using stopped-flow technique. The log of the second-order rate constants (k_2) obtained for tocopherols was found to correlate with their half-wave oxidation potentials ($E_{p/2}$); the same correlation was found for the reaction of tocopherols with peroxyl radical.

Acknowledgment. We are very grateful to Eisai Co. for the generous gift of α-, β-, γ-, and δ-tocopherols. We are also very grateful to Prof. Yoichi Kitamura for use of the stopped-flow spectrophotometer and his helpful discussions.

Registry No. α-Tocopherol, 59-02-9; γ-tocopherol, 7616-22-0; tocol, 119-98-2; β-tocopherol, 148-03-8; δ-tocopherol, 119-13-1; 5,7-dimethyltocol, 493-35-6.

Deoxygenation of Tertiary Alcohols Using Raney Nickel[†]

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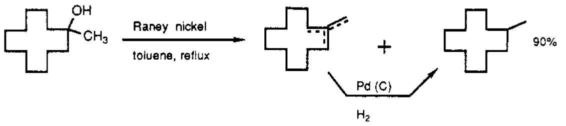
Introduction

Tertiary alcohols have been deoxygenated by using a variety of different routes.[1,2] These include reduction of tertiary alcohol thioformates using tributylstannane,[3] acid-catalyzed hydrogenolysis using palladium or platinum catalysts in the presence of hydrogen,[4] benzylic hydrogenolysis under dissolving metal conditions,[5] ionic deoxygenations using silanes and Lewis acids,[6] and the use of transition-metal catalysts.[7] During the course of our investigation of the oxidation of secondary alcohols to ketones using Raney nickel,[8] we found that tertiary alcohols were easily deoxygenated by Raney nickel under similar reaction conditions. Raney nickel has previously been used in reductive desulfurization reactions or as a hydrogenation catalyst in the reduction of nitro groups,[9] isoxazolidines,[10] and olefins.

Results and Discussion

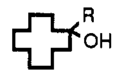
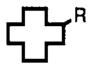
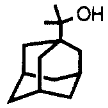
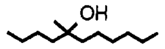
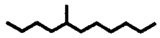
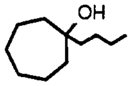
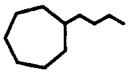
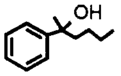
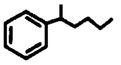
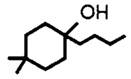
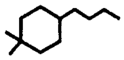
We report that the use of Raney nickel in toluene provides a mild and inexpensive means of efficiently deoxygenating tertiary alcohols under neutral conditions. Heating a toluene solution of 1-methyl-1-cyclododecanol with washed[11] Raney nickel for 40 min resulted in the formation of a mixture[12a] of methylcyclododecenes and methylcyclododecane (eq 1). Subsequent hydrogenation



(1)

of the olefins [Pd(C), H_2, EtOH, EtOAc] gave a 90% yield of methylcyclododecane.[12b] The deoxygenation and olefin reduction sequence could also be carried out in one step. For example, reaction of 1-methyl-1-cyclododecanol with a large excess of Raney nickel yielded exclusively methylcyclododecane in 90% yield after 12 h in refluxing toluene.[12c] We found that with other tertiary alcohols the reduction proceeded cleanly and in high yield as is illustrated by the results in Table I.

Table I

entry	alcohol	product(s)[a]	yield (%)[b]
			
1	R = CH_3		90
2	R = n-Bu		89
3	R = t-Bu		91[c]
4			90
			
5	R = TBDMS		86
6	R = Ac		90
7			80
8			83
9			94
10		 	71 13
11			90
12			99

[a] Products obtained after hydrogenation of the olefins. [b] All yields refer to isolated materials. [c] Yield of olefins.

tert-Butyldimethylsilyl ethers and acetates were stable to the reaction conditions as is demonstrated by entries

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[†] Dedicated to Professor Gilbert Stork on the occasion of his 65th birthday.

(1) For the deoxygenation of primary and/or secondary alcohols, see; Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc. Perkin Trans. 1* **1975**, 1574. Masamune, S.; Rossy, P. A.; Bates, G. S. *J. Am. Chem. Soc.* **1973**, *95*, 6452 and references cited therein. Hartwig, W. *Tetrahedron* **1983**, *39*, 2609. Ueno, Y.; Tanaka, C.; Okawara, M. *Chem. Lett.* **1983**, 795. Fujimoto, Y.; Tatsuno, T. *Tetrahedron Lett.* **1976**, 3325. Corey, E. J.; Achiwa, K. *J. Org. Chem.* **1969**, *34*, 3667. Garbisch, E. W.; Schreader, L.; Frankel, J. J. *J. Am. Chem. Soc.* **1967**, *89*, 4233. Watanabe, Y.; Araki, T.; Ueno, Y.; Endo, T. *Tetrahedron Lett.* **1986**, *27*, 5385. See also: Harrison, I. T.; Harrison, S. *Compendium of Organic Synthetic Methods*; Wiley: New York, 1971; Vol. 1–5 for a more complete listing of references.

(2) For isolated examples of the reductive deoxygenation of tertiary alcohols, see: Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098. Redlich, H.; Neumann, H. J.; Paulsen, H. *Chem. Ber.* **1977**, *110*, 2911. Pfenninger, J.; Heuberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328. Zderic, J. A.; Cabezas Rivera, M. E.; Limon, D. *J. Am. Chem. Soc.* **1960**, *82*, 6373.

(3) Barton, D. H. R.; Hartwig, W.; Motherwell, R. S. H.; Motherwell, W. B.; Stange, A. *Tetrahedron Lett.* **1982**, *23*, 2019.

(4) Khan, A. M.; McQuillin, F. J. *J. Chem. Soc.* C **1967**, 136. Peterson, P. E. *J. Org. Chem.* **1964**, *29*, 2325.

(5) Small, G. H.; Minella, A. E.; Hall, S. S. *J. Org. Chem.* **1975**, *40*, 3151.

(6) Adlington, M. G.; Orfanopolous, M.; Fry, J. L. *Tetrahedron Lett.* **1976**, 2955.

(7) Alper, H.; Salisova, M. *Tetrahedron Lett.* **1980**, *21*, 801.

(8) Krafft, M. E.; Zorc, B. *J. Org. Chem.* **1986**, *51*, 5482.

(9) Williams, H. W. R. *Can. J. Chem.* **1976**, *54*, 3377.

0022-3263/88/1953-0432$01.50/0

5 and 6 in Table I. Even tertiary neopentyl alcohols could be smoothly deoxygenated (entries 3 and 4).[12d] Alkyl chlorides were stable to Raney nickel in refluxing toluene (entry 11), but alkyl bromides were partially hydrogenolyzed under the reaction conditions (entry 10).

Several functional groups—ethoxyethyl ethers, epoxides, and olefins—were too sensitive to withstand the conditions of the reaction. Ethoxyethyl ethers and acetals reacted immediately and gave several products resulting from cleavage and deoxygenation. Raney nickel reacted with cyclooctene oxide, giving rise to a 1:4 mixture of cyclooctanol and cyclooctanone[8] after 2.5 h in refluxing toluene. Olefins were isomerized and partially reduced in the initial deoxygenation reaction and completely reduced during the catalytic hydrogenation reaction.

We feel that Raney nickel in refluxing toluene will provide an inexpensive and efficient method for the hydrogenolysis of tertiary alcohols. In addition to the stability of many functional groups to the mild reaction conditions, the convenient workup—filtration and solvent removal followed by catalytic hydrogenation—makes this deoxygenation procedure very attractive.

Experimental Section

General Information. Toluene was distilled from sodium immediately prior to use. Tetrahydrofuran (THF) and diethyl ether were distilled from potassium immediately prior to each use. Methylene chloride (CH_2Cl_2), diisopropylamine, triethylamine, and hexamethylphosphoramide (HMPA) were distilled from calcium hydride. ^1H NMR spectra were obtained at 270 MHz on a Bruker instrument. Chemical shifts are reported downfield relative to tetramethylsilane. IR spectra were obtained on a Perkin-Elmer Model 1320 infrared spectrophotometer. Low resolution mass spectra were obtained on a Finnigan 4510 GC/MS instrument. Chromatography refers to flash chromatography as reported by Still.[13] Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

All of the alcohols in listed Table I were prepared by the addition of the appropriate alkyllithium reagent to a ketone or ester.

General Procedure for the Addition of Alkyllithium Reagents to Ketones: Preparation of 5-Methyl-5-undecanol. To a stirred solution of 1.72 g of 2-octanone (13.5 mmol) in 40 mL of THF at −78 °C was added 12 mL of a 1.5 M solution of *n*-butyllithium in hexane (18 mmol) slowly down the edge of the cooled flask. After 15 min, the excess butyllithium was quenched with 1 mL of saturated aqueous sodium chloride. The reaction mixture was warmed to room temperature, washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, and evaporated to afford a mixture of starting ketone and 5-methyl-5-undecanol. Since enolization was a major side reaction, the *n*-butyllithium addition procedure was repeated twice. The resulting oil was chromatographed by using a 20:1 mixture of hexane in ethyl acetate to yield 2.0 g of 5-methyl-5-undecanol as a colorless oil (10.75 mmol, 80%): ^1H NMR ($CDCl_3$) δ 0.81 (t, 3 H, J = 7.0 Hz), 0.83 (t, 3 H, J = 7.0 Hz), 1.2–1.7 (m, 19 H); IR ($CHCl_3$) 3500, 2973, 2900, 1475, 1385, 1225 cm^{-1}. Anal. Calcd for $C_{12}H_{26}O$: C, 77.35; H, 14.06. Found: C, 77.25; H, 14.15. Yields for the preparation of other tertiary alcohols (entry, yield): (1, 67%), (2, 79%), (3, 50%), (7, 80%), (8, 65%), (9, 58%), (10, 69%), (12, 69%).

Preparation of 2-Methyl-13-acetoxy-2-tridecanol. To a stirred solution of 2-methyl-13-hydroxy-2-tridecanol (480 mg, 2.08 mmol) in 10 mL of methylene chloride at 0 °C was added acetic anhydride (0.26 mL, 2.71 mmol), triethylamine (0.6 mL, 4.16 mmol), and a catalytic amount of (dimethylamino)pyridine (DMAP). After 30 min at 0 °C, the reaction mixture was diluted with 80 mL of diethyl ether/hexane (1:1) and washed with successive portions of 5% HCl, saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was dried over anhydrous sodium sulfate, reduced to an oil, and chromatographed on silica gel by using hexane/ethyl acetate (7:3) to afford 2-methyl-13-acetoxy-2-tridecanol (521 mg, 1.91 mmol, 92%): ^1H NMR ($CDCl_3$) δ 1.20 (s, 6 H), 1.2–1.6 (m, 22 H), 2.05 (s, 3 H), 4.06 (t, 2 H, J = 6.5 Hz); IR ($CHCl_3$) 3445, 2945, 2870, 1725, 1473, 1395, 1368, 1255 cm^{-1}. Anal. Calcd for $C_{16}H_{32}O$: C, 70.54; H, 11.84. Found: C, 70.94; H, 12.02.

Preparation of 13-Bromo-2-methyl-2-tridecanol. To a stirred solution of 13-hydroxy-2-methyl-2-tridecanol (285 mg, 1.24 mmol) in 7 mL of methylene chloride at 0 °C was added 414 mg of carbon tetrabromide (1.25 mmol). Triphenylphosphine (433 mg, 1.65 mmol) was added slowly to prevent warming of the reaction mixture. Upon addition the reaction was warmed to room temperature. After 9 h at room temperature, the reaction mixture was diluted with ethyl acetate and hexane and washed twice with saturated sodium chloride, dried over anhydrous sodium sulfate, and concentrated to afford an oily solid. The residue was filtered through a 1-in. plug of silica gel by using ethyl acetate/hexane (1:9). The filtrate was concentrated to a clear oil and chromatographed on silica gel by using ethyl acetate/hexane (1:9) to afford 249 mg of 13-bromo-2-methyl-2-tridecanol as a clear oil (0.850 mmol, 69%): ^1H NMR ($CDCl_3$) δ 1.22 (s, 6 H), 1.2–1.5 (m, 18 H), 1.85 (t, 2 H, J = 6.5 Hz), 3.37 (t, 2 H, J = 6.5 Hz); IR ($CHCl_3$) 3445, 2895, 2745, 1568, 1378, 1220 cm^{-1}. Anal. Calcd for $C_{14}H_{29}OBr$: C, 57.33; H, 9.97. Found: C, 57.26; H, 10.11.

General Procedure for the Deoxygenation of Tertiary Alcohols. A solution of 200 mg (1.01 mmol) of 1-methyl-1-cyclododecanol in 3 mL of toluene was added to 400 mg of a Raney nickel slurry. [The Raney nickel was weighed as an aqueous slurry where most of the liquid had been removed before weighing. The weight of the Raney nickel slurry was equal to two times the weight of the alcohol. Immediately before each use the slurry was washed eight times with vigorous stirring with 8 mL of distilled water and two times with 1-propanol.] The residual water and the 1-propanol were azeotropically removed from the slurry very rapidly by using an efficient Dean–Stark trap and a hot oil bath (~140 °C). Less than 10 min was necessary for complete removal of the water. The remaining suspension was refluxed for 40 min with vigorous stirring, cooled to room temperature, and filtered through a pad of Celite by using 30% ethyl acetate in hexanes. (Caution, the Raney nickel may still be pyrophoric!) The solvent was removed in vacuo, leaving a pale oil which was diluted with a 1:1 mixture of ethanol and ethyl acetate and stirred under 1 atm of hydrogen for 8 h at room temperature in the presence of a catalytic amount of 5% Pd(C). Filtration and solvent removal yielded 181 mg of methylcyclododecane (90%).[14]

Acknowledgment. This work was supported by an Atlantic Richfield Foundation Grant of Research Corporation and the donors of the Petroleum Research Fund, administered by the American Chemical Society.

Registry No. $H_3CCO(CH_2)_5CH_3$, 111-13-7; $(H_3C)_2C(OH)(CH_2)_{11}OH$, 109183-00-8; $HOC(CH_3)_2(CH_2)_{11}OTBDMS$, 111772-84-0; $(H_3C)_2CH(CH_2)_{11}OTBDMS$, 111772-89-5; $(H_3C)_2C(OH)(CH_2)_{11}OAc$, 111772-85-1; $(H_3C)_2CH(CH_2)_{11}OAc$, 88591-30-4; $C6H_5C(OH)(CH_3)Bu$, 4396-98-9; $C_6H_5CH(CH_3)Bu$, 6031-02-3; HOC(C-

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(10) Kozikowski, A. P.; Stein, P. D. *J. Am. Chem. Soc.* **1982**, *104*, 4023. Curran, D. P. *J. Am. Chem. Soc.* **1982**, *104*, 4024.

(11) Fresh Raney nickel from Aldrich Chemical Company (50% slurry in water, pH 10) was used for the deoxygenation reaction. See the Experimental Section for the washing procedure. Unwashed Raney nickel did not deoxygenate tertiary alcohols at any appreciable rate. The 1-propanol washed Raney nickel was more reactive and its use permitted shorter reaction times as compared to Raney nickel washed with distilled water only.

(12) (a) For substrates which were deoxygenated very rapidly, olefin isomers were the major products. At longer reaction times, more alkane was obtained. (b) Attempted hydrogenation of the crude reaction mixture was unsuccessful. Addition of ethanol to the unfiltered reaction mixture followed by stirring for 24 h at room temperatures, under 1 atm of hydrogen, still yielded olefins as the major products. (c) With large excesses of Raney nickel (eight times the weight of the alcohol), complete conversion to alkane was observed with no change in the overall yield. (d) We were unable to hydrogenate the olefins obtained from the deoxygenation of 1-*tert*-butyl-1-cyclododecanol (entry 3) using a number of different conditions.

(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(14) All compounds gave satisfactory spectral data. All yields refer to homogeneous materials of >98% purity.

$H_3)_2(CH_2)_{11}Br$, 111772-86-2; $(H_3C)_2CH(CH_2)_{11}Br$, 111772-90-8; $(H_3C)_2CH(CH_2)_{10}CH_3$, 1560-96-9; $HOC(CH_3)_2(CH_2)_{11}Cl$, 111772-87-3; $(H_3C)_2CH(CH_2)_{11}Cl$, 111793-80-7; 1-methyl-1-cyclododecanol, 32400-09-2; methylcyclododecanol, 1731-43-7; 1-butyl-1-cyclododecanol, 16282-71-6; butylcyclododecanol, 102860-64-0; 1-*tert*-butyl-1-cyclododecanol, 111772-83-9; *tert*-butylcyclododecanol, 61682-11-9; 2-(3-adamantyl)-2-propanol, 775-64-4; 2-(3-adamantyl)propane, 773-32-0; 1-butyl-1-cycloheptanol, 3898-34-8; butylcycloheptane, 13152-41-5; 1-butyl 4,4-dimethylcyclohexan-1-ol, 111772-88-4; 1-butyl-4,4-dimethylcyclohexane, 111772-91-9; cyclododecanone, 830-13-7; cycloheptanone, 502-42-1; 4,4-dimethylcyclohexanone, 4255-62-3; 5-methyl-undecan-5-ol, 21078-80-8; 5-methylundecane, 1632-70-8; Raney nickel, 7440-02-0.

The Structures of Marvel's δ-Lactone and "Polymer"

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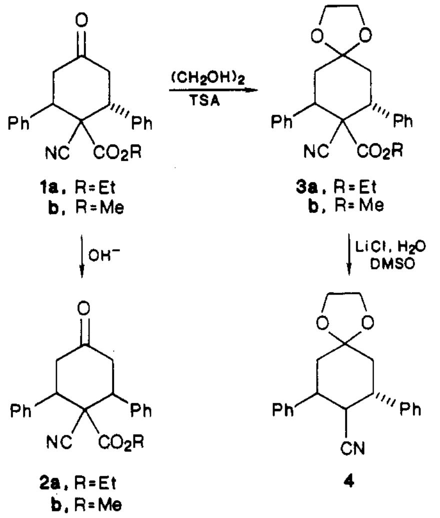
Received June 26, 1987

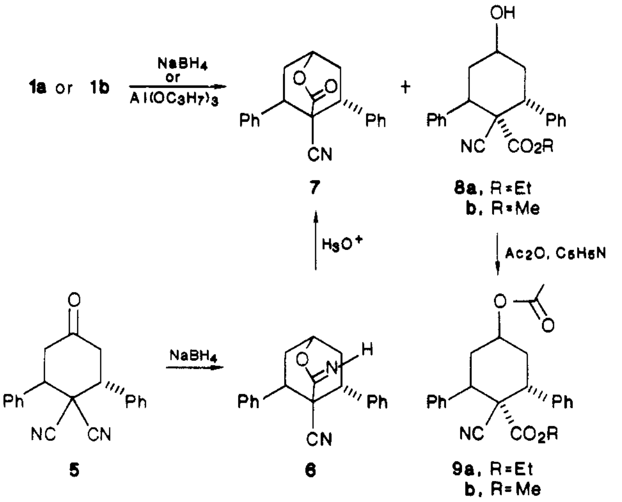
The Michael condensations of 1,5-disubstituted 1,4-pentadien-3-ones with certain addends provide efficient preparations of substituted cyclohexanones.[1] In the course of our studies[2] of Michael adducts, it became necessary to determine the configurations at C-2 and C-6 in two previously reported cyclohexanones: ethyl 1-cyano-2,6-diphenyl-4-oxocyclohexane-1-carboxylate (**1a**)[3] and 2,6-diphenyl-4-oxocyclohexane-1,1-dicarbonitrile (**5**).[4] Marvel and Moore[3] assumed that **1a** was one of the two possible meso isomers (phenyls cis) while NMR data[4c] indicated that the dicyano ketone **5** probably was the trans (±) isomer. We report here chemical and spectroscopic studies that make stereochemical assignments with certainty in **1a** and in **5**. We also present a complete elucidation of the products of the Meerwein–Ponndorf–Verley reduction of **1a** first reported by Marvel and Moore.[3]

Condensation of dibenzalacetone with ethyl cyanoacetate in ethanol or in ethyl ether with Triton B as the catalyst gave the oxo ethyl ester **1a**.[3] This material was converted by further treatment with base into the previously unknown isomeric ester **2a** (Scheme I). The behavior of **1a** parallels that of the trans methyl ester **1b**, which is known to be the labile product of the reaction of methyl cyanoacetate with dibenzalacetone and which can be isomerized by base to the cis isomer **2b**.[4c,5] Further chemical proof of the trans relationship of the phenyl substituents in **1a** was obtained by decarbalkoxylation[6] of the ethylene ketals (**3a** and **3b**) of the oxo esters **1a** and **1b**. In each case, the same cyano ketal **4** was obtained in good yield. The ^{13}C NMR spectrum (Table I) of **1a** exhibits a unique signal for each cyclohexanone ring carbon as expected for a trans relationship of the phenyl groups. In contrast, identical δ values for C-2/C-6 and for C-3/C-5 in **2a** confirm the meso character of this compound, presumably with a C-1 axial cyano group.[4c] The ^{13}C NMR spectrum of the dicyano ketone **5** (recorded also by Kingsbury[4c]) is consistent with a trans compound with rapidly equilibrating chair or twist conformations.

Scheme I



Scheme II



Sodium borohydride reduction of the dicyano ketone **5** gave the imino ester **6** in high yield (Scheme II). Compound **6** was obtained as a mixture of diastereomers about the C=NH unit in a ratio of ca. 7/3 as calculated from the appropriate signals in the ^{13}C NMR spectrum (Table II). Hydrolysis of **6** with aqueous HCl gave the δ-lactone **7** reported earlier.[3] Reduction of the ethyl ester **1a** by aluminum isopropoxide following Marvel and Moore[3] gave a mixture from which the δ-lactone **7** was readily isolated in 43% yield as an ether-insoluble precipitate. The formation of **7** from **5** as well as from **1a** provides conclusive evidence of **5** as the trans (±) isomer. The ether extract gave a syrup, which resisted all attempts at crystallization. The IR and ^1H NMR spectra of this material were inconsistent, however, with the "noncrystalline polymer" suggested[3] as the secondary product of the reduction as evidenced by the presence of the ethyl group. Chromatography of the oil on silica gel gave fractions that proved to be the hydroxy ester **8a**. The oil was identified from spectral data and by conversion to the solid acetate derivative **9a**.

Lactone **7** and the hydroxy ester **8a** also were obtained by $NaBH_4$ reduction of the ethyl ester **1a**. In similar fashion, the methyl ester **1b** was reduced to give **7**, accompanied by the noncrystalline hydroxy ester **8b**, which was characterized spectroscopically and by conversion to

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[1] Bergmann, E. D.; Ginsburg, D.; Pappo, R. *Org. React. (N.Y.)* **1959**, *10*, 179.

[2] Rowland, A. T.; Hohneker, J. A.; McDaniel, K. F.; Moore, D. S. *J. Org. Chem.* **1982**, *47*, 301.

[3] Marvel, C. S.; Moore, A. C. *J. Am. Chem. Soc.* **1949**, *71*, 28.

[4] (a) Tanaka, Y.; Imoto, M. *Kogyo Kagaku Zasshi* **1966**, *69*, 524. (b) Otto, H. H.; Triepel, J.; Schmelz, H.; Meyer-Schaar, J. *Arch. Pharm. (Weinheim, Ger.)* **1976**, *309*, 786. (c) Kingsbury, C. A.; Jordan, M. E. *J. Chem. Soc., Perkin Trans. 2* **1977**, 364.

[5] (a) Kohler, E. P.; Helmkamp, R. W. *J. Am. Chem. Soc.* **1924**, *46*, 1018. (b) Otto, H. H. *Arch. Pharm. (Weinheim, Ger.)* **1972**, *305*, 913.

[6] Krapcho, A. P.; Weimaster, J. F. *J. Org. Chem.* **1980**, *45*, 4105.

0022-3263/88/1953-0434$01.50/0