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SHORT COMMUNICATIONS

Dedicated to Full Member of the Russian Academy of Sciences N.S. Zefirov on His 70th Anniversary

Functional Derivatives of α-Bromocyclopropylmagnesium Bromides

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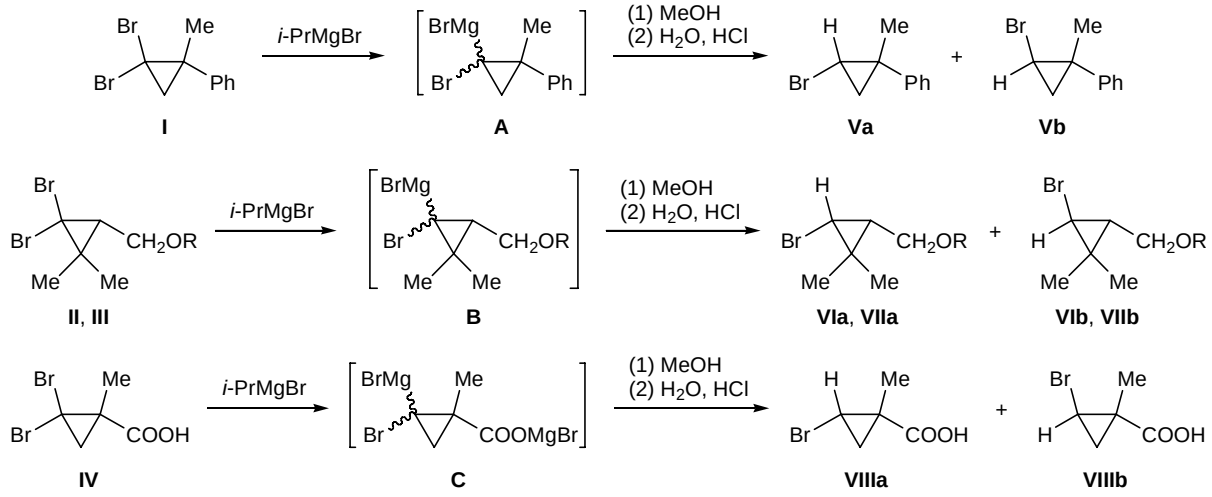
The present communication reports on the results of partial hydrodehalogenation of a series of functionalized geminal dibromocyclopropanes. These substrates attract interest as readily accessible precursors (or analogs) of practically important compounds [1, 2]. As shown in [3, 4], 1,1-dibromo-2-methyl-2-phenylcyclopropane (**I**) reacts with 3–4 equiv of Grignard compounds in THF at –60°C with subsequent decomposition of the reaction mixture with methanol to afford an approximately equimolar mixture of stereoisomeric monobromo derivatives (Scheme 1, see table). Analogous reaction with allyl ether **II** and acetate **III** also led to formation of ~1:1 mixtures of the corresponding stereoisomeric partial hydrodebromination products. The reaction mixtures contained neither products resulting from opening of cyclopropane ring nor other cyclopropane derivatives. Therefore, we concluded that under the given conditions the major or the only intermediates are α-bromocyclopropylmagnesium bromides **A** and **B**.

The depth of partial hydrodebromination of cyclopropanecarboxylic acid **IV** strongly depended on the amount of the Grignard compound. The complete conversion of acid **IV** was attained only with the use of 6 equiv of isopropylmagnesium bromide. It is known that hydrodebromination of acid **IV** with methyllithium is diastereoselective and enantioselective: it leads to formation of the corresponding *trans*-bromo-substituted carboxylic acid [5–7]. By contrast, the reaction of **IV** with isopropylmagnesium bromide gave

Scheme 1.



II, **VI**, R = CH_2=$CHCH_2$; **III**, **VII**, R = MeCO.

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Hydrodebromination of dibromocyclopropanes **I–IV**

Initial compound no.	*i*-PrMgBr, equiv (–60°C, 30 min)	Decomposition, min (MeOH, –60°C)	*cis*/*trans*-Isomer ratio,[a] %	Yield, %
I	2.5	5	34:66	87
II	3	10	37:63	79
III	3	10	45:55	95
IV	6	10	75:25	83

[a] The isomer ratio was determined from the intensity ratio of signals from the C**H**Br protons, δ 3.0–3.7 ppm.

a mixture of stereoisomeric acids **VIIIa** and **VIIIb**, the fraction of *cis* isomer **VIIIa** being about 75%.

Thus partial hydrodebromination of some functional derivatives of geminal dibromocyclopropanes by the action of isopropylmagnesium bromide in THF at –60°C, followed by treatment with methanol, gives the corresponding monobromo derivatives **V**–**VIII** in preparative yields without involving the other functional groups. Analogous reaction with dibromocyclopropanecarboxylic acid **IV** leads to predominant formation of *cis*-monobromide **VIIIa**.

Preparation of functionalized α-bromocyclopropylmagnesium bromides and their subsequent decomposition (*general procedure***).** A dry flask was filled with argon and charged with a solution of 1–3 mmol of dibromocyclopropane in 9 ml of anhydrous tetrahydrofuran. The solution was cooled to –65°C, and a solution of 2.5–6 equiv of isopropylmagnesium bromide in THF was added dropwise, maintaning the temperature within the range from –60 to –75°C. The mixture was stirred for 30 min and cooled to –70°C, 1 ml of methanol was added maintaining the temperature below –60°C, the mixture was allowed to warm up to 0°C, and 1 ml of water was added.

Compounds **V** and **VI** were isolated as follows. Petroleum ether, 20 ml, was added to the mixture, the organic layer was separated by decanting, the remaining suspension of magnesium salts was dissolved in 4 M hydrochloric acid and extracted with petroleum ether, and the organic extracts were combined, washed with water, dried over $MgSO_4$, and evaporated. The residue was subjected to chromatographic separation to isolate the corresponding *cis*- and *trans*-isomeric monobromocyclopropanes.

The reaction mixture obtained by addition of the Grignard compound to a solution of acid **IV** was diluted with 20 ml of chloroform at room temperature, and excess 15% hydrochloric acid was then added. The organic phase was separated, the aqueous phase was extracted with chloroform, the organic extract was shaken with a saturated solution of potassium carbonate, and the aqueous solution was washed with chloroform and acidified to pH 1 with concentrated hydrochloric acid. Acids **VIIIa** and **VIIIb** were extracted into chloroform, the extract was dried over magnesium sulfate, and the solvent was distilled off to obtain a mixture of *cis*- and *trans*-bromocyclopropanecarboxylic acids **VIIIa** and **VIIIb**.

***cis*-1-Bromo-2-methyl-2-phenylcyclopropane (Va)** [3]. Colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.34–1.40 m (2H, *J* = 4.6, 7.3 Hz), 1.45 s (3H), 3.08 d.d (1H, *J* = 4.6, 7.3 Hz), 7.18–7.37 m (5H).

***trans*-1-Bromo-2-methyl-2-phenylcyclopropane (Vb)** [3]. Colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.06 d.d (1H, *J* = 4.8, 6.3 Hz), 1.61 s (3H), 1.64 d.d (1H, *J* = 6.3, 8.0 Hz), 3.21 d.d (1H, *J* = 4.8, 8.0 Hz), 7.18–7.37 m (5H).

***cis*-1-Allyloxymethyl-2-bromo-3,3-dimethylcyclopropane (VIa)** [4]. Colorless oily substance. IR spectrum, ν, cm^{-1}: 3090, 3000–2865, 1730, 1650, 1470–1460, 1420, 1380, 1350 w, 1275, 1210, 1160–1140, 1000, 930, 680. ^{1}H NMR spectrum, δ, ppm: 1.07 d.d (1H, *J* = 6.8, 7.1 Hz), 1.14 s (3H), 1.16 s (3H), 2.99 d (1H, *J* = 7.5 Hz), 3.5 d.d (1H, *J* = 6.8, 10.6 Hz), 3.54 d.d (1H, *J* = 10.6, 7.1 Hz), 4.0 m (2H, *J* = 1.5, 5.8, 17.2, 10.4 Hz), 5.18 d.q (1H, *J* = 1.5, 10.4 Hz), 5.29 d.q (1H, *J* = 1.5, 17.2 Hz), 5.93 m (1H, *J* = 10.4, 5.8, 17.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.14, 26.19, 26.86, 29.67, 34.99, 68.31, 71.79, 117.05, 134.89. Mass spectrum (EI, 70 eV; retention time 6.16 min), *m*/*z* (I_{rel}, %): 218, 220 (0.016) $[M]^+$, 175, 177 (0.11) $[M - C_3H_7]^+$, 161, 163 (1.7) $[M - C_3H_5O]^+$, 147, 149 (5) $[M - C_4H_7O]^+$, 139 (9.6) $[M - Br]^+$.

***trans*-1-Allyloxymethyl-2-bromo-3,3-dimethylcyclopropane (VIb)** [4]. Colorless oily substance. IR spectrum, ν, cm^{-1}: 3085, 3000–2870, 1740, 1650, 1460, 1420, 1380, 1300, 1270–1250, 1205, 1145, 1100–

1090, 1000, 935, 820 w, 680. ^{1}H NMR spectrum, δ, ppm: 1.14 s (3H), 1.28 s (3H), 1.25 m (1H, *J* = 4.3 Hz), 2.71 d (1H, *J* = 4.3 Hz), 3.36 d.d, (1H, *J* = 8.1, 10.9 Hz), 3.58 d.d (1H, *J* = 5.9, 10.9 Hz), 3.98 m (2H, *J* = 1.5, 5.8, 5.5 Hz), 5.19 d.d (1H, *J* = 1.5, 10.5 Hz), 5.28 d.d (1H, *J* = 1.5, 17.2 Hz) 5.91 m (1H, *J* = 10.5, 17.2, 5.8, 5.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 19.43, 21.81, 24.45, 33.15, 33.71, 68.52, 71.46, 117.08, 134.73.

***cis*-2-Bromo-3,3-dimethylcyclopropylmethyl acetate (VIIa).** Colorless oily substance. IR spectrum, ν, cm^{-1}: 3000–2880, 1740, 1460, 1380, 1240, 1150 w, 1125 w, 1050, 1000, 990, 930–920 w, 905 w, 850 w, 810 w, 710 w, 695 w. ^{1}H NMR spectrum, δ, ppm: 1.12 m (1H, *J* = 7.6 Hz), 1.16 s (3H), 1.17 s (3H), 2.07 s (3H), 3.0 d (1H, *J* = 7.6 Hz), 4.12–4.21 m (2H). ^{13}C NMR spectrum, δ_C, ppm: 19.95, 22.19, 22.62, 24.88, 29.63, 34.35, 63.36, 170.99. Mass spectrum (EI, 70 eV; retention time 8.56 min), *m*/*z* (I_{rel}, %): 222, 220 (0.02) $[M]^+$, 163, 161 (0.11) $[M - C_2H_3O_2]^+$, 147, 149 (2.7) $[M - C_3H_5O_2]^+$, 141 (10) $[M - Br]^+$.

***trans*-2-Bromo-3,3-dimethylcyclopropylmethyl acetate (VIIb).** Colorless oily substance. IR spectrum, ν cm^{-1}: 3000–2880, 1740, 1460, 1380, 1240, 1150 w, 1125 w, 1050, 1000, 990, 920–930 w, 905 w, 850 w, 810 w, 710 w, 695 w. ^{1}H NMR spectrum, δ, ppm: 1.16 s (3H), 1.28 s (3H), 1.30 m (1H, *J* = 4.3, 4.5, 8.1 Hz), 2.07 s (3H), 2.75 d (1H, *J* = 4.3 Hz), 3.98 d.d (1H, *J* = 11.9, 8.1 Hz), 4.12–4.21 m (1H, *J* = 11.9, 4.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 19.55, 20.85, 24.27, 26.74, 31.97, 33.22, 63.40, 170.88. Mass spectrum (EI, 70 eV; retention time 8.56 min) *m*/*z* (I_{rel}, %): 222, 220 (0.02) $[M]^+$, 163, 161 (0.11) $[M - C_2H_3O_2]^+$, 147, 149 (2.7) $[M - C_3H_5O_2]^+$, 141 (10) $[M - Br]^+$.

***cis*-2-Bromo-1-methylcyclopropanecarboxylic acid (VIIIa)** [6, 7]. Colorless crystals. ^{1}H NMR spectrum, δ, ppm: 1.32 d.d (1H, *J* = 7.6, 6.7 Hz), 1.41 s (3H), 1.81 d.d (1H, *J* = 6.7, 5.8 Hz), 3.02 d.d (1H, *J* = 7.6, 5.8 Hz), 10.6 s (1H).

***trans*-2-Bromo-1-methylcyclopropanecarboxylic acid (VIIIb)** [6, 7]. Colorless crystals. ^{1}H NMR spectrum, δ, ppm: 1.09 d.d (1H, *J* = 5.5, 5.8 Hz), 1.48 s (3H), 1.92 d.d (1H, *J* = 8.2, 5.8 Hz), 3.57 d.d (1H, *J* = 5.5, 8.2 Hz), 10.6 s (1H).

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in $CDCl_3$ on a Varian VXR-400 spectrometer (400 and 100 MHz, respectively); the chemical shifts were measured relative to tetramethylsilane as internal reference. The IR spectra were obtained on a UR-20 instrument from samples prepared as films (liquids) or mulls in mineral oil (crystalline substances). The mass spectra were run on a Finnigan MAT SSQ-7000 GC–MS system using a 25-m OV-1 quartz capillary column.

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