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(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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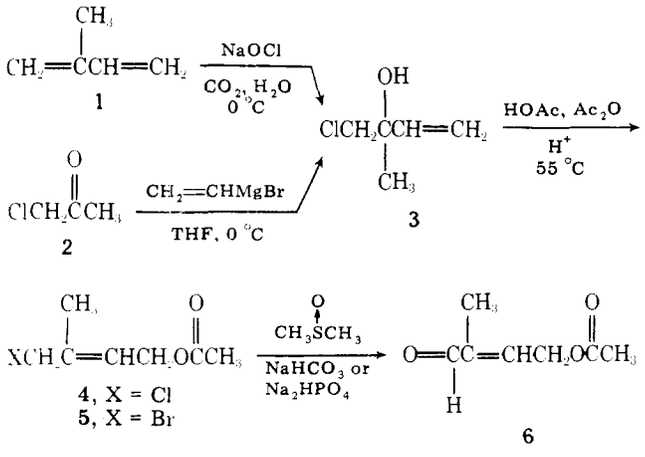
One of the commercial syntheses of vitamin A involves the preparation of 4-acetoxy-2-methyl-2-butenal (**6**) [also known as β-formylcrotyl acetate and γ-acetoxytiglicaldehyde] as a key intermediate.[2] Recently, Wehrli and Schaer have reported[3] an extremely simple route to this aldehyde (**6**) starting 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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685 cm^{-1}; NMR (Me_4Si, CCl_4) δ 5.68 (t, J = 7 Hz, vinyl H), 4.57 (d, J = 7 Hz, CH_2OAc), 4.09 (s, "Z" CH_2Cl), 3.99 (s, "E" CH_2Cl), 2.02 (s, $OC(=O)CH_3$), 1.85 (br s, vinyl CH_3).

Conversion of Allylic Bromide 5 to 4-Acetoxy-2-methyl-2-butenal (6). A mixture of 1.10 g (5.3 mmol) of 4-bromo-3-methyl-2-buten-1-ol acetate (**5**)[17] and 500 mg (5.95 mmol) of sodium bicarbonate in 8 mL of anhydrous dimethyl sulfoxide was stirred vigorously at room temperature for approximately 20 h. The product was isolated by diluting the mixture with 75 mL of water and extracting thoroughly with carbon tetrachloride. Chromatography[18] on silica gel (40 mL, elution with hexane–10% ether) afforded 610 mg (81%) of aldehyde **6** as a 4:1 mixture[19] of E/Z stereoisomers, the spectral properties of which were identical with those previously reported[20] for this same compound.

Conversion of Allylic Chloride 4 to 4-Acetoxy-2-methyl-2-butenal (6). To a 25-mL flask equipped with an efficient stirrer and Vigreux column were added 536 mg (3.3 mmol) of 4-chloro-3-methyl-2-buten-1-ol acetate (**4**), 4 mL of anhydrous dimethyl sulfoxide, 662 mg (3.80 mmol) of K_2HPO_4, 138 mg (1.02 mmol) of KH_2PO_4,[21] and 40 mg (0.38 mmol) of sodium bromide. This mixture was then heated, protected from atmospheric moisture, at 80 °C (bath temperature) for 18 h. The product was isolated by cooling the mixture to room temperature, pouring it into 40 mL of water, and extracting thoroughly with carbon tetrachloride. VPC analysis (6 ft × $\frac{1}{8}$ in. SE-30 column, oven temperature 165 °C, flow 30 mL/min) indicated the crude product (452 mg, 97% yield) to consist mainly of two components: aldehyde **6** (retention time 2.3 min, >83% of the mixture) and an unidentified higher boiling component (14% of the mixture, retention time 5.0 min). NMR analysis[19] indicated the absence of the Z stereoisomeric aldehyde (**6**) in the crude product. Purification of this material[18] was achieved via chromatography on silica gel as described above, affording (*E*)-4-acetoxy-2-methyl-2-butenal (**6**)[20] in approximately 80% yield.

Registry No.—**3**, 7437-62-9; (*E*)-**4**, 24529-80-4; (*Z*)-**4**, 24529-81-5; (*E*)-**5**, 32659-14-6; (*Z*)-**5**, 32659-13-5; **6**, 26586-02-7; (*Z*)-**6**, 69551-41-3.

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(11) For an analogous rearrangement process, see J. H. Babler and D. O. Olsen, *Tetrahedron Lett.*, 351 (1974).
(12) Sodium bicarbonate could not be utilized under these reaction conditions. The water liberated when $NaHCO_3$ functions as a base apparently promoted hydrolysis of the acetate moiety, leading to an unstable intermediate which could not be isolated and identified.
(13) Alcohol **3** was prepared by addition of an ether solution of chloroacetone to 1.3 equiv of vinylmagnesium bromide in tetrahydrofuran at 0 °C. For the experimental details, see ref 9.
(14) The rearrangement proceeded too slowly at room temperature.
(15) VPC analysis (6 ft × $\frac{1}{8}$ in., SE-30 column, oven temperature 150 °C, flow 28 mL/min) indicated that >96% of the distillate was a 6:1 mixture of E/Z stereoisomers (retention times 2.7 and 2.4 min, respectively). This ratio was also consistent with that determined by NMR analysis. The *E* stereoisomer was characterized by a singlet at δ 3.99 (CH_2Cl), whereas the corresponding signal for the *Z* stereoisomer was δ 4.09 (CH_2Cl, singlet).
(16) W. Oroshnik and R. A. Mallory, *J. Am. Chem. Soc.*, **72**, 4608 (1950).
(17) Allylic bromide **5** [E/Z ratio: 70:30] was prepared using the method given in ref 5.
(18) On a large scale, fractional distillation would be more convenient to separate aldehyde **6** from the minor impurities present in the crude product.
(19) Determined by NMR analysis. The *E* stereoisomer was characterized by a singlet at δ 9.54 (CHO), whereas the corresponding signal for the *Z* stereoisomer was δ 10.23 (singlet, CHO).
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(21) In the absence of potassium phosphate monobasic, the yield of (*E*)-4-acetoxy-2-methyl-2-butenal (**6**) was only ~60% (79% crude yield).

Thermolysis of Diazodicyanoimidazole: Products and Rates, the Effect of 18-Crown-6

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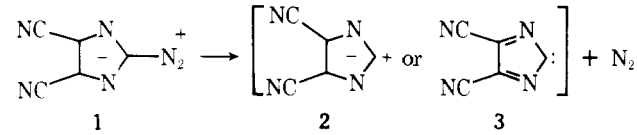
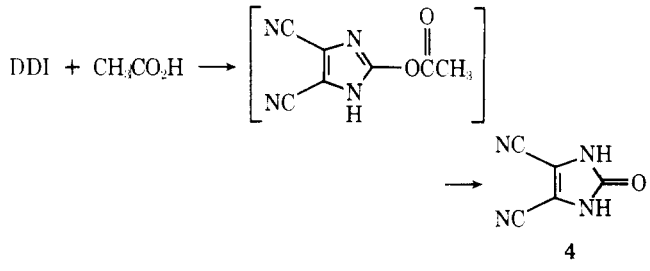
The intermediate from thermolysis of diazodicyanoimidazole (DDI, 1) is highly electrophilic; for example, it is trapped by aryl halides to form stable aromatic haloylides.[3] Structure **2**, with the negative charge stabilized by the two cyano groups and the aromatic sextet, has been suggested for this intermediate.[3] Form **3** is also a possible structure. If the intermediate is best represented by **2** rather than **3**, then nitrogen elimination should be enhanced in polar solvents due to solvation of **2**. In addition, since the solid phase stability of DDI is greatly increased in the crystalline 18-crown-6 complex, the solution phase stability of the DDI·18-crown-6 complex is of interest. A similar stabilization has been noted for aryldiazonium salts stabilized as "host–guest" complexes.[4,5]



1 2 3

The decomposition of DDI in acetic acid gives 4,5-dicyano-2-imidazolone (**4**) which has been previously prepared by other methods.[11]



4

In hot water or aqueous acetic acid DDI gives a quantitative amount of nitrogen but the product is intractable.

In benzonitrile the product from DDI thermolysis is the fused heterocycle **6** which probably forms by reaction of the intermediate nitrilium ylide **5** with a second mole of benzonitrile.

The rate of nitrogen elimination from DDI is first order and correlates with the Y value of solvent.[6] The trend is toward a *slower* rate of decomposition in more polar media. This would seem to reflect a greater solvation of starting material which retards the nitrogen extrusion process in more polar

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