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Synthesis of 3,4-Dibromo-3,4,4-trichloro-1-phenylbutan-1-one and 1-Aryl-2-bromo-3,4,4-trichlorobut-3-en-1-ones from 3,4,4-Trichlorobut-3-enoic Acid

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Abstract—Bromination of 3,4,4-trichlorobut-3-enoic acid in boiling carbon tetrachloride led to the formation of 2-bromo-3,4,4-trichlorobut-3-enoic acid as a result of replacement of hydrogen in the CH_2 group. The reaction at 40°C involved the double C=C bond to give 3,4-dibromo-3,4,4-trichlorobutanoic acid. The brominated acids were converted into the corresponding chlorides which were used to acylate benzene, toluene, and bromobenzene according to Friedel–Crafts. The acylation was not selective, and only the reaction of 3,4-dibromo-3,4,4-trichlorobutanoyl chloride with benzene gave 3,4-dibromo-3,4,4-trichloro-1-phenylbutan-1-one as the only product. 1-Aryl-2-bromo-3,4,4-trichlorobut-3-en-1-ones were synthesized by bromination of the corresponding 1-aryl-3,4,4-trichlorobut-3-en-1-ones which were prepared previously by Friedel–Crafts acylation of substituted benzenes with 3,4,4-trichlorobut-3-enoyl chloride.

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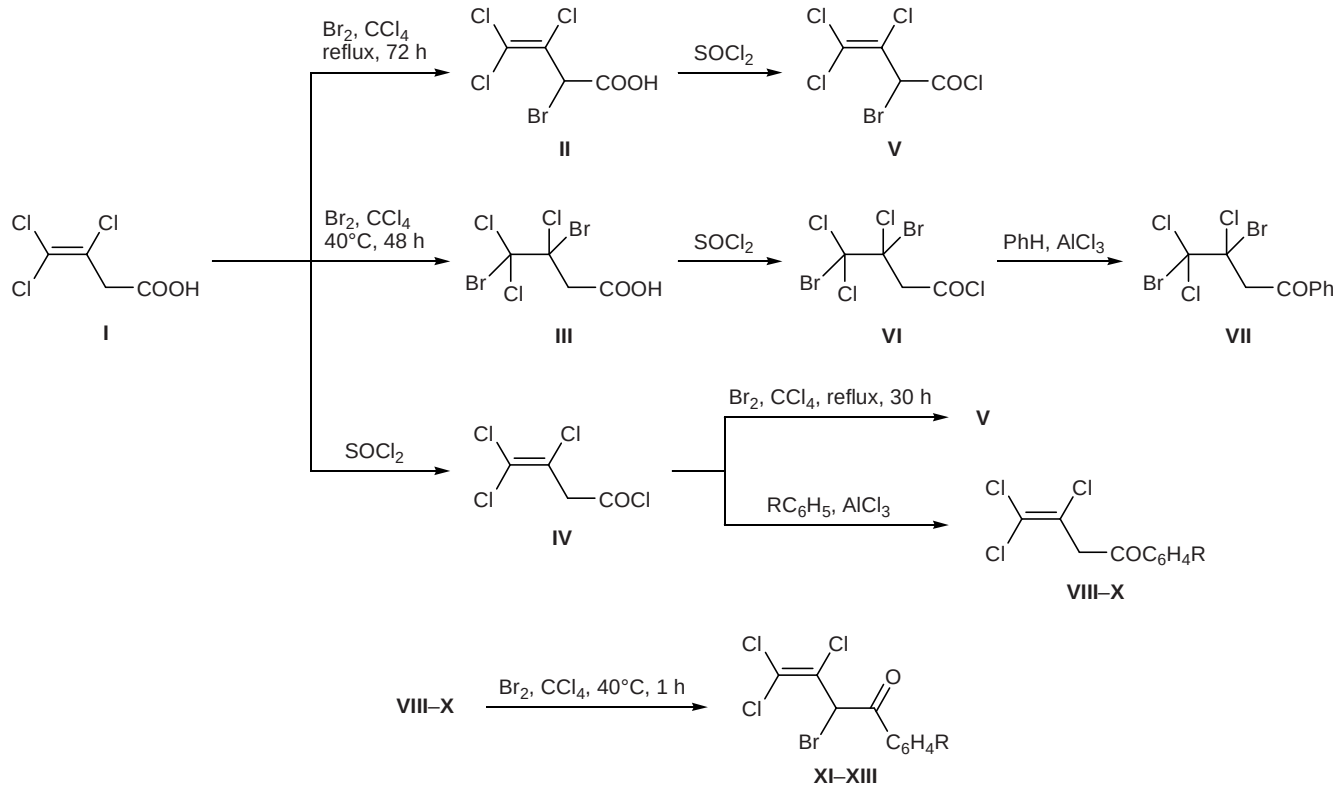
Accessible 3,4,4-trichlorobut-3-enoic acid (**I**) which is readily obtained from trichloroethylene dimer [1] contains several potential reaction centers and is a convenient starting material for the synthesis of various polyfunctional compounds [2, 3]. We previously reported on the chlorination of acid **I** with quantitative formation of pentachlorobutanoic acid [3]; however, its bromination has not been studied so far. Nevertheless, bromine-and chlorine-containing carboxylic acids attract interest from both preparative (due to the presence of reactive C–Br bonds in their molecules) and practical viewpoints. Polyhalogenated carboxylic acids exhibit a broad spectrum of useful properties, in particular they are extractants for rare-earth elements, promotors of Ziegler–Natta catalysts, flammable inhibitors, and biologically active substances [4–8].

The goal of the present work was to study the bromination of 3,4,4-trichlorobut-3-enoic acid (**I**) and possible way of synthesis of polychlorobromo-substituted acids and ketones.

We previously found that the bromination of acid **I** follows different pathways, depending on the reaction conditions. The reaction with bromine in boiling carbon tetrachloride was complete in 72 h; it involved replacement of hydrogen in the CH_2 group and resulted in the formation of 57% of 2-bromo-3,4,4-trichlorobut-3-enoic acid (**II**). We also isolated 3,4-dibromo-3,4,4-trichlorobutanoic acid (**III**) as by-product (yield 4%); it was formed via bromine addition at the double C=C bond in the initial acid. When the bromination in carbon tetrachloride was carried out at 40°C, the reaction was complete in 48 h, and bromine addition product **III** was isolated in 53% yield, while the yield of substitutive bromination product **II** did not exceed 5%. In this case, the reaction required initiation by irradiation with a filament lamp (no bromination occurred in the dark). By contrast, the substitutive bromination in boiling carbon tetrachloride was equally successful in the dark and on exposure to light. Compounds **II** and **III** are characterized by considerably different solubilities, and they were separated by fractional crystallization from hexane.

Unlike acid **I**, the bromination of acid chloride **IV** in carbon tetrachloride both under reflux and at room temperature resulted in replacement of hydrogen in the CH_2 group with formation of 2-bromo-3,4,4-trichlorobut-3-enoyl chloride (**V**). From the preparative view-

Scheme 1.



VIII, **XI**, R = H; **IX**, **XII**, R = 4-Me; **X**, **XIII**, R = 4-Br.

point, it is advisable to carry out the reaction under reflux. In this case, the reaction is complete in 30 h, and compound **V** is formed in 65% yield. The reaction at room temperature required 10 days to be complete. Dibromo acid **III** was converted into the corresponding chloride **VI** in 97% yield by standard procedure, i.e., by treatment with thionyl chloride. Acid chloride **V** was synthesized in a similar way from acid **II**, but the yield of **V** did not exceed 75%.

The structure of bromo-substituted carboxylic acids **II** and **III** and the corresponding acid chlorides **V** and **VI** was determined on the basis of their elemental analyses and IR, ^{1}H NMR, and mass spectra. In addition, the molecular weights of acids **II** and **III** were determined by titrimetry. In the IR spectra of acids **II** and **III**, stretching vibrations of the carbonyl groups appeared as strong absorption bands at 1738 and 1718 cm^{-1}, respectively. The C=O bands in the spectra of acid chlorides **V** and **VI** were located at higher frequencies, at 1801 and 1817 cm^{-1}, respectively. Stretching vibrations of the double C=C bond in **II** and **V** gave rise to absorption bands at 1589 and 1585 cm^{-1}. IR absorption bands in the regions 692–814 and 596–648 cm^{-1} were assigned to vibrations of the C–Cl and C–Br bonds in compounds **II**, **III** and **V**, **VI**, respectively.

The ^{1}H NMR spectrum of acid **III** contained a singlet at δ 3.86 ppm from protons of the CH_2 group and a broadened singlet from the acidic proton at δ 11.31 ppm. In the ^{1}H NMR spectrum of **VI**, the CH_2 signal appeared as a singlet at δ 4.34 ppm. Acid **II** displayed in the spectrum a singlet at δ 5.93 ppm from the CHBr proton (δ 6.13 ppm in the spectrum of chloride **V**) and a broadened singlet at δ 10.97 ppm due to the COOH group.

No molecular ion peaks were observed in the mass spectra of both acids **II** and **III** and acid chlorides **V** and **VI**. Fragmentation of these compounds under electron impact involves elimination of hydrogen chloride, bromine atoms, decarboxylation (**II**, **III**), and subsequent profound decomposition with rupture of C–C bonds. The intensity ratios for the isotope clusters were consistent with the presence of four halogen atoms in molecules **II** and **V** and five halogen atoms in **III** and **VI** [9, 10].

Friedel–Crafts acylation of benzene with 3,4-dibromo-3,4,4-trichlorobutanoyl chloride (**VI**) gave 66%

of 3,4-dibromo-3,4,4-trichloro-1-phenylbutan-1-one (**VII**), whereas the acylation with the same reagent of substituted benzenes, such as toluene, *p*-xylene, and *p*-bromobenzene, was not selective (complex mixtures of products were formed). Presumably, the process was accompanied by dehydrobromination, rearrangements with migration of bromine atom, and arylation of the ketones thus formed. The ^{1}H NMR spectra of the reaction mixtures (after removal of excess aromatic substrates) contained a singlet at δ 6.7 ppm from the CHBr and vinylic =CH protons and a singlet at δ 4.26 ppm, which may be assigned to C**H**Ph proton. Furthermore, the signal intensity ratio for aromatic protons and aliphatic protons in the acyl fragment indicated the presence of two aromatic rings in the molecule of one of the products. Likewise, the acylation of benzene and its derivatives with 2-bromo-3,4,4-trichlorobut-3-enoyl chloride (**V**) was accompanied by analogous processes, as followed from similarity of the ^{1}H NMR spectra of the product mixtures obtained in the acylation with acid chlorides **V** and **VI**. The IR spectra of the reaction mixtures contained several strong carbonyl absorption bands in the region 1690–1702 cm^{-1}, which also confirmed formation of several products. The product mixtures were difficult to separate, and we failed to isolate individual compounds therefrom.

The structure of 3,4-dibromo-3,4,4-trichloro-1-phenylbutan-1-one (**VII**) was confirmed by its analytical and spectral data. In the IR spectrum of **VII**, the carbonyl band was located at 1699 cm^{-1}, stretching vibrations of the aromatic C=C bonds appeared at 1580 and 1595 cm^{-1}, and vibrations of the C–Cl and C–Br bonds were characterized by absorption bands in the regions 689–799 and 548–623 cm^{-1}, respectively. The ^{1}H NMR spectrum of ketone **VII** contained a singlet at δ 4.38 ppm due to methylene protons, and aromatic protons gave rise to multiplets in the region δ 7.30–8.12 ppm.

With a view to obtain polyhalogenated aryl ketones we examined bromination of 1-aryl-3,4,4-trichlorobut-3-en-1-ones **VIII**–**X** which were synthesized previously by Friedel–Crafts acylation of the corresponding benzenes with acid chloride **IV** [3]. Reactions of compounds **VIII**–**X** with bromine in carbon tetrachloride both at room temperature and under reflux involved replacement of hydrogen in the CH_2 group. Under the optimal conditions (40°C, 1 h), the corresponding 1-aryl-2-bromo-3,4,4-trichlorobut-3-en-1-ones **XI**–**XIII** were obtained in 92–98% yield. Their structure was determined on the basis of their IR, ^{1}H NMR, and mass spectra and elemental analyses.

Stretching vibrations of the C=O bonds in ketones **XI**–**XIII** were characterized by strong IR absorption bands at 1698–1706 cm^{-1}, and bands in the regions 1584–1602 and 1572–1580 cm^{-1} were assigned to vibrations of the C=C bonds. Ketones **XI**–**XIII** showed in the ^{1}H NMR spectra singlets at δ 6.63–6.70 ppm from the CHBr protons, which unambiguously indicated that the reaction occurred as replacement of hydrogen in the CH_2 group by bromine. Aromatic protons resonated in the region δ 7.27–7.95 ppm. In the mass spectra of ketones **VII** and **XI**–**XIII** we observed no molecular ion peaks; the fragment ion peaks corresponded to elimination of halogen atoms and hydrogen chloride, followed by decomposition of the carbon skeleton.

Ketones **VII** and **XI**–**XIII** attract interest as convenient synthons for the preparation of polyfunctional compounds; it is known that halogenated ketones are used in the synthesis of antihelminthics, insecticides, and other biologically active substances [11, 12].

EXPERIMENTAL

The IR spectra were recorded in KBr on a Protege-460 spectrometer with Fourier transform. The ^{1}H NMR spectra were measured on a Tesla-567A instrument (100 MHz) from solutions in $CDCl_3$ using tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Hewlett–Packard HP 5890/5972 GC–MS system (HP-5MS capillary column, 30 m×0.25 mm, film thickness 0.25 μm, 5% of phenylmethylsilicone; injector temperature 250°C). The molecular weights of acids **II** and **III** were determined by titration with a 0.1 N alcoholic solution of sodium hydroxide.

2-Bromo-3,4,4-trichlorobut-3-enoic acid (II). A mixture of 10 g (53.8 mmol) of 3,4,4-trichlorobut-3-enoic acid (**I**) and 3 ml (58.4 mmol) of bromine in 50 ml of anhydrous carbon tetrachloride was heated for 72 h under reflux. The mixture was washed with an aqueous solution of Na_2SO_3 to remove residual bromine and with water and dried over sodium sulfate. The solvent was removed under reduced pressure, 50 ml of hexane was added to the solid residue, the mixture was heated to the boiling point, the undissolved material was filtered off, the filtrate was cooled to 0°C, and the precipitate was filtered off, washed with cold hexane, and dried under reduced pressure. Yield 8.06 g (57%), mp 83–85°C. IR spectrum, ν, cm^{-1}: 2500–3300 (COOH); 1738 (C=O); 1589 (C=C); 722, 814 (C–Cl); 648 (C–Br). ^{1}H NMR spectrum, δ,

ppm: 5.93 s (1H, CHBr), 10.97 br.s (1H, COOH). Found, %: C 18.08; H 0.90; Hlg 69.78. *M* 265. Calculated, %: C 17.91; H 0.75; Hlg 69.42. *M* 268.32.

The material insoluble in hexane was 3,4-dibromo-3,4,4-trichlorobutanoic acid (**III**); it was purified by recrystallization from carbon tetrachloride. Yield 4%, mp 148–150°C. IR spectrum, ν, cm^{-1}: 2450–3200 (COOH); 1718 (C=O); 692, 773, 805 (C–Cl); 596 (C–Br). ^1H NMR spectrum, δ, ppm: 3.86 s (2H, CH_2), 11.31 br.s (1H, COOH). Found, %: C 13.61; H 1.23, Hlg 75.98. *M* 347. Calculated, %: C 13.76; H 0.87; Hlg 76.21. *M* 349.23.

Following an analogous procedure, the reaction was carried out at 40°C (reaction time 48 h) under irradiation with a filament lamp. The products were separated in a similar way.

2-Bromo-3,4,4-trichlorobut-3-enoyl chloride (V). A solution of 18.5 g (89 mmol) of 3,4,4-trichlorobut-3-enoyl chloride (**IV**) and 5 ml (97.3 mmol) of bromine in 50 ml of anhydrous carbon tetrachloride was heated for 30 h under reflux. The solvent was distilled off under atmospheric pressure, and the residue was distilled under reduced pressure. Yield 16.6 g (65%), bp 76–77°C (2 mm), d_4^{20} = 1.836. IR spectrum, ν, cm^{-1}: 1801 (C=O); 1585 (C=C); 729, 701 (C–Cl); 599 (C–Br). ^1H NMR spectrum, δ, ppm: 6.13 s (1H, CHBr). Found, %: C 16.90; H 0.76; Hlg 76.95. $[M - HCl]^+$ 248. Calculated, %: C 16.75; H 0.35; Hlg 77.32. *M* 286.77.

3,4-Dibromo-3,4,4-trichlorobutanoyl chloride (VI). Thionyl chloride, 5 ml (69.6 mmol), was added dropwise to a solution of 8 g (22.9 mmol) of acid **III** in 30 ml of anhydrous carbon tetrachloride, and the mixture was stirred for 30 min and heated under reflux until hydrogen chloride no longer evolved (test with a litmus paper). The solvent and excess thionyl chloride were distilled off first under atmospheric pressure and then under reduced pressure (1 mm). The residue was 8.25 g (98%) of compound **VI** which required no additional purification, d_4^{20} = 2.008. IR spectrum, ν, cm^{-1}: 1817 (C=O); 694, 758, 788 (C–Cl); 599, 623 (C–Br). ^1H NMR spectrum, δ, ppm: 4.34 s (2H, CH_2). Found, %: C 12.90; H 0.99; Hlg 81.81. $[M - 2Br]^+$ 206. Calculated, %: C 13.07; H 0.55; Hlg 82.03. *M* 367.68.

An analogous procedure was used to obtain 2-bromo-3,4,4-trichlorobut-3-enoyl chloride (**V**) (yield 75%); the product was identical to a sample prepared by bromination of 3,4,4-trichlorobut-3-enoyl chloride (**IV**) as described above.

3,4-Dibromo-3,4,4-trichloro-1-phenylbutan-1-one (VII). Acid chloride **VI**, 8.5 g (23 mmol), was mixed with 3.7 g (27.8 mmol) of anhydrous aluminum(III) chloride, 5.45 g (69.8 mmol) of anhydrous benzene was added to the resulting complex, and the mixture was stirred for 4 h at 20°C and for 2 h at 45°C, diluted with 15 ml of methylene chloride, and poured into 100 ml of 0.1 N hydrochloric acid. The organic phase was separated, washed with water, a solution of sodium carbonate, and water again, and dried over $MgSO_4$. The solvent was distilled off, and the residue was recrystallized from hexane. Yield 6.22 g (66%), mp 88–90°C. IR spectrum, ν, cm^{-1}: 1699 (C=O); 1595, 1580 (C=C); 799, 748, 689 (C–Cl); 548, 623 (C–Br). ^1H NMR spectrum, δ, ppm: 4.38 s (2H, CH_2), 7.50–7.60 m (3H, H_{arom}), 7.90–8.10 m (2H, H_{arom}). Found, %: C 29.18; H 2.08; Hlg 64.71. $[M - 2Br - HCl]^+$ 212. Calculated, %: C 29.34; H 1.72; Hlg 65.02. *M* 409.33.

General procedure for the bromination of 1-aryl-3,4,4-trichlorobut-3-en-1-ones VIII–X. Bromine, 45 mmol, was added dropwise under stirring to a solution of 40 mmol of ketone **VIII–X** in 40 ml of anhydrous carbon tetrachloride, heated to 40°C. The mixture was then heated to 60°C, stirred for 30 min at that temperature, washed with a solution of Na_2SO_3 to remove excess bromine and with water until neutral reaction, and dried over $CaCl_2$. The solvent was removed, and the solid residue was purified by recrystallization from hexane (compound **XI**) or methanol (**XII**, **XIII**).

2-Bromo-3,4,4-trichloro-1-phenylbut-3-en-1-one (XI). Yield 98%, mp 65–66°C. IR spectrum, ν, cm^{-1}: 1706 (C=O); 1582, 1592 (C=C); 709, 750, 847 (C–Cl); 551 (C–Br). ^1H NMR spectrum, δ, ppm: 6.70 s (1H, CHBr), 7.49–7.65 m (3H, H_{arom}), 7.86–7.95 m (2H, H_{arom}). Found, %: C 36.90; H 2.03; Hlg 56.55. $[M - HCl]^+$ 290. Calculated, %: C 36.57; H 1.84; Hlg 56.71. *M* 328.42.

2-Bromo-3,4,4-trichloro-1-(4-methylphenyl)but-3-en-1-one (XII). Yield 96%, mp 95–97°C. IR spectrum, ν, cm^{-1}: 1698 (C=O); 1580, 1602 (C=C); 707, 752, 822 (C–Cl); 545 (C–Br). ^1H NMR spectrum, δ, ppm: 2.45 s (3H, Me), 6.68 s (1H, CHBr) 7.27 d and 7.35 d (1H each, H_{arom}), 7.78 d and 7.86 d (1H each, H_{arom}). Found, %: C 38.54; H 2.58; Hlg 54.70. $[M - HCl]^+$ 302. Calculated, %: C 38.58; H 2.35; Hlg 54.39. *M* 340.45.

2-Bromo-1-(4-bromophenyl)-3,4,4-trichlorobut-3-en-1-one (XIII). Yield 92%, mp 96–98°C. IR spec-

trum, ν, cm^{-1}: 1698 (C=O); 1572, 1584 (C=C); 716, 764, 825 (C–Cl); 546 (C–Br). ^1H NMR spectrum, δ, ppm: 6.63 s (1H, CHBr) 7.70 br.s (2H, H_{arom}), 7.75 br.s (2H, H_{arom}). Found, %: C 29.72; H 1.65; Hlg 65.39. $[M - HCl]^+$ 368. Calculated, %: C 29.49; H 1.24; Hlg 65.35. *M* 407.32.

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