: $R_1=Br$, $R_2=R_3=H$
36: $R_2=OH$, $R_1=R_3=H$
37: $R_2=OH$, $R_3=NO_2$, $R_1=H$



16: $R_1=Ac$, $R_2=NO_2$
31: $R_1=R_2=H$
32: $R_1=Ac$, $R_2=H$
33: $R_1=OAc$, $R_2=H$

Chart 1

As an analogous nitro-dealkylation, the nitration (nitro-dealkylation and nitro-deacylation) in polyalkylacyl-benzene series was reviewed.[8] In the resin acid, Cambie's group recently found that the nitration of 12-acetyl ester (**14**) yielded 12,14-dinitro ester (**15**) (nitro-deacylation) and 12-acetyl-13-nitro ester (**16**) (nitro-dealkylation).[9] However, our case is different from the above example in the relative position of the isopropyl and carbonyl group (*meta* in ours (**11**) and *ortho* in Cambie's compound (**14**)).

In order to examine the effect of substituent on this nitration, some methyl 7-oxo-dehydroabietates having a substituent in 12 or 14 position were selected and 12-hydroxy (**18**←**17**),[9b] 12-acetoxy (**19**←**17**),[9b] 12-methoxy (**21**←**20**),[9b] 12-bromo (**23**←**22**),[3b] 12-nitro (**24**←**4**),[3]

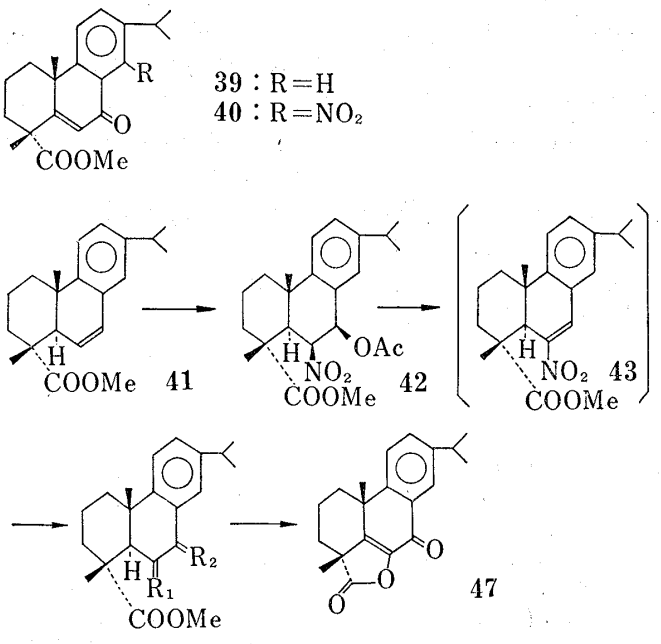
8) *a*) D.V. Nightingale, *Chem. Rev.*, **40**, 117 (1947); *b*) R.O.C. Norman and R. Taylo, "Electrophilic Substitution in Benzenoid Compounds," Elsevier Publishing Company, 1965, p. 258, 260.
9) *a*) R.C. Cambie and R.A. Franich, *Chem. Commun.*, **1970**, 845; *b*) *Idem*, *Aust. J. Chem.*, **24**, 117 (1971).

14-hydroxy (**26**←**25**←**12**)[1] and 14-nitro-7-oxo ester (**12**)[1] were synthesized by the usual method.

12-Substituted 7-oxo esters (**18**, **19**, **21** and **23**) were smoothly nitrated (fuming HNO_3 (d=1.47)–conc.H_2SO_4) to give exclusively the corresponding 13-nitro-deisopropyl esters (**18** and **19**→**27**; **21**→**28**; **23**→**29**). The substituted site was confirmed by the analysis of aromatic region of their nuclear magnetic resonance (NMR) spectra and by the following chemical conversion. The NMR spectra of the nitration products (**27**: 7.12 (s; 11-H), 8.78 (s; 14-H),[10] **28**: 7.02 (s; 11-H), 8.46 (s; 14-H),[10] **29**: 7.78 (s; 11-H), 8.43 (s; 14-H)[10]) clearly show that these substituents occupy the 12 and 13 positions and 13-isopropyl group has disappeared. This observation is also supported by the chemical interrelation. 12-Hydroxy-13-nitro-7-oxo ester (**27**) is converted into the corresponding methoxyl compound (**28**) and can also be obtained by nitration of 12-acetoxy-7-oxo ester (**30**) synthesized from **31**[11] *via* **32** and **33**. Reduction of 12-bromo-13-nitro-7-oxo ester (**29**) and 13-nitro-7-oxo ester (**10**)[5] gave the same amine (**34**).

Table I

Nitric acid (density)	Conc. HNO_3 (d=1.38)	Fuming HNO_3 (d=1.45)	Fuming HNO_3 (d=1.47)	Fuming HNO_3 (d=1.52)
Starting-material (**26**)	quantitative			
11-Nitro ester (**35**)		36%	19%	
13-Nitro ester (**36**)		13%	24%	
11,13-Dinitro ester (**37**)			21%	69%



44: R_1=NOH, R_2=H_2
45: R_1=H_2, R_2=NOH
46: R_1=NOH, R_2=O

Chart 2

In contrast, nitration (fuming HNO_3 (d=1.47)–conc.H_2SO_4) of 14-hydroxy-7-oxo ester (**26**) did not proceed selectively, but gave a mixture consisting of three products; 11-nitro (**35**: 1.33 (4-Me), 1.56 (10-Me), 7.34 (s; 12-H)),* 13-nitro (**36**: 1.29, 1.36 (4- and 10-Me), 6.96, 8.16 (d, 1H each, J=8 Hz; 11- and 12-H)) and 11,13-dinitro ester (**37**: 1.36 (4-Me), 1.62 (10-Me), 8.22 (s; 12-H)). The dinitro compound (**37**) was also obtained as a sole product from **38**[12] and **36** under more drastic condition (fuming HNO_3 (d=1.52)–conc.H_2SO_4). The structures of these products (**35**, **36** and **37**) are indicated by the chemical shift of 10-Me and the NMR pattern of aromatic protons. The 10-Me chemical shifts of **35** and **37** appeared in a lower field by the effect of their 11-nitro group. The ratio of the

10) The chemical shift due to 14-H appeared in a lower magnetic field than that of other aromatic protons by the effect of 7-oxo group.
11) M. Ohta and L. Ohmori, *Chem. Pharm. Bull.* (Tokyo), **5**, 91 (1957).
12) It is unpublished datum that the 14-hydroxy ester (**38**) is synthesized by deisopropylation of **26**.

products depends on the concentration of nitric acid. The milder nitration (conc.HNO_3 (d=1.38)–conc.H_2SO_4) did not proceed, but other nitrations ((i) fuming HNO_3 (d=1.45)– and (ii) fuming HNO_3 (d=1.52)–conc.H_2SO_4) gave mononitro esters (**35** and **36**) and dinitro ester (**37**), respectively (Table I).

With respect to the nitro group having a counter-electronic effect to hydroxyl and halogen groups, 12- (**24**) and 14-nitro ester (**12**) were not nitrated to give only the starting material.

Nitration (fuming HNO_3 (d=1.47)–conc.H_2SO_4) of Δ^5-7-oxo ester (**39**)[5a] gave quite a different result from that of 7-oxo esters described above. 14-Nitro ester (**40**) was the only product and its structure was confirmed from the NMR spectrum of its product (**40**) in which the signal for 14-H in a lower field (**39**: 8.00 (br s, 1H))* had disappeared and pattern due to 11- and 12-H (7.63 (s; 2H)) was still observed (*cf.* **39**: 7.43 (br s, 2H; 11-H, 12-H)).* Also, 14-nitro ester (**12**) having the known structure was converted to **40**.

Finally, the effect of 6,7-double bond in place of 7-oxo group on the nitration was examined. The usual nitration (fuming HNO_3 (d=1.47)–conc.H_2SO_4) of **41**[13] gave only an inseparable mixture. While a milder nitration (conc.HNO_3 (d=1.38)–Ac_2O) did not give a substitution product of the aromatic C-ring, but gave an addition product to the double bond. NMR spectrum of the product (**42**: 2.90 (d, 1H, J=12 Hz; 5α-H), 5.05 (dd, 1H, J=6, 12 Hz; 6α-H), 6.55 (d, 1H, J=6 Hz; 7α-H), 7.06—7.12 (m, 3H; arom.H)) supports this structure. The configuration between 6-nitro and 7-acetoxyl groups is assumed to be *β-cis* in the boat form of B-ring by their coupling constants ($J_{5,6}$=12 Hz, $J_{6,7}$=6 Hz)[14] and lower shift (1.51) due to one of the methyl groups (effect of spatial neighboring nitro group). Easy *trans*-elimination between 7-acetoxy and 6-hydrogen of **42** gave Δ^6-6-nitro ester (**43**), which having a 6-substituent in *trans*-A/B ring fusion, is expected firstly to be important for many synthetic projects, but could not be derived to the anticipated useful compound as follow. Catalytic hydrogenation of **43** gave an oxime (**44**), whose physical constant (mp 162—163°, NMR: 3.20 (s; 5-H), 3.86 (s; 7-H)) was completely different from that (mp 72—73°) of the 7-oxime (**45**).[15] Accordingly, the position of nitro and acetoxyl groups in the original ester (**42**) was confirmed. As hydrolysis of the oxime (**44**) did not progress to the expected course, its oxidative cleavage was carried out to give only the 7-oxo compound (**46**) and subsequently was converted to the known lactone (**47**).[5a,16]

The nitration (with deisopropylation) of 7-oxo ester (**11**) to give 13-(**10**) and 14-nitro product (**12**) gave a clue for the opening of this study. In the examination of substituent effect on the nitration, exclusive syntheses of 13- or 14-nitro derivatives were found out. These products are considered to be useful intermediates for our project in future.

Experimental

Nitration of Methyl 7-Oxo-dehydroabietate (11) to Methyl 14-Nitro-7-oxo-dehydroabietate (12) and Methyl 13-Nitro-7-oxo-dehydrodeisopropylabietate (10)——7-Oxo ester (**11**)[7] (500 mg) was added to a solution of f.HNO_3 (d=1.47) (2.5 ml)–conc.H_2SO_4 (0.25 ml) under ice–salt cooling. After the reaction mixture was stirred for 30 min, ice water was added and it was extracted with ether. The extract was washed with sat. Na_2CO_3 aq. and sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave colorless crystals, whose GLC (260°) showed it consisted of two components (**12**, t_R=5.5 min and **10**, t_R=3.95 min in a ratio of 48: 52). They are chromatographed on neut. Al_2O_3 (50 g) to separate two crystalline fractions: (i) (80 mg) in benzene elution and (ii) (425 mg) in benzene–$CHCl_3$ elution. Each of the fractions was recrystallized twice

13) G. Dupont, R. Dulon, G. Ourisson, and C. Thiabault, *Bull. Soc. Chim. France*, **1955**, 708.
14) Dihedral angles ($\phi_{5,6}$=10°, $\phi_{6,7}$=40—45°) were measured from the Dreiding model (*β-cis*, 6-NO_2/7-OAc and boat B-ring) of **42**. The calculated coupling constants $J_{5,6}$(Calcd.)=12 Hz, $J_{6,7}$(Calcd.)=7.27—6.20 Hz obtained by substitution of the observed angles to the Karplus equation, closely resemble the observed value $J_{5,6}$(obs.)=12 Hz, $J_{6,7}$(obs.)=6 Hz.
15) M. Ohta, *Yakugaku Zasshi*, **75**, 289 (1955).
16) R.C. Cambie and R.A. Franich, *Aust. J. Chem.*, **24**, 571 (1971).

from MeOH–H_2O to give pale yellow plates (**12**) (35 mg; 6% yield), mp 187—189°,[17] from the former and colorless needles (**10**) (72 mg; 14% yield), mp 155.5—156.5°,[5] from the latter. Both products were identified with the respective authentic samples (mixed mp, infrared (IR), NMR and t_R).

The nitration of **11** only gave the starting material under the mild condition (i) conc.HNO_3 (d=1.38)–Ac_2O (0.03: 1) and (ii) conc.HNO_3 (d=1.38)–conc.H_2SO_4 (20: 1). Using the other condition (i) f.HNO_3 (d=1.52)–conc.H_2SO_4 (20: 1), (ii) f.HNO_3 (d=1.52)–70% $HClO_4$ (4: 1), and (iii) f.HNO_3 (d=1.52)–f.H_2SO_4 (60% SO_3) (4: 1), the same products (**12**) and (**10**) were obtained in about same ratio.

Methyl 12-Hydroxy-7-oxo-dehydroabietate (18) and Methyl 12-Acetoxy-7-oxo-dehydroabietate (19) from 17——12-Acetoxy ester (**17**)[9b] (500 mg) in AcOH (35 ml) was oxidized with CrO_3 (700 mg) in AcOH (14 ml)–H_2O (4 ml) under stirring for 24 hr at room temperature. The solvent was evaporated after MeOH (7 ml) was added, and the resulting residue was extracted with ether. The extract was washed with 5% Na_2CO_3 aq., then sat. NaCl aq., and was dried over Na_2SO_4. Removal of the solvent gave oil (364 mg), which was chromatographed on silica gel to isolate a homogeneous oil (**19**) (301.5 mg; 58% yield), bp 150° (bath temp.)/10^{-3} mmHg, in petr. ether–ether (9: 1) elution. *Anal.* Calcd. for $C_{23}H_{30}O_5$: C, 71.73; H, 7.69. Found: C, 71.84; H, 7.92. IR: 1770, 1730, 1688. NMR: 1.21, 1.23 (d, 3H each J=6 Hz; iso-C_3H_7), 1.28, 1.34 (s, 3H each; 4- and 10-Me), 1.76 (s, 3H; 12-OAc), 3.66 (s, 3H; 4-COOMe), 7.00 (s, 1H; 11-H), 8.00 (s, 1H; 14-H).

Unpurified ester (**19**) (1.36 g) was chromatographed on deactivated Al_2O_3 (neut. Al_2O_3 (100 g) and H_2O (1 ml)) to isolate crystals (852 mg) in MeOH elution. They were recrystallized from MeOH to give pale yellow prisms (**18**) (635 mg; 44% yield) mp 262—263.5°.[18] *Anal.* Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.30; H, 8.19. IR: 3160, 1738, 1655. NMR (CF_3COOH): 1.30 (d, 6H; J=7 Hz; iso-C_3H_7), 1.35, 1.48 (s, 3H each; 4- and 10-Me), 3.86 (s, 3H; 4-COOMe), 7.02 (s, 1H; 11-H), 8.15 (s, 1H; 14-H).

Methyl 12-Methoxy-7-oxo-dehydroabietate (21) from 20——12-Methoxy ester (**20**) (1.01 g)[9b] was oxidized as in the case of **17**. Crystals (664 mg) purified by chromatography, were recrystallized from petr. ether–ether to give colorless prisms (**21**) (565 mg; 54% yield), mp 100.5—101.5°. *Anal.* Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.70; H ,8.39. IR: 1728, 1668. NMR: 1.20, 1.22 (d, 3H each, J=7 Hz; iso-C_3H_7), 1.28, 1.34 (s, 3H each; 4- and 10-Me), 3.65 (s, 3H; 4-COOMe), 3.90 (s, 3H; 12-OMe), 6.76 (s, 1H; 11-H), 7.90 (s, 1H; 14-H).

Methyl 12-Bromo-7-oxo-dehydroabietate (23) from 22——12-Bromo ester (**22**) (2.37 g)[3a] was oxidized as in the case of **17**. Crystals (2.08 g) purified by chromatography, were recrystallized from MeOH to give pale yellow needles (**23**) (1.6 g; 65% yield), mp 118—121°.[19] *Anal.* Calcd. for $C_{21}H_{27}O_3Br$: C, 61.91; H, 6.63; Br, 19.66. Found: C, 61.26; H, 6.51; Br, 19.87. IR: 1720, 1688. NMR: 1.24, 1.26 (d, 3H each, J=6 Hz; iso-C_3H_7), 1.28, 1.35 (s, 3H each; 4- and 10-Me), 3.67 (s, 3H; 4-COOMe), 7.55 (s, 1H; 11-H), 7.92 (s, 1H; 14-H).

Methyl 12-Nitro-7-oxo-dehydroabietate (24) from 4——12-Nitro ester (**4**)[3] (1 g) was oxidized as in the case of **17**. Crystals (322 mg) purified by chromatography, were recrystallized from MeOH to give yellow plates (**24**) (240 mg; 23% yield), mp 137.5—139.5°. *Anal.* Calcd. for $C_{21}H_{27}O_5N$: C, 67.54; H, 7.29; N, 3.75. Found: C, 67.26; H, 7.19; N, 3.77. IR: 1740, 1700, 1535. NMR: 1.28, 1.30 (d, 3H each, J=7 Hz; iso-C_3H_7) 1.30, 1.36 (s, 3H each; 4- and 10-Me), 3.67 (s, 3H; 4-COOMe), 7.62 (s, 1H; 11-H), 8.10 (s, 1H; 14-H).

Methyl 14-Hydroxy-7-oxo-dehydroabietate (26) from 12 *via* 25——14-Nitro-7-oxo ester (**12**)[17] (3.6 g) was refluxed in conc.HCl aq. (31.3 ml)–MeOH (39.5 ml) with Sn (7.8 g) for 12 hr. The reaction mixture was extracted with ether after 30% NaOH aq. (81 ml) was added and then, the extract was washed with sat. NaCl aq. and was dried over Na_2SO_4. An oil (3.0 g) resulted by removal of the solvent, was chromatographed on silica gel (150 g) to isolate a homogeneous oil (**25**) (2.54 g; 76% yield) in petr. ether–ether (4: 1) elution. IR (CCl_4): 3520, 3300, 1725, 1640. NMR* (CCl_4): 1.18, 1.27 (s, 3H each; 4- and 10-Me), 1.20 (d, 6H, J=7 Hz; iso-C_3H_7), 3.61 (s, 3H; 4-COOMe), 6.45, 7.10 (d, 1H each, J=8 Hz; 11- and 12-H), 6.85 (br. s, 2H; 14-NH_2).

14-Amino-7-oxo ester (**25**) (2.54 g) was treated in pyridine (42 ml) with $NaNO_2$ (6.3 g)–80% H_3SO_4 aq. (140 ml) under ice-cooling and it was stirred for 60 min. After ice-water (600 ml) and urea (4.2 g)were added, the mixture was stirred for 30 min more, then heated on steam bath for 90 min and was extracted with ether. The extract was washed with 5% Na_2CO_3 aq., sat. NaCl aq. and was dried over Na_2SO_4. An oil resulted by removal of ether, was chromatographed on silica gel (80 g) to isolate a homogeneous oil (1.16 g) in petr. ether–ether (9: 1) elution. The oil was crystallized from MeOH to give pale yellow plates (**26**) (451 mg; 18% yield), mp 68—70°. *Anal.* Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.37; H, 8.29. IR: 1725, 1635. NMR: 1.21, 1.23 (d, 3H each J=7 Hz; iso-C_3H_7), 1.25, 1.34 (s, 3H each; 4- and 10-Me), 3.67 (s, 3H; 4-COOMe), 6.77, 7.37 (d, 1H each, J=8 Hz; 11- and 12-H).

Nitration of Methyl 12-Hydroxy-7-oxo-dehydroabietate (18), Methyl 12-Acetoxy-7-oxo-dehydroabietate

17) W.J. Considine and H.H. Zeiss, *J. Org. Chem.*, **24**, 253 (1959).
18) W.L. Meyer and C.W. Sigel, *Tetrahedron Letters*, **1967**, 2485. The compound (**18**) was already synthesized through the other route, but mp 238—240° reported is different from that of ours.
19) G.A. Tolstikov, M.P. Irismetov, and M.I. Goryaev, *Tr. Inst. Khim. Nauk. Akad. Nauk. Kaz. SSR*, **19**, 72 (1967). Different reagent ($KMnO_4$) was used in the oxidation and mp 128—128.5° of **23** was reported.

(19) and Methyl 12-Acetoxy-7-oxo-dehydrodeisopropylabietate (30) to Methyl 12-Hydroxy-13-nitro-7-oxo-dehydrodeisopropylabietate (27)——(i) 12-Hydroxy ester (**18**) (200 mg) was nitrated with f.HNO_3 (d=1.47) (1.4 ml)–conc.H_2SO_4 (0.07 ml) as in the case of **11**. The ether extract was washed with 5% Na_2CO_3 aq. and the aqueous layer was extracted with $CHCl_3$ after it was acidified. The extract (acidic fraction) was washed with sat. NaCl aq., dried over Na_2SO_4 and removal of the solvent gave an oil (203.5 mg), which consisted of almost one product (t_R=2.8 min). The oil was crystallized from MeOH to give pale yellow needles (**27**) (96.5 mg; 48% yield), mp 151—152°. *Anal.* Calcd. for $C_{18}H_{21}O_6N$: C, 62.24; H, 6.10; N, 4.03. Found: C, 62.22; H, 6.13; N, 4.06. IR: 3280, 1720, 1690, 1578, 1325. NMR: 1.29, 1.35 (s, 3H each; 4- and 10-Me), 3.68 (s, 3H; 4-COOMe), 7.12 (s, 1H; 11-H), 8.78 (s, 1H; 14-H).

(ii) 12-Acetoxy ester (**19**) (309.5 mg) was nitrated as in the case of (i). The resulting crystals (195.5 mg) from acidic part were crystallized from petr. ether–ether to give pale yellow needles (**27**) (134.5 mg; 48% yield), mp 148.5—150° (Identification by mixed mp, IR and NMR).

(iii) 12-Acetoxy ester (**30**) (249 mg) was nitrated as in the case of (i). The resulting crystals (**27**) from acidic part were recrystallized from MeOH to give pale yellow needles (**27**) (20 mg; 8% yield), mp 147—148° (Identification by mixed mp and IR).

12-Acetoxy ester (**30**) was synthesized from methyl dehydrodeisopropylabietate (**31**)[11] *via* **32** and **33** in accordance with the method in the corresponding methyl podocarpate series.[20] Physical data of these compounds[21] were indicated as follows. Methyl 12-acetoxy-7-oxo-dehydrodeisopropylabietate (**30**); IR (CCl_4): 1768, 1728, 1200. NMR*: 1.26, 1.32 (s, 3H each; 4- and 10-Me), 2.30 (s, 3H; 12-OAc), 3.64 (s, 3H; 4-COOMe), 8.10—6.90 (m, 3H; 11, 13 and 14-H). Methyl 12-acetoxy-dehydrodeisopropylabietate (**33**); IR (CCl_4): 1765, 1730, 1205. Methyl 12-acetyl-dehydrodeisopropylabietate (**32**); IR (CCl_4): 1730, 1685. NMR*: 1.18, 1.26 (s, 3H each; 4- and 10-Me), 2.51 (s, 3H; 12-Ac), 3.63 (s, 3H; 4-COOMe), 7.10 (d, 1H, J= 8 Hz; 14-H), 7.67 (dd, 1H, J=8, 2 Hz; 13-H), 7.92 (d, 1H, J=2 Hz; 11-H).

Nitration of Methyl 12-Methoxy-7-oxo-dehydroabietate (21) to Methyl 12-Methoxy-13-nitro-7-oxo-dehydrodeisopropylabietate (28)——12-Methoxy ester (**21**) (302 mg) was nitrated as in the case of **11**. The resulting oil (284 mg) was crystallized from petr. ether–$CHCl_3$ to give colorless needles (**28**) (263.5 mg; 87% yield), mp 189—190°. *Anal.* Calcd. for $C_{19}H_{23}O_6N$: C, 63.14; H, 6.42; N, 3.88. Found: C, 63.15; H, 6.47; N, 4.23. IR: 1722, 1688. NMR: 1.31, 1.36 (s, 3H each; 4- and 10-Me), 3.68 (s, 3H; 4-COOMe), 4.04 (s, 3H; 12-OMe), 7.02 (s, 1H; 11-H), 8.46 (s, 1H; 14-H).

The product (**28**) was also obtained by methylation of 12-hydroxy-13-nitro ester (**27**) with CH_2N_2–ether solution (Identification by mixedmp, IR and t_R).

Nitration of Methyl 12-Bromo-7-oxo-dehydroabietate (23) to Methyl 12-Bromo-13-nitro-7-oxo-dehydrodeisopropylabietate (29)——12-Bromo ester (**23**) (300 mg) was nitrated as in the case of **11**. The resulting oil (327.5 mg) was chromatographed on silica gel (20 g) to isolate crystals in petr. ether–ether (9: 1) elution. The crystals were recrystallized from petr. ether–$CHCl_3$ to give colorless plates (**29**) (235.5 mg; 79% yield), mp 154—156°. *Anal.* Calcd. for $C_{18}H_{20}O_5NBr$: C, 52.68; H, 4.88; N, 3.41; Br, 19.51. Found: C, 52.63; H, 4.88; N, 3.52; Br, 18.98. IR: 1730, 1690. NMR: 1.33, 1.37 (s, 3H each; 4- and 10-Me), 3.70 (s, 3H; 4-COOMe), 7.78 (s, 1H; 11-H), 8.43 (s, 1H; 14-H).

Reduction of Methyl 12-Bromo-13-nitro-7-oxo-dehydrodeisopropylabietate (29) and Methyl 13-Nitro-7-oxo-dehydrodeisopropylabietate (10) to Methyl 13-Amino-7-oxo-dehydrodeisopropylabietate (34)——(i) A solution of 12-bromo-13-nitro ester (**29**) (195 mg) in AcOH (20 ml)–conc.H_2SO_4 (0.2 ml) was shaken with 10% Pd-C (400 mg) under H_2-atmosphere until absorption of H_2 gas (160 ml). After 5% Na_2CO_3 aq. was added into the residue resulted by removal of the solvent, the mixture was extracted with ether. The extract was washed with sat. NaCl aq., dried over Na_2SO_4 and was evaporated to give an oil (139.5 mg), which was repeatedly crystallized from MeOH to give pale yellow needles (**34**) (24 mg), mp 163.5—172.5°. ii) 13-Nitro ester (**10**)[5] (215 mg) in MeOH (50 ml) was hydrogenated (10% Pd–C (200 mg)) as in the case of (i). The residue resulted by removal of the solvent was recrystallized from MeOH to give pale yellow needles (**34**) (54 mg), mp 170—175°. *Anal.* Calcd. for $C_{18}H_{23}O_3N$: C, 71.73; H, 7.69; N, 4.65. Found: C, 71.32; H, 7.81; N, 4.20. IR (CCl_4): 3480, 3400, 1722, 1690. NMR*: 1.22, 1.32 (s, 3H each; 4- and 10-Me), 3.64 (s, 3H; 4-COOMe), 6.72—7.30 (m, 3H; 11, 12 and 14-H).

Both samples in (i) and (ii) were identical (mixed mp and IR).

Nitration of Methyl 14-Hydroxy-7-oxo-dehydroabietate (26)——(i) 14-Hydroxy ester (**26**) (300 mg) was nitrated as in the case of **18**.

a) Acidic Part: After the alkaline extract (5% Na_2CO_3 aq.) was acidified and then was extracted with $CHCl_3$, the organic layer was washed with sat. NaCl aq., dried over Na_2SO_4 and was evaporated. The resulting residue (200 mg) was chromatographed on silicic acid (30 g) to successively separate two oily fractions, (84 mg; 25% yield) and (85 mg; 28% yield) in petr. ether–ether (4: 1) elution. The former was crystallized from $CHCl_3$–petr. ether to give pale yellow needles (**37**) (72 mg; 21% yield), mp 168—169°. *Anal.* Calcd. for $C_{18}H_{20}O_8N_2$: C, 55.10; H, 5.14; N, 7.14. Found: C, 54.93; H, 5.11; N, 6.96. IR: 1725, 1660, 1535, 1525,

20) E. Wenkert and B.G. Jackson, *J. Am. Chem. Soc.*, **80**, 217 (1958).
21) These compounds (**30**), (**33**) and (**32**) were not be purified to samples for the elemental analysis.

1355, 1335. NMR: 1.36 (s, 3H; 4-Me), 1.62 (s, 3H; 10-Me), 3.70 (s, 3H; 4-COOMe), 8.22 (s, 1H; 12-H). The latter was crystallized from ether to give pale yellow prisms (**36**) (72 mg; 24% yield), mp 151—153°. *Anal.* Calcd. for $C_{18}H_{21}O_6N$: C, 62.24; H, 6.10; N, 4.03. Found: C, 62.41; H, 6.21; N, 3.93. IR: 1730, 1638, 1515, 1346. NMR: 1.29, 1.36 (s, 3H each; 4- and 10-Me), 3.70 (s, 3H; 4-COOMe), 6.96, 8.16 (d, 1H each, J=8 Hz; 11- and 12-H).

b) Neutral Part: After the acidic part in aqueous layer was taken off, neutral part obtained from ether extract was chromatographed on Florisil (15 g) to isolate an oil (**35**) (64 mg; 19% yield) in petr. ether–ether (19: 1) elution. GC-MASS. Calcd. for $C_{21}H_{27}O_6N$: 389. Found: 389. IR (CCl_4): 1732, 1660. NMR*: 1.22 (q, 6H, J=6 Hz; iso-C_3H_7), 1.33 (s, 3H; 4-Me), 1.56 (s, 3H; 10-Me), 3.67 (s, 3H; 4-COOMe), 7.34 (s, 1H; 12-H).

(ii) The ester (**26**) (98 mg) was nitrated with conc.HNO_3 (d=1.38) (2.0 ml)–conc.H_2SO_4 (0.1 ml) as in the case of (i). An oil (96 mg) obtained as neutral part was identical with the starting material (**26**).

(iii) The ester (**26**) (300 mg) was nitrated with conc.HNO_3 (d=1.45) (4.0 ml)–conc.H_2SO_4 (0.2 ml) as in the case of (i). 14-Hydroxy-13-nitro ester (**36**) (40 mg; 13% yield) from the acidic part and 14-hydroxy-11-nitro ester (**35**) (122 mg; 36% yield) from the neutral part were resulted.

(iv) The ester (**26**) (220 mg) was nitrated with f.HNO_3 (d=1.52) (2 ml)–conc.H_2SO_4 (0.1 ml) as in the case of (i). 11,13-Dinitro-14-hydroxy ester (**37**) (173 mg; 69% yield) was only obtained from the acidic part.

Methyl 11,13-Dinitro-14-hydroxy-7-oxo-dehydrodeisopropylabietate (37)——(i) From **36**: 14-Hydroxy-13-nitro ester (**36**) (90 mg) was nitrated with f.HNO_3 (d=1.52) (2 ml)–conc.H_2SO_4 (0.1 ml) as in the case of **26**. The product (106 mg) (from the acidic part) was recrystallized from MeOH to give pale yellow needles (**37**) (64 mg; 63% yield), mp 167.5—169° (Identification by mixed mp, IR and t_R).

(ii) From **38**: 14-Hydroxy ester (**38**)[12] (146 mg) was nitrated as in the case of (i) and the product was recrystallized from petr. ether–$CHCl_3$ to give pale yellow needles (**37**) (93 mg; 49% yield), mp 176—179° (Identification by mixed mp and IR).

Nitration of Methyl Δ^5-7-Oxo-dehydroabietate (39) to Methyl Δ^5-14-Nitro-7-oxo-dehydroabietate (40)——Nitration reagent (f.HNO_3 (d=1.47) (0.26 ml)–conc.H_2SO_4 (1.04 ml)) was added to a solution of the ester (**39**)[5a] (330 mg) in conc.H_2SO_4 (1.65 ml). After it was strongly shaken until the unsoluble part was disappeared, the mixture was poured into water and extracted with ether. The extract was treated as in the case of **11**. The resulting crystals (264 mg) were chromatographed on Florisil (30 g) to isolate crystals (135 mg) in petr. ether–ether (1: 2) elution and then were recrystallized from MeOH–H_2O to give colorless needles (**40**) (100 mg; 27% yield), mp 197—198.5°. *Anal.* Calcd. for $C_{21}H_{25}O_2N$: C, 67.90; H, 6.78; N, 3.77. Found: C, 68.10; H, 6.79; N, 3.78. IR: 1729: 1660, 1613, 1540. NMR: 1.20, 1.25 (d, 3H each, J=6.5 Hz; iso-C_3H_7), 1.53, 1.61 (s, 3H each; 4- and 10-Me), 3.70 (s, 3H; 4-COOMe), 6.11 (s, 1H; 6-H), 7.63 (s, 2H; 11- and 12-H).

Methyl Δ^5-14-Nitro-7-oxo-dehydroabietate (40) from 12——14-Nitro ester (**12**)[17] (200 mg) in AcOH (5 ml) was oxidized with SeO_2 (150 mg) under reflux for 1 hr. The mixture was poured into ice water, extracted with ether, and the extract was washed with sat. Na_2CO_3 aq. and then H_2O. After drying over Na_2SO_4, removal of the solvent gave crystals (192 mg), which were chromatographed on Florisil (15 g) to isolate crystals (95 mg) in petr. ether–ether (1: 2) elution and were recrystallized from MeOH–H_2O to give colorless needles (**40**) (89 mg; 45% yield), mp 198—200° (Identification by mixed mp, IR, NMR).

Nitration of Methyl Δ^6-Dehydroabietate (41) to Methyl 7β-Acetoxy-6β-nitro-dehydroabietate (42)——Δ^6-Ester (**41**)[13] (1.11 g) in Ac_2O (11 ml) was slowly nitrated with HNO_3 (d=1.38)–Ac_2O (1: 10) (5.5 ml) under ice-cooling and it was stirring for 1 hr. The mixture was treated as in the case of **11**. The resulting oil (1.4 g) was chromatographed on silica gel (40 g) to isolate an oil (927 mg) in petr. ether–ether (4: 1) elution and then, was crystallized from petr. ether to give colorless prisms (**42**), (554 mg; 37% yield) mp 140—141°. *Anal.* Calcd. for $C_{23}H_{31}O_6N$: C, 66.16; H, 7.48; N, 3.36. Found: C, 65.78; H, 7.45; N, 3.39. IR: 1726, 1741, 1557, 1225. NMR: 1.23 (d, 6H, J=6 Hz; iso-C_3H_7), 1.35 (s, 3H; 10-Me), 1.51 (s, 3H; 4-Me), 2.06 (s, 3H; OAc), 2.90 (d, 1H, J=12 Hz; 5-H), 3.52 (s, 3H; 4-COOMe), 5.05 (dd, 1H, J=6, 12 Hz; 6-H), 6.55 (d, 1H, J=6 Hz; 7-H), 7.06—7.12 (m, 3H; 11, 12 and 14-H).

Methyl 6-Oxo-dehydroabietate Oxime (44) from 42 *via* Methyl Δ^6-6-Nitro-dehydroabietate (43)——A solution of **42** (108 mg) in 1N KOH aq. (20 ml)–MeOH (10 ml) was stirred for 12 hr at room temperature. The solution was diluted with H_2O and was extracted with ether. The extract was washed with sat. NaCl aq., dried over Na_2SO_4 and evaporated to give an oil (**43**)[22] (58 mg). IR (CCl_4): 1730, 1325. NMR: 1.17 (s, 3H; 10-Me), 1.24 (d, 6H, J=6 Hz; iso-C_3H_7), 1.37 (s, 3H; 4-Me), 3.65 (s, 3H; 4-COOMe), 3.80 (d, 1H, J=3 Hz; 5-H), 7.12—7.18 (m, 3H; 11, 12 and 14-H), 7.62 (d, 1H, J=3 Hz; 7-H). A solution of the crude ester (**43**) (7.13 g) in AcOEt (50 ml) was shaken with 10% Pd-C (2 g) under H_2-atmosphere. The filtrate was evaporated and the resulting crystals were recrystallized from petr. benzine to give colorless needles (**44**) (4.56 g; 67% yield), mp 162—163°. *Anal.* Calcd. for $C_{21}H_{29}O_3N$: C, 73.43; H, 8.51; N, 4.08. Found: C, 73.42; H, 8.58; N, 4.29. IR: 3410, 1719. NMR: 1.16 (s, 3H; 10-Me), 1.25 (d, 6H, J=6 Hz; iso-C_3H_7), 1. 56(s, 3H; 4-Me), 3.20 (s, 1H; 5-H), 3.62 (s, 3H; 4-COOMe), 3.86 (s, 3H; 7-H), 7.25—7.03 (m, 3H; 11, 12 and 14-H), 7.64 (s, 1H; 6-NOH, disappeared with D_2O).

22) The compound (**43**) was directly prepared by treatment of the nitration mixture of **41** on alumina.

Methyl 6,7-Dioxo-dehydroabietate 6-Monooxime (46) from 44——Ozone gas passed through a solution of 6-oxime (**44**) (4.560 g) in AcOEt (100 ml) for 90 min under dryice–acetone cooling. The residue resulted by removal of the solvent, was diluted with H_2O and was extracted with ether. The extract was washed with sat. NaCl aq. dried over Na_2SO_4 and was evaporated to give an oil (5.49 g), which was chromatographed on silica gel (60 g) to isolate crystals in petr. ether–ether (9: 1) elution and was crystallized from MeOH–H_2O to give yellow prisms (**46**) (3.49 g; 73% yield), mp 109—110°. *Anal.* Calcd. for $C_{21}H_{27}O_4N$: C, 70.56; H, 7.61; N, 3.92. Found: C, 70.14; H, 7.45; N, 4.00. IR: 3430, 1737, 1638. NMR: 1.25 (s, 3H; 10-Me), 1.28 (d, 6H, J=7 Hz; iso-C_3H_7), 1.60 (s, 3H; 4-Me), 3.66 (s, 3H; 4-COOMe), 3.68 (s, 1H; 5-H), 7.37 (d, 1H, J=9 Hz; 11-H), 7.56 (dd, 1H, J=2, 9 Hz; 12-H), 7.93 (d, 1H, J=2 Hz; 14-H).

Δ^5-6-Hydroxy-7-oxo-dehydroabietic Acid 15→6-Lactone (47) from 46——A solution of the oxime (**46**) (1.02 g) and AcOK (500 mg) in Ac_2O (25 ml) was refluxed at 160° for 45 min. After the reaction mixture was diluted with H_2O to decompose Ac_2O and was extracted with ether, the extract was washed with 5% Na_2CO_3 aq., then sat. NaCl aq. and dried over Na_2SO_4. Removal of the solvent gave an oil, which was chromatographed on silica gel (50 g) to isolate crystals in petr. ether–ether (9: 1) elution. The crystals were recrystallized from MeOH to give colorless needles (**47**) (173 mg; 20% yield), mp 188—189°, which was identical (mixed mp and NMR) with the authentic sample).[16]

Acknowledgement The authors are indebted to Mr. Yoshiteru Tōjō for his valuable assistant. Financial support from the Ministry of Education (Grant-in-Aid for Scientific Research, No. 67031 (1972)) are gratefully acknowledged.