Brief Communications

Reactions of (1*S*,3*S*)-3-acetoxymethyl-1-(2-acetoxyvinyl)-2,2-dimethylcyclopropane with haloforms under conditions of phase-transfer catalysis

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Heating of (1*S*,3*S*)-3-acetoxymethyl-1-(2-acetoxyvinyl)-2,2-dimethylcyclopropane with bromoform under phase-transfer catalysis affords dibromocyclopropane *via* addition of dibromocarbene to the double bond. In an analogous reaction with chloroform, the trichloromethyl anion adds to the double bond in the α-position with respect to the acetoxy group.

Key words: dicyclopropanes, (+)-3-carene, dibromocyclopropanes, phase-transfer catalysis, enol ester.

gem-Dihalocyclopropanes possessing high reactivity and biological activity can conveniently be synthesized by addition of dihalocarbenes to olefins, which depends on the electrophilicity of substituents at the double bond.[1—3] For this reason, it was of interest to study the effect of a cyclopropane fragment on dihalocyclopropanation of olefins containing an electron-deficient double bond.

Enol acetate **2** prepared by ozonization of (+)-3-carene[4] (**1**) was made to react with dihalocarbenes (generated from $CHCl_3$ and $CHBr_3$) under conditions of phase-transfer catalysis (Scheme 1). Cyclopropanation of the double bond in enol acetate **2** was found to occur only in the reaction with dibromocarbene, yielding (1*S*,3*S*)-3-acetoxymethyl-1-(2,2-dibromo-3-acetoxycyclopropyl)-2,2-dimethylcyclopropane (**3**). When a mixture of $CHCl_3$ and enol acetate **2** was stirred in a basic medium at elevated temperature in the presence of a phase-transfer catalyst, addition of the trichloromethyl anion to the double bond in the α-position with respect to the acetoxy group was effected to give (1*R*,3*S*)-1-(2-acetoxy-3,3,3-trichloropropyl)-3-acetoxymethyl-2,2-dimethylcyclopropane (**4**).

Different reaction products for $CHCl_3$ and $CHBr_3$ can be due to an equilibrium between $CHal_3^-$ and $:CHal_2$ generated from haloforms under phase-transfer catalysis

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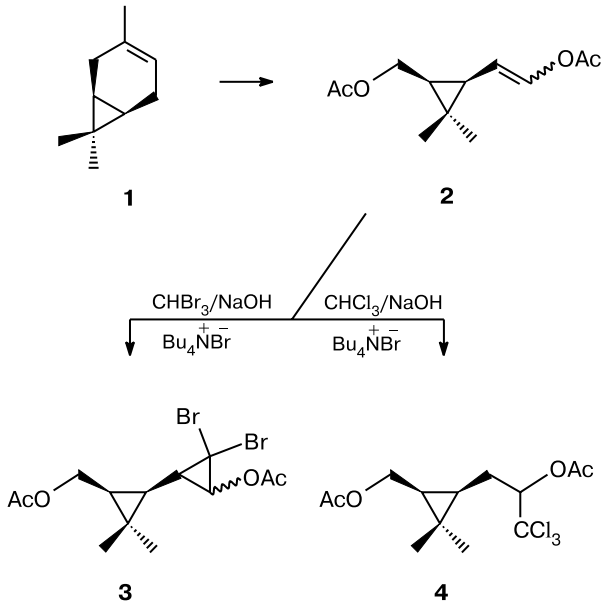
Scheme 1



conditions and to their different reactivities in reactions with olefins containing electron-deficient double bonds (*e.g.,* enol acetate **2**).[5—7] Enol acetate **2**, in which the double bond is activated by a cyclopropanyl fragment, can react with a less electrophilic and more reactive dibromocarbene. Such an activation is insufficient for cycloaddition of more electrophilic dichlorocarbene; as a result, the CCl_3^- anion enters into the reaction. The cycloaddition of dibromocarbene to enol acetate **2** is stereospecific; this is evident from the ratio of *cis/trans*-isomers (1.5 : 1, ^{13}C NMR data), which is the same as in the starting olefin **2** and consistent with the literature data.[8,9]

Doubled signals in the ^1H and ^{13}C NMR spectra of compound **4** suggest the presence of two diastereomers about the chiral $\underline{C}CCl_3$ center in a ratio of ~1.5 : 1.

Hence, dibromocarbene generated in the reaction of diacetate **2** with bromoform under phase-transfer catalysis conditions is added to the double bond to give dibromocyclopropane **3**, while the reaction with chloroform under analogous conditions affords an adduct containing a trichloromethyl group in the α-position relative to the acetoxy group.

Experimental

IR spectra were recorded on a Specord M-80 instrument (thin film) in the 400—4000 cm^{-1} range. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75.46 MHz, respectively) in $CDCl_3$ with Me_4Si as the internal standard. Chemical shifts are referenced to the δ scale. Specific rotation was measured in $CHCl_3$ on a Perkin—Elmer 241 MS polarimeter. GLC analysis was carried out on a Chrom-5 chromatograph (column 1200 × 3 mm, SE-30 silicone (5%) on Chromaton *N*-AW-DMSC (0.16—0.20 mm) as a stationary phase, working temperature 50—300 °C, helium as a carrier gas).

(1*S*,3*S*)-3-Acetoxymethyl-1-(2-acetoxyvinyl)-2,2-dimethylcyclopropane (2) was prepared as described earlier.[4]

(1*S*,3*S*)-3-Acetoxymethyl-1-(2,2-dibromo-3-acetoxycyclopropyl)-2,2-dimethylcyclopropane (3). A mixture of diacetate **2** (0.5 g, 2.2 mmol), Bu^n_4NBr (0.021 g, 0.066 mmol), $CHBr_3$ (0.83 g, 3.28 mmol), EtOH (0.04 mL), and freshly calcined NaOH (0.37 g, 9.25 mmol) in 6 mL of CH_2Cl_2 was refluxed with stirring for 72 h. The reaction mixture was diluted with 100 mL of AcOEt, washed with 3% HCl and brine (15 mL each), and dried with Na_2SO_4. The solvent was removed, and the residue was chromatographed on SiO_2 in hexane—AcOEt (19 : 1) to give compound **3** (0.36 g, 41%) as a mixture of *cis/trans*-isomers in a ratio of 1.5 : 1, $[\alpha]_D^{20}$ +7.54 (*c* 2.1, $CHCl_3$), R_f 0.71 (Silufol, hexane—AcOEt, 4 : 1). Found (%): C, 38.45, H, 4.32, Br, 38.72. $C_{13}H_{18}O_4Br_2$. Calculated (%): C, 39.19, H, 4.52, Br, 40.20. IR, ν/cm^{-1}: 1740, 1720 (C=O); 688, 604 (CBr_2). ^1H NMR, δ: 0.81—0.96 (m, 1 H, H(3)); 0.98, 1.05, 1.07, 1.09 (all s, 6 H, C(2)Me_2); 1.12—1.22 (m, 1 H, H(1)); 1.97, 1.99, 2.00, 2.02 (all s, 6 H, 2 MeCO); 2.04—2.15 (m, 1 H, C(1)CH); 3.85—3.97, 4.05—4.20 (both m, 3 H, CH_2, OCH). ^{13}C NMR, δ: 14.8, 15.2 and 28.6, 28.6 (all q, $(\underline{C}H_3)_2C$); 18.9 (s, C(2)); 24.5, 24.6 and 25.1, 25.2 (all q, $\underline{C}H_3CO$); 28.6, 28.9 (both d, C(3)); 30.4, 30.6 (both s, CBr_2); 45.4 (d, C(1)); 46.0, 46.3 (both d, $\underline{C}HC(1)$); 57.6, 58.3 (both d, OCH); 62.0, 62.2 (both t, CH_2); 169.7, 171.2 (both s, C=O).

(1*R*,3*S*)-1-(2-Acetoxy-3,3,3-trichloropropyl)-3-acetoxymethyl-2,2-dimethylcyclopropane (4). A mixture of diacetate **2** (0.5 g, 2.2 mmol), Bu^n_4NBr (0.021 g, 0.066 mmol), $CHCl_3$ (0.26 mL, 3.34 mmol), and freshly calcined NaOH (0.39 g, 9.32 mmol) in 6 mL of CH_2Cl_2 was refluxed with stirring for 6 h. The reaction mixture was diluted with 100 mL of AcOEt, washed with 3% HCl and brine (15 mL each), and dried with Na_2SO_4. The solvent was removed, and the residue was chromatographed on SiO_2 in hexane—AcOEt (19 : 1) to give compound **4** (0.41 g, 53%) as a mixture of diastereoisomers in a ratio of 1.5 : 1, $[\alpha]_D^{20}$ +12.23 (*c* 1.5, $CHCl_3$), R_f 0.78 (Silufol, hexane—AcOEt, 4 : 1). Found (%): C, 45.12; H, 5.43; Cl, 30.79. $C_{13}H_{19}O_4Cl_3$. Calculated (%): C, 45.15; H, 5.49; Cl, 30.82. IR, ν/cm^{-1}: 1765, 1720 (C=O); 660, 630, 600 (CCl_3). For the minor diastereomer, ^1H NMR, δ: 0.63—0.72 (m, 1 H, H(1)); 0.89—0.97 (m, 1 H, H(3)); 1.04, 1.09 (both s, 3 H each, C(2)Me_2); 1.92—1.97 (m, 2 H, C(1)CH_2); 2.08, 2.23 (both s, 2×3 H, 2 MeCO); 3.95 (dd, 1 H, C(3)CH_α, J = 12 Hz, J = 9 Hz); 4.28 (dd, 1 H, C(3)CH_β, J = 12 Hz, J = 7.2 Hz); 5.69 (dd, 1 H, $CHCCl_3$, J = 10 Hz, J = 2.9 Hz). ^{13}C NMR, δ: 14.8, 28.5 (both q, $(\underline{C}H_3)_2C$); 17.2 (s, C(2)); 22.7 (d, C(1)); 21.2, 23.5 (both q, 2 $\underline{C}H_3CO$); 25.7 (t, $\underline{C}H_2C(1)$); 28.2 (d, C(3)); 61.7 (t, CH_2O); 80.9 (d, $\underline{C}CCl_3$), 99.7 (s, CCl_3); 169.2, 171.1 (both s, 2 CO).

For the major diastereomer, ^1H NMR, δ: 0.68—0.75 (m, 1 H, H(1)); 0.95—1.01 (m, 1 H, H(3)); 1.09, 1.13 (both s, 3 H each, C(2)Me_2); 1.95—2.03 (m, 2 H, C(1)CH_2); 2.05, 2.21 (both s, 2×3 H, 2 MeCO); 4.11 (d, 2 H, C(3)CH_2, J = 7 Hz); 5.57 (dd, 1 H, $CHCCl_3$, J = 10 Hz, J = 2.9 Hz). ^{13}C NMR, δ: 12.2, 28.3 (both q, $(\underline{C}H_3)_2C$); 17.5 (s, C(2)); 22.6 (d, C(1)); 21.1, 23.3 (both q, 2 $\underline{C}H_3CO$); 25.6 (t, $\underline{C}H_2C(1)$); 28.2 (d, C(3));

62.1 (t, CH_2O); 80.6 (d, $\underline{C}CCl_3$), 99.6 (s, CCl_3); 169.2, 171.1 (both s, 2 CO) (signals of the CO groups coincide in the spectra of both diastereomers).

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