bond dipoles with approximately the same orientation are introduced at the same distance: (1) H-CH_2CH_2-CO_2H *vs.* Cl-$CH_2CH_2CO_2H$, for which $\Delta pK = 0.9$ and $\Delta\mu = \mu(CCl) - \mu(CH) \approx \mu(CH_3Cl) = 1.9$ D; (2) $NH_2CH_2CO_2H$ *vs.* H-$NH_2{}^+CH_2CO_2H$, for which $\Delta pK = 2.2$ and $\Delta\mu \approx 1.3$ D. If the value of D_E govering the charge–dipole interaction were the same in both pairs, the value of ΔpK observed for (1) would require that the charge–dipole contribution to ΔpK for (2) be 0.6 pK unit, which is 27% of the observed total ΔpK. However, this direct comparison of HN and ClC dipoles disregards the large difference in size between Cl and H. The value of Tanford's d which should be assigned to an NH dipole may be much less than the 1.5 Å which is required for halogen–carbon dipoles, and the estimate of 0.6 pK unit must be considered as an upper limit on the contribution of the NH dipole to the value of ΔpK for glycine; the actual contribution may be very much less.

In the sequence NH, SH, SeH, the magnitude of the bond dipole decreases sharply. From the dipole moments[22] and molecular geometries[23] of NH_3, H_2S, and H_2Se, these bonds moments may be estimated to be 1.3, 0.7 and 0.3 D if the contributions of lone pair moments are assumed to be negligible. These estimated bond dipole moments contain errors due to the unknown magnitudes of the lone pair moments in H_nX; the effects of such errors on estimates of the dipolar contribution to ΔpK will tend to cancel with the effects on ΔpK of the corresponding lone pair moments in the substituted carboxylic acids. This cancellation will in general, however, not be complete.

Although the magnitude of the variation in ΔpK which should result from changes in the XH bond moment (or from changes in the mean orientation of the XH dipole) cannot be quantitatively estimated, it is clear that a difference of *ca.* 1 D between the effective NH and SeH moments is probable; if the effect on ΔpK from this source had a magnitude about equal to its estimated maximum possible value, it could account for the observed total variation in ΔpK. Since that variation, however, lies well within the range which could be accounted for by changes in the value of D_E for charge–charge interactions, at least a major part of it very probably arises from an increase in the efficiency of transmission of the effect of a charge as the atom which bears that charge increases in size.

Registry No.—Selenoglycolic acid, 25244-47-7; selenoglycolic methyl ester, 25244-48-8.

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Free-Radical Bromination of Methyl Abietate by N-Bromosuccinimide and Solvolysis of the Products

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The major product from the solvolysis of the methyl bromoabietate formed by the NBS–methyl abietate reaction was methyl 12α-methoxyabietate. The structure was proved by independent synthesis from 12α-hydroxyabietic acid. Methyl 18-methoxyabietate was also formed. The three possible methyl methoxydehydroabietates were obtained as secondary reaction products from the methyl dehydroabietate formed during the NBS–abietate reaction. They have also been prepared by the solvolysis of NBS–methyl dehydroabietate reaction products. The structures of the intermediate bromo compounds have been assigned by analogy to the ethers.

As one approach to the identification of a methyl methoxyabietate obtained by photolysis of methyl neoabietate in methanol,[2] preparation of similar compounds from methyl abietate (**1**) by free-radical bromination followed by methanolysis of the bromides was investigated. Bromination with N-bromosuccinimide (NBS) followed by dehydrobromination[3] has been used to make dehydroabietic acid from abietic acid. In the present investigation methyl dehydroabietate (**10**) was still the major product, but a fair yield of ethers was also obtained.

On the basis of the identity of its uv spectrum with that of methyl abietate and the splitting pattern of the C_{12} proton[4] in its nmr spectrum,[5] it should be **2a**. This structure was confirmed by comparison with an authentic sample prepared from methyl 12α-hydroxyabietate[6] (**2b**). Of the minor products, only one exhibited the uv absorption characteristic of an abietate structure. Its gas chromatographic behavior was identical with that of the ether obtained by photolysis and subsequently identified as methyl 18-methoxyabietate[2] (**6a**).

The other products had uv and ir spectra which were consistent with aromatic structures, indicating that **10**

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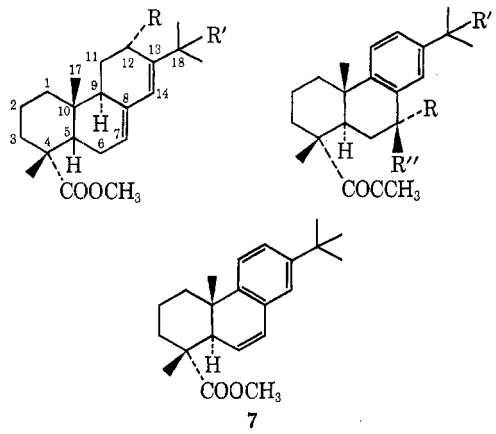
(2) J. C. Sircar and G. S. Fisher, *Chem. Ind. (London)*, 26 (1970).

(3) O. Jeger, O. Durst, and G. Buchi, *Helv. Chim. Acta*, **30**, 1853 (1947).

(4) (a) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, p 77. (b) J. C. Sircar and G. S. Fisher, *J. Org. Chem.*, **34**, 404 (1969).

(5) Nmr spectra were run in deuteriochloroform on a Varian A-60 spectrometer unless otherwise specified. Frequencies are given in cps with tetramethylsilane as internal standard. s = singlet, d = doublet, t = triplet, m = multiplet. The mention of firm names of trademarks does not imply that they are endorsed or recommended by the Department of Agriculture over others not mentioned.

(6) W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller, and G. W. Hedrick, *J. Org. Chem.*, **30**, 3190 (1965).



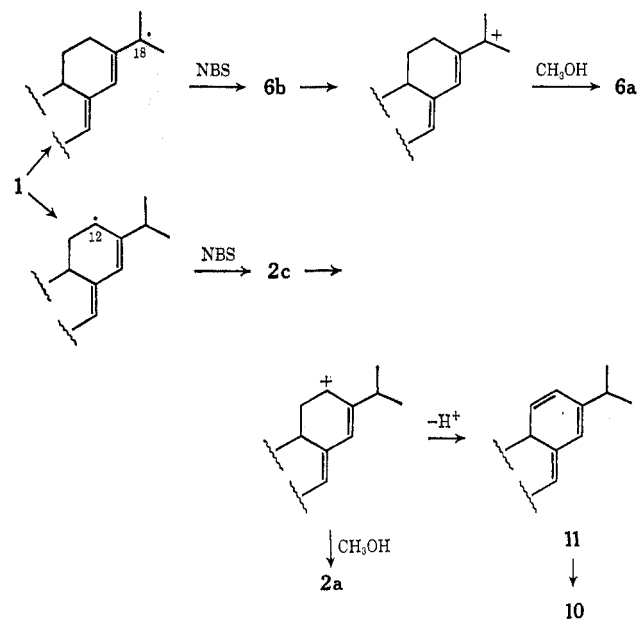
7

1, R = R′ = H
2a, R = OCH_3; R′ = H
b, R = OH; R′ = H
c, R = Br; R′ = H
6a, R = H; R′ = OCH_3
b, R = H; R′ = Br
3, R = OCH_3; R′ = R″ = H
4, R = R″ = H; R′ = OCH_3
5, R = R′ = H; R″ = OCH_3
8, R = R′ = OCH_3; R″ = H
9, R = H; R′ = R″ = OCH_3
10, R = R′ = R″ = H

formed during bromination of **1** and was also brominated by the NBS. Hence, pure **10** was brominated and solvolyzed under the same conditions. Bromination was somewhat slower than in the case of **1** and there was much less evolution of HBr. In addition to the products in question, two products with longer glpc emergence times were formed. On the basis of spectral data, the secondary products from methyl abietate, in order of emergence, were methyl Δ^6-dehydrodehydroabietate (**7**), methyl 7β-methoxydehydroabietate (**5**), methyl 7α-methoxydehydroabietate (**3**), and methyl 18-methoxydehydroabietate (**4**). One of the two additional products was isolated by column chromatography and shown to be methyl 7α,18-dimethoxydehydroabietate (**8**). On the basis of relative emergence times and yield, the other one is assumed to be the corresponding 7β isomer (**9**). The 18-methoxy derivatives accounted for only about 20% of the products. Similar selectivity for the C_7 position was observed in the autoxidation of **10**.[7]

The observed predominance of the α-quasiaxial ethers can be rationalized on the basis of a combination of steric and stereoelectronic factors. The stereoelectronic requirements for the formation of allylic radicals or ions greatly enhances the reactivity of quasiaxial allylic substituents.[8,9] Formation of axial or quasiaxial products from such ions and radicals is also favored.[8,9] Of the six allylic positions in **1**, 6α and 12β are quasiequatorial. The 6β position is synaxial to the methyl groups at C_4 and C_{10}. The 9α position is allylic to the 7 double bond, but a p orbital at C_9 cannot conjugate with the whole diene system. Hence, failure to get detectable amounts of ether formation at these four positions is reasonable. Since the abietic diene system is the most stable abietadiene system,[10] allylic rearrangement products would not be expected. The great predominance of **2a** over **6a** reflects the fact that the 12α position is quasiaxial and relatively unhindered,[6] while rotation of the isopropyl group to an H-axial conformation involves a crowding of the methyl groups,[11] which becomes more severe in the derived ion or radical. Copious evolution of HBr with formation of **10** during bromination of **1** is a further result of the stereoelectronic enhancement of the reactivity of the 12α bromine.[9] The primary product (**2c**) would aromatize immediately in the presence of acid (Scheme I).

SCHEME I



The influence of these same factors also determines the distribution of products from **10**, but compared to the vinyl group of **1**, the phenyl group of **10** is less effective in conjugating with the neighboring p orbital.[12] Hence, there is less dehydrobromination, a greater proportion of 18-methoxy products, and a significant yield of the 7β isomer. The quasiaxial 7α position is still the most reactive one. This is in accord with the observations of Meyer[11] that tetralin is more reactive than cumene and contrary to Walling's report that cumene reacts more rapidly than tetralin with NBS.[13]

Since solvolysis of the bromides is an SN1 reaction,[14,15] they would not necessarily have the same configuration as the ethers, but we consider that they do because the same steric and stereoelectronic factors which control the solvolysis steps will also govern the bromination steps.[7]

Experimental Section[16]

Bromination of Methyl Abietate (1) with NBS.—A mixture of "Vazo"[5] (AIBN) (104 mg) and N-bromosuccinimide (10.01 g,

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(8) E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, **78**, 6269 (1956).
(9) H. L. Goering and R. R. Josephson, *ibid.*, **84**, 2779 (1962).
(10) H. Takeda, W. H. Schuller, and R. V. Lawrence, *J. Org. Chem.*, **33**, 1683 (1968).
(11) J. A. Meyer, V. Stannet, and M. Szwarc, *J. Amer. Chem. Soc.*, **83**, 25 (1961).
(12) R. Hoffman, *Tetrahedron Lett.*, 3819 (1965).
(13) C. Walling, A. L. Rieger, and D. D. Tanner, *J. Amer. Chem. Soc.*, **85**, 3129 (1963).
(14) T. I. Wrigley and W. G. Young, *ibid.*, **80**, 4604 (1958).
(15) H. L. Goering, T. D. Nevitt, and E. F. Silversmith, *ibid.*, **77**, 5026 (1955).
(16) Melting points are uncorrected. Analyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tenn. 37921. Infrared spectra were obtained with a Perkin-Elmer infrared spectrophotometer, Model 21. Ultraviolet spectra and rotations were determined in 95% ethanol. Analytical gas chromatographic analyses were performed at 245° on a Varian-Aerograph Model 1200 using a 10 ft × 3/16 in. column packed with 5% Versamid-900 on 60–80 mesh Chromosorb W. Unless otherwise mentioned, methyl arachidate was used as an internal standard for determination of relative retention times (α).

0.0568 mol) was added to a solution of methyl abietate (1) (17.93 g, 0.0568 mol) in dry carbon tetrachloride (180 ml) and the mixture heated on a steam bath for 5 min, until the reaction was complete as indicated by the disappearance of the heavy NBS. The hot solution was filtered and the solvent removed under vacuum (1 mm) at 50°. The crude bromo compound (20 g) spontaneously generated hydrogen bromide, so it was used immediately for the methanolysis.

13-Isopropyl-12α-methoxypodocarpa-7,13-dien-15-oic Acid Methyl Ester (Methyl 12α-Methoxyabietate) (2a). A. Solvolysis[17] of the Bromoabietates.—The crude bromo compounds (20 g) from above were dissolved in anhydrous methanol (1500 ml, AR) mixed with fused potassium acetate (7.40 g, 0.0644 mol), and refluxed for 8 hr. Methanol was removed by distillation under reduced pressure and the residual oil was extracted with ether as usual to give a brown oil (18.89 g). Glpc analysis showed the following composition: methyl dehydroabietate (α = 2.16), 29%; Δ^6-dehydrodehydroabietate (7) (α = 2.32), 5%; methyl abietate (1) (α = 2.51), 26%; methyl 7β-methoxydehydroabietate (5) (α = 2.59), methyl 7α-methoxydehydroabietate (3) (α = 2.89), 7%; methyl 12α-methoxyabietate (2a) (α = 3.38), 27%; methyl 18-methoxydehydroabietate (4) (α = 3.57), 1.0%; methyl 18-methoxyabietate (6a) (α = 4.11), 1.6%; and three other minor products, 3.5% (none of them above 2%).

The solvolysis product (9.15 g) was chromatographed over silica gel (E. Merck, 70-325 mesh ASTM, 239 g). Elution with 80% benzene–*n*-hexane mixture (700 ml) and benzene (600 ml) gave resin acid ester mixtures (3.1 g) containing methyl dehydroabietate, methyl abietate, and a little methyl palustrate. Further elution with 20–30% ether–benzene mixture (300 ml) gave semisolid mixtures of ethers, which on trituration with methanol gave white solids. Recrystallization from methanol gave methyl 12α-methoxyabietate (2a) (1.82 g) as white needles; mp, 113–4°. Another recrystallization from methanol gave the analytical sample: mp 115°; $[\alpha]^{26}D$ −72°; λ_{max}^{EtOH} 236, 242, and 251 mμ (ϵ_{max}^{242} 26,700); λ^{Nujol} 5.85, 8.10, 9.30, 11.40, and 12.40 μ; nmr (cps) 352 (s, 1 H, C_{14}-proton), 330 (m, 1 H, (C_7-proton), 227 (t, 1 H, $J_{a,e}$ = 2 cps, C_{12}-β-proton), 218 (s, 3 H, C_{15}-O-CH_3), 202 (s, 3 H, C_{12}-α-OCH_3), 76 (s, C_{16}-protons), 63 (d, J = 7 cps, C_{19}- or C_{20}-protons), 65 (d, J = 7 cps, C_{19}- or C_{20}-protons), 49 (s, 3 H, C_{17}-protons).

Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89; O, 13.85. Found: C, 76.07; H, 9.72; O, 14.05.

Mother liquor from the crude 12α-methoxyabietate (2a) was used to isolate methoxydehydroabietates **3**, **4**, and **5**.

B. Methylation of Methyl 12α-Hydroxyabietate (2b).—A sample of 56% sodium hydride (2.95 g) suspended in mineral oil was washed several times with dry *n*-pentane and once with 1,2-dimethoxyethane. The suspension of sodium hydride in 1,2-dimethoxyethane (15 ml) was added to a solution of methyl 12α-hydroxyabietate[6] (1.66 g) in 1,2-dimethoxyethane (40 ml). The whole mixture was refluxed for 10 min and then methyl iodide (9 ml) was added. Refluxing was continued for 5 hr. The solvent was removed under reduced pressure and the residual oil was diluted with water and extracted with ether as usual to give crude methyl 12α-methoxyabietate (2a) (1.91 g). The crude solid was recrystallized from methanol three times to give white crystals of 2a: mp 111–113°; $[\alpha]^{26}D$ −71.5°; λ_{max}^{EtOH} 242 mμ (ε 26,000); mmp with solvolysis product (mp 115°) 113–115°. The ir and nmr spectra of the product are superimposable on those of methyl 12α-methoxyabietate (2a) obtained from solvolysis products. Glpc retention times and enrichment with one another also confirmed identity of the two products.

Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.35; H, 9.79.

13-Isopropyl-7α-methoxypodocarpa-8,11,13-trien-15-oic Acid Methyl Ester (Methyl 7α-Methoxydehydroabietate)[18] (3); 13-Isopropyl-7β-methoxypodocarpa-8,11,13-trien-15-oic Acid Methyl Ester (Methyl 7β-Methoxydehydroabietate (5); and 13-Isopropyl-18-methoxypodocarpa-8,11,13-trien-15-oic Acid Methyl Ester (Methyl 18-Methoxydehydroabietate) (4).—The mother liquor (1.9 g) from the trituration and recrystallization of 2a was chromatographed over Woelm neutral alumina (activity I, 50 g). Elution with *n*-hexane (Fraction 1,200 ml) and benzene–hexane mixtures (each fraction 50 ml) with increasing amounts of benzene gave mixtures of ethers, partially separated from one another.

Elution with 15% benzene–*n*-hexane (50 ml) gave in Fraction 7 (and others), 18-methoxydehydroabietate (4) as a colorless oil (100 mg) which gave in the glpc one major peak (α = 3.57) (46%) along with five minor peaks (54%). The fraction did not have any characteristic absorption in the uv: λ^{film} 5.81 (>C=O), 6.71 (aromatic), 8.07 (ester C—O), and 9.35 (C—O—CH_3) μ; nmr (cps) 427 (m, aromatic protons), 220 (s, C_{15}-OCH_3), 184 (s, C_{18}-OCH_3), 90 (s, C_{19}- and C_{20}-protons), 77 (s, C_{16}-protons), 73 (s, C_{17}-protons).

Elution further with 30% benzene–*n*-hexane (50 ml) gave in Fraction 11 (64 mg), 7β-methoxydehydroabietate (5) (33%) as a colorless oil admixed with 7α-methoxydehydroabietate (3) (23%), 18-methoxydehydroabietate [+12α-methoxyabietate (2a)] (4) (15%), and other minor ethers (29%): no uv absorption λ^{film} 5.81, 6.71, 8.07, and 9.35 μ; nmr (cps) (after eliminating signals for known compounds), 428 (m, aromatic protons), 219 (s, C_{15}-OCH_3), 206 (s, C_7-β-OCH_3), 202 (b, $W_{1/2}$ = 11 cps, C_7 α-proton), 78 (s, C_{16}-protons), 71 (s, C_{17}-protons), 74 (d, overlapped with the C_{16}- and C_{17}-singlets, J = 7 cps, C_{19}- and C_{20}-protons).

Elution with 50% benzene–hexane mixture (250 ml) gave in Fractions 12 to 16 a white solid (250 mg) which on recrystallization afforded methyl 7α-methoxydehydroabietate (3); mp 98.5°; λ^{Nujol} −5.83, 6.71, 8.05, and 9.30 μ; nmr (cps) 428 (b, 3H, C_{11}-, C_{12}-, and C_{14}-protons, aromatic), 256 (t, 1 H, J = 3 cps, C_7-β-proton), 221 (s, 3 H, C_{15}-OCH_3), 205 (s, 3 H, C_7-α-OCH_3), 165 (m, C_{13}-proton), 78 (s, 6 H, C_{16}- and half of the doublet of C_{19}- and C_{20}-protons), 71 (s, 6 H, C_{17}- and half of the doublet of C_{19}- and C_{20}-protons, J = 7 cps).

Anal. Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.92; H, 9.49.

Intermediate fractions (50 ml each) gave mixtures of ethers as found by glpc. Methoxydehydroabietates (3, 4, and 5) have been further confirmed by synthesis from dehydroabietate (*vide infra*).

Bromination of Methyl Dehydroabietate with NBS.—Bromination of methyl dehydroabietate (1.55 g, 0.00495 mol) in carbon tetrachloride (40 ml) was carried out for 8–9 min with NBS (0.897 g, 0.00502 mol) and Vazo[5] (10 mg) as usual at reflux. Removal of solvent gave the bromides as a pale yellow oil which was used in the next step, solvolysis.

13-Isopropyl-7α-methoxypodocarpa-8,11,13-trien-15-oic Acid Methyl Ester (Methyl 7α-Methoxydehydroabietate) (3) and 13-Methoxyisopropyl-7α-methoxypodocarpa-8,11,13-trien-15-oic Acid Methyl Ester (Methyl 7α,18-Dimethoxydehydroabietate) (8).—The crude bromides (1.83 g) from above were dissolved in dry methanol (165 ml), mixed with anhydrous potassium acetate (0.879 g, 0.00762 mol), and refluxed for 8 hr. Usual work-up gave a semisolid residue (1.83 g). Glpc analysis of the crude product gave the following composition: methyl dehydroabietate (α = 2.15) (28%); methyl Δ^6-dehydrodehydroabietate (α = 2.28) (7) (2%); methyl 7β-methoxydehydroabietate (α = 2.59) (5) (15%); methyl 7α-methoxydehydroabietate (α = 2.89) (3) (36%); methyl 18-methoxydehydroabietate (α = 3.57) (4) (5%); methyl 7α-18-dimethoxydehydroabietate (α = 4.38) (8) (6%); and methyl 7β-18-dimethoxydehydroabietate (α = 3.98) (5%) plus one minor broad peak (2%). All the known compounds were identified by their relative retention time.

The crude solvolysis product (1.83 g) was chromatographed over silica gel (50 g) as usual. Elution with 75% benzene–*n*-hexane (225 ml) gave in Fractions 4–7 only methyl dehydroabietate (320 mg) identified by its retention time. Further elution with 20% ether–benzene mixture (200 ml) gave in Fractions 15 and 16 a solid (1.14 g) containing 3, 4, 5, and 7 mainly. Recrystallization of the solid from aqueous methanol gave methyl 7α-methoxydehydroabietate (3) (350 mg), mp 92–5°; mixture melting point with the analytical sample (mp 98.5°) was undepressed. Ir, nmr of the sample were identical with those of 3 obtained earlier from abietate. It has been further confirmed by relative retention time. The mother liquor was used to isolate methyl Δ^6-dehydrodehydroabietate (7) and also identify the methyl 7β-methoxydehydroabietate (5) and methyl 18-methoxydehydroabietate (4) by their relative retention times.

(17) G. H. Whitham and J. A. F. Wickramsinghe, *J. Chem. Soc.*, 1655 (1964).

(18) One report of a methyl methoxydehydroabietate (mp 111°) was found in the literature [R. Lombard and J. P. Baltzinger, *C. R. Acad. Sci*, **236**, 1970 (1953)], but the properties fit the 7α-hydroxydehydroabietate, reported later by Dupont, *et al.*[19]

(19) G. Dupont, R. Dulou, G. Ourisson, and C. Thibault, *Bull. Soc. Chim. Fr.*, 708 (1955).

Further elution with 20% ether–benzene (100 ml) gave in Fraction 17, methyl 7α-18-dimethoxydehydroabietate (**8**) (47 mg) as a white solid, mp 129–133°. This, on recrystallization from ether, gave the analytical sample: mp 141–143°; λ^{Nujol} 5.83, 6.68, 8.05, and 9.35 μ, no λ_{max}; nmr (cps) 429 (s, 3 H, aromatic protons), 258 (t, J = 3 cps, 1 H, C_7-β-proton), 223 (s, 3 H, C_{15}-OCH_3), 206 (s, 3 H, C_7-α-OCH_3), 185 (s, 3H, C_{18}-OCH_3), 91 (s, 6 H, C_{19}- and C_{20}-protons), 79 (s, 3 H, C_{16}-protons), 71 (s, 3 H, C_{17}-protons).

Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.65; H, 9.05.

13-Isopropyl-podocarpa-6,8,11,13-tetraen-15-oic Acid Methyl Ester (Methyl Δ^6-Dehydrodehydroabietate) (7).—The mother liquor from the recrystallization of **3** above was evaporated to dryness and the residual oil (745 mg), composed of methyl Δ^6-dehydrodehydroabietate (**7**), methyl 7β-methoxydehydroabietate (**5**), methyl 7α-methoxydehydroabietate (**3**), and methyl 18-methoxydehydroabietate (**4**) (identified **3**, **4**, and **5** by their known relative retention times) was chromatographed over alumina (25 g).

Elution with 30% benzene–hexane mixture (200 ml) (Fraction 9, 10) and 40% benzene–hexane mixture (100 ml) (Fraction 11) gave methyl Δ^6-dehydrodehydroabietate[19] (**7**) as oil (120 mg) with 80% purity. Impurities are **3** and **5**. Further elution with 40% benzene–hexane mixture (50 ml) (Fraction 12) gave pure **7** (26 mg): λ_{max}^{EtOH} 265 and 220 mμ; λ^{neat} 3.37 (aromatic), 5.80 (>C=O), 6.25 (>C=C<), 6.42, 6.73 (aromatic), 8.06 (C–O ester), 9.27, 12.18 (aromatic), and 14.57 (*cis*-CH=CH) μ; nmr (cps) 428 (m, 34, aromatic protons), 394 (a pair of doublets, J_{AB} = 9 cps, J_{AX} = 3 cps, 1 H, C_7-proton), 346 (a pair of doublets, J_{AB} = 9 cps, J_{AX} = 2.5 cps, 1 H, C_6-proton), 220 (s, 3 H, C_{15}-OCH_3), 177 (t, J = 3 cps, C_5-proton), 166 (m, J = 7 cps, C_{18}-proton), 85 (s, 3 H, C_{16}-protons), 75 (d, J = 7 cps, C_{19}- and C_{20}-protons), 65 (s, 3 H, C_{17}-protons).

The identity was further confirmed by the relative retention time in 15% DEGS column (6 × 3/16 in.) at 230° with the known data (methyl stearate[20] as internal standard).

Further elution with benzene (100 ml) (Fraction 21) and 10% ether–benzene (200 ml) (Fraction 22, 23) gave solid **3** (131 mg) mixed with **5**.

Registry No.—**1**, 127-25-3; NBS, 128-08-5; **2a**, 25236-84-4; **3**, 25236-85-5; **4**, 25236-86-6; **7**, 18492-76-7; **8**, 25236-88-8.

Acknowledgment.—We wish to thank Mr. G. Bourdreaux of Southern Utilization Research and Development Division, New Orleans, Louisiana, for taking the nmr spectra.

(20) F. H. Max Nestler and D. F. Zinkel, *Anal. Chem.*, **39**, 1118 (1967).

Synthesis of N,N,N′-Trifluoroamidines[1]

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The dehydrofluorination of 1,1-bis(difluoramino)alkanes yielded the corresponding N,N,N′-trifluoroalkylamidines in good yield. The geometric isomers of these compounds were separated, and conformations are proposed. The direct fluorination of fluoroalkylamidines in the solid phase produced only one isomer of the corresponding N,N,N′-trifluoroamidines, $R_fC(=NF)NF_2$. The addition of methanol to the fluorimino group followed by fluorination gave $R_fC(NF_2)_2OCH_3$.

The fluorination of nitrogen bases with elemental fluorine has received considerable attention during recent years.[2] The solution fluorination of amines[3] and N-alkylcarbamates or -ureas[4] have yielded the corresponding alkyl difluoramines, and the fluorination of nitro aromatic amines produced nitro aromatic difluoramines.[5]

The synthesis of N-haloamidines to give N-chloro-, -bromo-, and -iodoamidines has been studied extensively.[6–9] The synthesis of the first N-fluoroamidine, tetrafluoroformamidine, has been reported[10] as well as some reactions involving this compound.[2,11] Our interest in other N,N,N′-trifluoroamidines prompted us to investigate methods of preparing these compounds by two methods: (a) the dehydrofluorination of terminal geminate difluoramino compounds, and (b) the direct fluorination of amidines.

Terminal geminate difluoraminoalkanes are readily prepared by the reaction of difluoramine with aldehydes.[12] The dehydrofluorination of these compounds with base occurs rapidly to give moderate to high yields of N,N,N′-trifluoroamidines. The kinetics of the base-catalyzed dehydrofluorination of several difluoraminoalkanes has been studied previously,[13,14] but dehydrofluorination has not been applied to the synthesis of trifluoroamidines on a laboratory scale. Solution fluorination was not a practical method for the synthesis of trifluoroamidines, although trace amounts of N-fluoramino compounds were detected in the solution fluorination of acetamidine, butyramidine, and heptafluorobutyramidine.[9] The solid phase fluorination of electronegatively substituted amidines yielded the desired trifluoroamidines whereas considerable decomposition and C-fluorination resulted when unsubstituted alkyl amidines were fluorinated.

Results and Discussion

In this study the compounds prepared by dehydrofluorination were N,N,N′-trifluoropropionamidine (**1**), N,N,N′-trifluorohexanamidine (**2**), and 2-chloro-N,N,-N′-trifluoropropionamidine (**3**). The *syn* and *anti* iso-

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