of an acyl halide.[32] Acidification of the initial bicarbonate wash liquor followed by extraction with dichloromethane showed the presence of phenylacetic acid (mass spectrum was identical with the literature spectrum[31b]) as well as other organic material.

3,3-Dimethyl-1-butyne. A single product (70%) was formed, which was identified as 2-fluoro-3,3-dimethylbutanal on the basis of the IR (aldehyde carbonyl stretching at 1710 cm^{-1}) and ^1H NMR spectra [^1H NMR ($CDCl_3$) δ 1.1 (*t*-Bu), 3.5 (d, J = 43 Hz, CHF), 10.6 (broad CHO)] of the reaction mixture. The ^1H NMR spectrum is similar to that of the chloro and bromo analogues,[33] and the observed CHF coupling constant is also indicative of this structure.[34] The mass spectrum of the major product also agreed well with the proposed structure: mass spectrum, *m/e* (rel intensity) 118 (1), 98 (35), 83 (10), 69 (70), 55 (98), 41 (100).

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Registry No.—Hypofluorous acid, 14034-79-8.

References and Notes

(1) (a) Based on work performed under the auspices of the Division of Basic Energy Sciences of the U.S. Department of Energy. (b) Present address: Helene Curtis Industries, Inc., Chicago, Ill. 60639. (c) Undergraduate Research Student, Indiana University Northwest, Gary, Indiana 46408.
(2) M. H.Studier and E. H. Appelman, *J. Am. Chem. Soc.*, **93,** 2349 (1971).
(3) E. H. Appelman, R. Bonnett, and B. Mateen, *Tetrahedron*, **33,** 2119 (1977).
(4) J. C. Hindman, A. Svirmickas, and E. H. Appelman, *J. Chem. Phys.*, **57,** 4542 (1972).
(5) L. Pauling, "The Chemical Bond", Cornell University Press, Ithaca, N.Y., 1960, p 63.
(6) E. Muller, *Methoden Org. Chem. (Houben-Weyl), 4th Ed., 1962,* **5,** Part 3, 768 (1962).
(7) A. Detoeuf, *Bull. Soc. Chim. Fr.*, **31,** 169 (1922).
(8) E. H. Appelman and H. Kim, *J. Chem. Phys.*, **57,** 3272 (1972).
(9) V. Markownikoff, *C. R. Hebd. Seances Acad. Sci.*, **82,** 668 (1875).
(10) A. Feldstein and C. A. VanderWerf, *J. Am. Chem. Soc.*, **76,** 1626 (1954).
(11) R. Fuchs and C. A. VanderWerf, *J. Am. Chem. Soc.*, **76,** 1631 (1954).
(12) A. Kergomard and G. Farges, *Bull. Soc. Chim. Fr.*, 51 (1963).
(13) G. Aranda, J. Jullien, and J. A. Martin, *Bull. Soc. Chim. Fr.*, 1890 (1965).
(14) A. Rosowsky in "*Heterocyclic Compounds with Three- and Four-Membered Rings, Part 1*", A. Weissberger, Ed., Wiley-Interscience, New York, 1964, p 1.
(15) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59,** 737 (1959).
(16) S. Patai, Ed., "*The Chemistry of the Ether Linkage*", Interscience, London, 1967.
(17) (a) J. Biggs, N. B. Chapman, and V. Wray, *J. Chem. Soc. B*, 66 (1971); (b) *ibid.*, 63 (1971); (c) *ibid.*, 71 (1971).
(18) J. Novak and J. Antosova, *Collect. Czech. Chem. Commun.*, **35,** 1096 (1970).
(19) M. J. Klug and A. J. Markovetz, *Adv. Microb. Physiol.*, **5,** 1 (1971).
(20) W. Weigert, H. Klebe, A. Meffert, G. Kaebisch, and A. Langenfeld, Ger. Offen. 2 160 613 (June 20, 1973); *Chem. Abstr.*, **79,** 65718f (1973).
(21) N. Matsumura, N. Sonoda, and S. Tsutsumi, *Tetrahedron Lett.*, 2029 (1970).
(22) A. Dansi and C. Pasini, *Gazz. Chim. Ital.*, **81,** 508 (1951).
(23) R. Breslow, J. Brown, and J. J. Gajewski, *J. Am. Chem. Soc.*, **89,** 4383 (1967).
(24) R. N. McDonald and P. Schwab, *J. Am. Chem. Soc.*, **86,** 4866 (1964).
(25) J. K. Stille and D. D. Whitehurst, *J. Am. Chem. Soc.*, **86,** 4871 (1964).
(26) R. F. Merritt and J. K. Ruff, *J. Org. Chem.*, **30,** 328 (1965).
(27) M. Hudlicky, "Chemistry of Organic Fluorine Compounds", 2nd. ed., Ellis Horwood Ltd., Chichester, 1976, p 36–41.
(28) J. A. Martin, *C. R. Hebd. Seances Acad. Sci.*, **261,** 4385 (1965).
(29) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, San Francisco, 1967, p 96.
(30) J. Jullien, J. A. Martin, and R. Ramanadin, *Bull. Soc. Chim. Fr.*, 171 (1964).
(31) (a) E. Stenhagen, S. Abrahamsson, and F. W. McLafferty, Eds., Registry of Mass Spectral Data", Wiley, New York, 1974, pp 443, 971; (b) *ibid.*, p 282.
(32) C. J. Pouchert, Ed., "The Aldrich Library of Infrared Spectra", 2nd ed., Aldrich Chemical Co., Milwaukee, Wis., 1975, p 375.
(33) P. Duhamel, L. Duhamel, and J. Gralak, *Bull. Soc. Chim. Fr.*, 3641 (1970).
(34) D. P. Wyman, B. L. Shapiro, and P. R. Kaufman, *Can. J. Chem.*, **43,** 2433 (1965).

Efficient Synthesis of 3-Substituted Aspartic Acids[1]

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3-Substituted aspartic acids are a class of physiologically interesting amino acids. For example, 3-hydroxyaspartic acid,[2] 3-methylaspartic acid,[3] 3-phenylaspartic acid,[4] 3-aminoaspartic acid (2,3-diaminosuccinic acid),[4] and their derivatives are attractive substances as a possible antagonist of aspartic acid, and some of these possess antibacterial activity. Of these, 3-aminoaspartic acid derivatives are also important intermediates for biotin[5] and 3-fluoroaspartic acid,[6] which is a useful precursor of 5-fluorouracil.[7] With regard to the synthesis of 3-aminoaspartic acid, two conventional methods are known: the first method is an amination of dibromosuccinic acid with benzylamine, followed by debenzylation;[8a,b] the second is a newer method by photodimerization of *N*-acylglycinate.[9]

In this regard, we have attempted to exploit the more versatile method for the synthesis of the 3-substituted amino acids in the course of studies on the synthesis of amino acids and related compounds. Most recently, we have found that 2-acetoxyamino acid derivatives were useful cationic synthons, which reacted with various nucleophiles to afford 2-substituted amino acid derivatives in excellent yields.[10] In the present study, this finding has been extended to the C–C bond formation by the reaction with carbanion as a nucleophile; this paper describes that the method has effected a potentially general synthesis of 3-substituted aspartic acids, especially 3-aminoaspartic acid derivatives as shown in Scheme I.

The reaction of ethyl 2-acetoxyglycinate (**1**), which was prepared by the anodic oxidation of ethyl *N*-acetylaminomalonate,[11] with an anionic source possessing the glycine skeleton (**2**) proceeded smoothly in the presence of sodium hydride. After the reaction mixture was worked up in the usual manner, the products were purified by column chromatography on silica gel. The resulting *N*-acetyl-3-substituted-aspartic acid derivatives (**3**) were identified by IR and NMR spectroscopies as described in the Experimental Section. When diethyl *N*-acetylaminomalonate (**2a**), diethyl *N*-formylaminomalonate (**2b**), diethyl *N*-carbobenzoxyaminomalonate (**2c**), and ethyl 2-(*N*-acetylamino)cyanoacetate (**2d**) as the carbanion sources having glycine skeleton were used, the corresponding coupling products (**3a–d**) were obtained in high yields. Of these, the compound **3d** was isolated as crystals in 55% yield, which seemed to be a single isomer; unfortunately, the stereochemistry was not determined in this study. Subsequently, these coupling products were hydrolyzed with hydrochloric acid to afford the desired 2,3-diaminosuccinic acid (**4**), which was a diastereomeric mixture of (±) and meso forms, in a good yield as shown in the Experimental Section.

The synthetic method was further applied to the preparation of other 3-substituted aspartic acid analogues. The reaction of the acetoxyglycinate (**1**) with ethyl acetoacetate and ethyl cyanoacetate afforded diethyl *N*-acetyl-3-acetylaspartate (**5**)[12] and diethyl *N*-acetyl-3-cyanoaspartate (**6**), respectively, in good yields. Further attempts to prepare the 2-methylaspartic acid derivative were carried out using ethyl *N*-acetyl-2-acetoxyalaninate (**1'**). As a typical example, diethyl *N*-acetyl-3-cyano-2-methylaspartate (**6'**) was synthesized in

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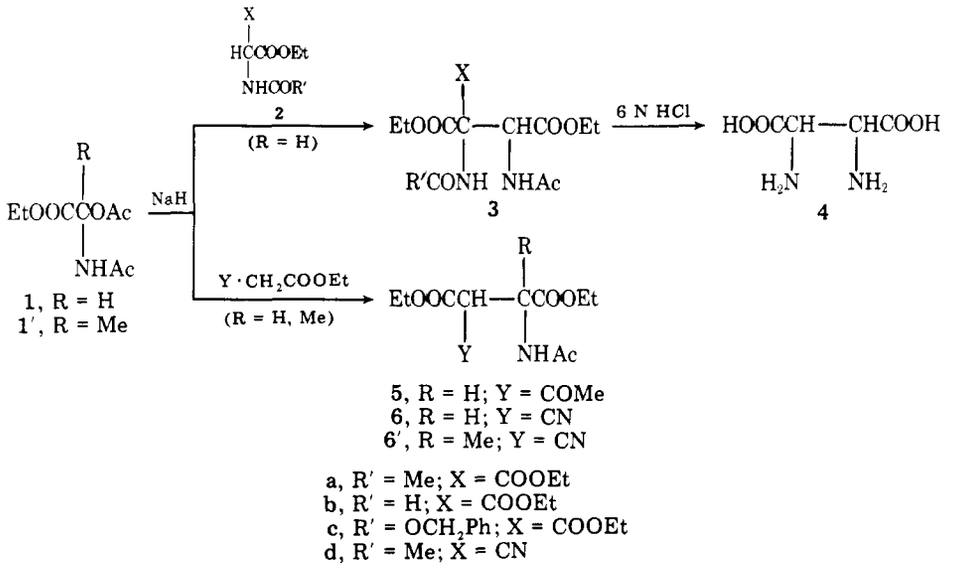
Scheme I



a good yield without formation of elimination product (dehydroalanine derivative) and Michael adduct to the dehydro compound. These results suggest that the reaction would proceed via the acylimine intermediate as postulated previously.[10]

Experimental Section

General. All melting points are uncorrected. Melting points were measured by the use of a Yamato melting point apparatus. IR spectra were recorded on a Shimadzu IR-27G infrared spectrophotometer. NMR spectra were obtained using a Hitachi Perkin-Elmer R-20A high-resolution NMR spectrometer with Me_4Si as internal standard.

Starting Materials. Ethyl *N*-acetyl-2-acetoxyglycinate (**1**) and ethyl *N*-acetyl-2-acetoxyalaninate (**1'**) were prepared by the method previously reported by us.[11]

Synthesis of 3-Aminoaspartic Acid Derivatives (3). General Procedure. To a stirred suspension of 65% sodium hydride (0.88 g, 0.024 mol) and diethyl *N*-acylaminomalonate (**2**) (0.02 mol) in tetrahydrofuran (20 mL) was added a solution of **1** (4.06 g, 0.02 mol) in tetrahydrofuran (10 mL) at 0–5 °C for 15 min. After the mixture was stirred for 2 h at room temperature, the mixture was evaporated to dryness in vacuo. The oily residue was extracted with ethyl acetate and the solution was washed with water and dried over magnesium sulfate. Then the solution was evaporated to dryness in vacuo and the resulting product was purified by column chromatography on silica gel using $CHCl_3$ as an eluent.

Diethyl *N*-acetyl-3-(*N*-acetylamino)-2-ethoxycarbonylaspartate (3a): obtained as a syrup; yield 95%; IR (Nujol) ν_{max} 3320, 1750, 1670, 1520 cm^{-1}; NMR (CCl_4) δ 1.24 (t, 6 H, $2COOCH_2CH_3$), 1.32 (t, 3 H, $COOCH_2CH_3$), 1.93, 2.04 (two s, 6 H, $2COCH_3$), 4.08, 4.15, 4.28 (three q, 6 H, $3COOCH_2CH_3$), 5.26 (d, 1 H, CH, J = 7.7 Hz), 7.24 (s, 1 H, NH), 7.69 (d, 1 H, NH, J = 7.7 Hz). Anal. Calcd for $C_{15}H_{24}O_8N_2$: C, 49.99; H, 6.71; N, 7.77. Found: C, 50.08; H, 6.74; N, 7.86.

Diethyl *N*-acetyl-3-(*N*-formylamino)-2-ethoxycarbonylaspartate (3b): obtained as a syrup; yield 84%; IR (Nujol) ν_{max} 3300, 1750, 1670, 1520 cm^{-1}; NMR ($CDCl_3$) δ 1.23, 1.25, 1.33 (three t, 9 H, $3COOCH_2CH_3$), 2.02 (s, 3 H, $COCH_3$), 4.13, 4.25, 4.34 (three q, 6 H, $3COOCH_2CH_3$), 5.63 (d, 1 H, CH, J = 8.0 Hz), 7.22 (br, 1 H, NH), 7.77 (d, 1 H, NH, J = 8.0 Hz), 8.16 (d, 1 H, CHO, J = 1.5 Hz). Anal. Calcd for $C_{14}H_{22}O_8N_2$: C, 48.55; H, 6.40; N, 8.09. Found: C, 48.39; H, 6.38; N, 7.98.

Diethyl *N*-acetyl-3-[*N*-(benzyloxycarbonyl)amino]-2-ethoxycarbonylaspartate (3c): obtained as a syrup; yield 92%; IR (Nujol) ν_{max} 3400, 1750, 1690, 1515 cm^{-1}; NMR (CCl_4) δ 1.20 (t, 6 H, $2COOCH_2CH_3$), 1.33 (t, 3 H, $COOCH_2CH_3$), 1.95 (s, 3 H, $COCH_3$), 4.14, 4.21, 4.33 (three q, 6 H, $3COOCH_2CH_3$), 5.15 (s, 2 H, CH_2), 5.52 (d, 1 H, CH, J = 8.4 Hz), 6.39 (s, 1 H, NH), 7.35 (s, 5 H, Ph), 7.57 (d, 1 H, NH, J = 8.4 Hz). Anal. Calcd for $C_{21}H_{28}O_9N_2$: C, 55.74; H, 6.24; N, 6.19. Found: C, 55.86; H, 6.24; N, 6.26.

Diethyl *N*-acetyl-3-(*N*-acetylamino)-3-cyanoaspartate (3d): obtained as crystals; yield 55%; mp 122–126 °C (ethyl acetate–diisopropyl ether); IR (Nujol) ν_{max} 3250, 1760, 1660, 1530 cm^{-1} [13]; NMR ($CDCl_3$) δ 1.31, 1.34 (two t, 6 H, $2COOCH_2CH_3$), 2.02, 2.18 (two s, 6 H, $2COCH_3$), 4.29 (q, 4 H, $2COOCH_2CH_3$), 5.14 (d, 1 H, CH, J = 7.8 Hz), 7.21 (d, 1 H, NH, J = 7.8 Hz), 8.06 (s, 1 H, NH). Anal. Calcd for $C_{13}H_{19}O_6N_3$: C, 49.83; H, 6.11; N, 13.41. Found: C, 49.82; H, 6.13; N, 13.44.

Synthesis of 3-Aminoaspartic Acid (4). A mixture of **3a** (3.6 g, 0.01 mol) and 6 N hydrochloric acid (60 mL) was heated at 90–100 °C for 4 h. The solution was evaporated to dryness in vacuo and the residue was dissolved in water (10 mL). Then the solution was treated with ion exchange resin, Amberlite IR 120 (H^+ form). After the resin was washed with water, the amino acid was eluted with 5% ammonia. The eluate was evaporated to dryness in vacuo and the resulting crystals were washed with methanol to afford diaminosuccinic acid [3-aminoaspartic acid (**4**)]: yield 1.33 g; 90%; mp 260–285 °C dec;[8a] IR (Nujol) ν_{max} 3470, 2100, 1630 cm^{-1}. Anal. Calcd for $C_4H_8O_4N_2$: C, 32.43; H, 5.44; N, 18.91. Found: C, 32.15; H, 5.49; N, 18.60. By the same treatment, the compounds **3b, 3c,** and **3d** were converted into **4** in 85–90% yields.

Synthesis of Diethyl *N*-Acetyl-3-acetylaspartate (5). According to the general procedure for preparation of 3-aminoaspartic acid derivatives, the reaction of ethyl acetoacetate with **1** was carried out to give **5** in 80% yield: 86–88 °C (ethyl acetate–diisopropyl ether); IR (Nujol) ν_{max} 3340, 1725, 1715, 1650, 1545 cm^{-1}; NMR ($CDCl_3$) δ 1.23, 1.27 (two t, 6 H, $2COOCH_2CH_3$), 2.01 (s, 3 H, $COCH_3$), 2.32 (s, 3 H, C_3-$COCH_3$), 4.18, 4.22 (two q, 4 H, $2COOCH_2CH_3$), 4.28 (d, 1 H, C_3-H, J = 4.5 Hz), 5.25 (dd, 1 H, C_2-H, J = 4.5, 8.7 Hz), 6.66 (d, 1 H, NH, J = 8.7 Hz). Anal. Calcd for $C_{12}H_{19}O_6N$: C, 52.74; H, 7.01; N, 5.13. Found: C, 52.68; H, 7.05, N, 5.11.

Synthesis of Diethyl *N*-Acetyl-3-cyanoaspartate (6). Ethyl cyanoacetate reacted with **1** as described above to afford **6** in 65% yield: mp 82–85 °C (ethyl acetate–diisopropyl ether); IR (Nujol) ν_{max} 3260, 2320, 1750, 1665, 1550 cm^{-1}; NMR ($CDCl_3$) δ 1.31, 1.33 (two t, 6 H, $2COOCH_2CH_3$), 2.14 (s, 3 H, $COCH_3$), 4.30, 4.33 (two q, 4 H, $2COOCH_2CH_3$), 4.38 (d, 1 H, C_3-H, J = 3.75 Hz), 5.33 (dd, 1 H, C_2-H, J = 3.75, 7.5 Hz), 6.92 (d, 1 H, NH, J = 7.5 Hz). Anal. Calcd for $C_{11}H_{16}O_5N_2$: C, 51.96; H, 5.55; N, 11.02. Found: C, 51.72; H, 5.41; N, 10.87.

Synthesis of Diethyl *N*-Acetyl-3-cyano-2-methylaspartate (6'). This compound (**6'**) was prepared by the reaction of **1'** and ethyl cyanoacetate in 80% yield: mp 79–82 °C (ethyl acetate–diisopropyl ether); IR (Nujol) ν_{max} 3270, 2260, 1740, 1650, 1550 cm^{-1}; NMR ($CDCl_3$) δ 1.30 (t, 6 H, $2COOCH_2CH_3$), 1.79 (s, 3 H, CH_3), 1.98 (s, 3 H, $COCH_3$), 4.25 (q, 4 H, $2COOCH_2CH_3$), 4.76 (s, 1 H, CH), 6.65 (s, 1 H, NH). Anal. Calcd for $C_{12}H_{18}O_5N_2$: C, 53.32; H, 6.71; N, 10.37. Found: C, 53.23; H, 6.69; N, 10.35.

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Registry No.—**1**, 62183-05-5; **1'**, 62183-00-0; **2a**, 1068-90-2; **2b**, 6326-44-9; **2c**, 3005-66-1; **2d**, 4977-62-2; **3a**, 69440-23-9; **3b**, 69440-24-0; **3c**, 69454-63-3; **3d**, 69440-25-1; *dl*-**4**, 29276-73-1; **5**, 69440-26-2; **6**, 69440-27-3; **6'**, 69440-28-4; ethyl cyanoacetate, 105-56-6.

References and Notes

(1) Syntheses of Amino Acids and Related Compounds. 22. Part 21, ref 6.
(2) T. Ishiyama, T. Furuta, M. Takai, and Y. Okimoto, *J. Antibiot.*, **23**, 821 (1975).
(3) D. W. Woolley, *J. Biol. Chem.*, **235**, 3238 (1960).
(4) P. K. Chang, L. J. Sciarini, and R. E. Handschumacher, *J. Med. Chem.*, **16**, 1277 (1973).
(5) For example, S. Laviell, S. Bory, B. Moreau, M. J. Luche, and A. Marquet, *J. Am. Chem. Soc.*, **100**, 1558 (1978), and references cited therein.
(6) K. Matsumoto, Y. Ozaki, T. Iwasaki, H. Horikawa, and M. Miyoshi, *Experientia*, in press.
(7) Our unpublished data.
(8) (a) W. Wenner, *J. Org. Chem.*, **13**, 26 (1948); (b) H. McKennis, Jr., and A. S. Yard, *J. Org. Chem.*, **23**, 980 (1958).
(9) N. Obata and K. Niimura, *J. Chem. Soc., Chem. Commun.*, 238 (1977).
(10) Y.Ozaki, T. Iwasaki, H. Horikawa, M. Miyoshi, and K. Matsumoto, *J. Org. Chem.*, **44**, 391 (1979).
(11) T. Iwasaki, H. Horikawa, K. Matsumoto, and M. Miyoshi, *J. Org. Chem.*, **42**, 2419 (1977).
(12) D. Ben-Ishai, J. Altman, Z. Bernstein, and N. Peled, *Tetrahedron*, **34**, 467 (1978); the report described a synthesis of a *N*-benzoyl-3-acetylaspartic acid derivative by a reaction of methyl α-methoxyhippurate with methyl acetoacetate in the presence of $BF_3{\cdot}OEt_2$.
(13) The characteristic absorption of CN group was not observed.

Facile Synthesis of 4-Acetoxy-2-methyl-2-butenal, a Vitamin A Precursor, from Isoprene Chlorohydrin

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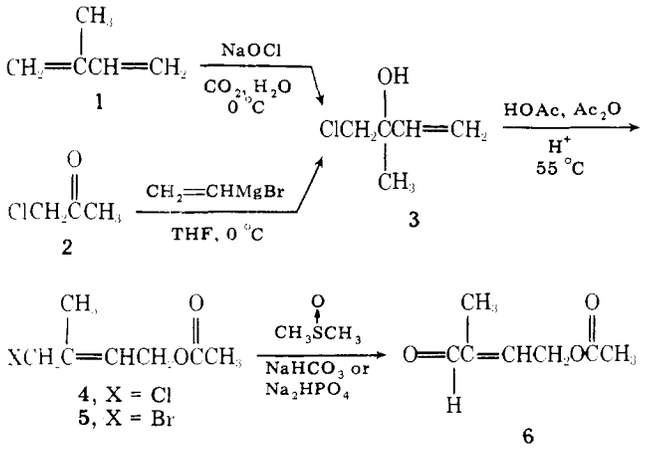
One of the commercial syntheses of vitamin A involves the preparation of 4-acetoxy-2-methyl-2-butenal (**6**) [also known as β-formylcrotyl acetate and γ-acetoxytiglicaldehyde] as a key intermediate.[2] Recently, Wehrli and Schaer have reported[3] an extremely simple route to this aldehyde (**6**) starting from isoprene (**1**). This present note discusses a similarly facile method that we have developed for converting isoprene to aldehyde **6** (Scheme I).

It is well known[4] that certain primary alkyl halides can be oxidized to aldehydes using dimethyl sulfoxide (Me_2SO) in the presence of a weak nonnucleophilic base. The required precursor to γ-acetoxytiglicaldehyde (**6**) using this oxidation step would be 4-bromo-3-methyl-2-buten-1-ol acetate (**5**) or the corresponding chloride (**4**).[5] As a model system for the desired transformation (i.e., **5** → **6**), 1-bromo-3,7-dimethyl-2,6-octadiene (geranyl bromide) was treated with 1 equiv of sodium bicarbonate in Me_2SO at room temperature for 15 h. Instead of obtaining the expected aldehyde (citral), NMR and IR analysis indicated the product to be a mixture of trienes

Scheme I



derived from a competing elimination reaction. Similar results were obtained when either 1-bromo-3-propyl-2-hexene[6] or 1-bromo-2-octene[7] was treated under the same conditions.

This failure to oxidize a primary allylic bromide to the corresponding α,β-unsaturated aldehyde using Me_2SO is consistent with results of similar experiments by Ganem and Boeckman.[8] In view of these negative results, it was much to our surprise that allylic bromide **5** was oxidized to the corresponding aldehyde (**6**) in 80% yield using Me_2SO in the presence of sodium bicarbonate at room temperature.

Since bromide **5** was difficult[5] to obtain in good yield and to purify, we decided to develop an efficient synthesis of the corresponding chloride (**4**). Addition of vinylmagnesium bromide to chloroacetone (**2**) afforded[9] an excellent yield of isoprene chlorohydrin (**3**).[10] Subsequent treatment of the latter compound with glacial acetic acid containing 1 equiv of acetic anhydride and a strong acid catalyst[11] went quite smoothly to give the corresponding rearranged primary allylic acetate (**4**) as the sole isolated product in 80% yield.

Treatment of primary allylic chloride **4** with dimethyl sulfoxide and 1 equiv of sodium bicarbonate proved to be a sluggish reaction, even at a temperature of 80 °C. However, in the presence of a catalytic amount (5–10%) of sodium bromide, chloride **4** could be oxidized to the corresponding aldehyde (**6**) using dimethyl sulfoxide and 1 equiv of a suitable base at 80 °C. The reaction conditions chosen for this oxidation are quite critical insofar as the yield of aldehyde **6** is concerned. The best yield of aldehyde **6** was obtained when potassium phosphate dibasic (K_2HPO_4) was employed as the nonnucleophilic base[12] for this high-temperature oxidation. A further improvement in yield was achieved by the addition of a small amount of potassium phosphate monobasic (KH_2PO_4) as a buffer.

An added feature to the oxidation of allylic chloride **4** at 80 °C was the discovery that under the reaction conditions (*Z*)-4-acetoxy-2-methyl-2-butenal slowly, but quantitatively, isomerized to the more stable *E* stereoisomer, which could be isolated in >80% yield after purification of the reaction product. If the oxidation reaction was stopped after 5 h, isolation of the product indicated the presence of unreacted starting material (**4**) as well as aldehyde **6** as a 6:1 mixture of *E*/*Z* stereoisomers. However, after 18 h using identical conditions, none of the *Z* stereoisomer could be detected by NMR analysis. In view of the stereoselectivity of this oxidation step and the ease of preparing 1,4-haloacetate derivatives of isoprene, the method reported in this note is an attractive one for synthesis of (*E*)-4-acetoxy-2-methyl-2-butenal (**6**).

Experimental Section

General. Reactions were carried out under a nitrogen atmosphere. The isolation of reaction products was accomplished by extracting with the specified solvent. The combined extracts were washed thoroughly with saturated brine and then dried over anhydrous magnesium sulfate. The solvent was removed from the dried extracts by using a rotary evaporator under reduced pressure. Evaporative distillation refers to bulb-to-bulb (Kugelrohr) short-path distillation. The NMR spectra were recorded with a Varian EM-360 spectrometer and infrared spectra were obtained using a Beckman Acculab 1 spectrophotometer.

4-Chloro-3-methyl-2-buten-1-ol Acetate (4). A solution of 127 mg (0.67 mmol) of *p*-toluenesulfonic acid monohydrate in 3.0 mL of glacial acetic acid was added dropwise to a chilled (~15 °C, bath temperature) mixture of 767 mg (6.37 mmol) of 1-chloro-2-methyl-3-buten-2-ol (**3**)[13] and 1.0 mL (10.6 mmol) of acetic anhydride in 3.0 mL of glacial acetic acid. This solution was then heated at 55 °C[14] (bath temperature) for 18 h. After cooling the reaction mixture to room temperautre, it was poured cautiously into 80 mL of 10% aqueous sodium hydroxide solution mixed with 40 g of cracked ice. Extraction of the product with ether, followed by evaporative distillation, afforded 827 mg (80%) of allylic chloride **4** as a 6:1 mixture[15] of *E*/*Z* stereoisomers: bp 35–45 °C (bath temperature, 0.1 mm) [lit.[16] bp 91–93 °C (10 mm)]; IR ν_{max} (film) 1740 (C=O), 1235, 1025, 960,

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