Hepta(methoxycarbonyl)cycloheptatriene halo derivatives

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A reaction of potassium hepta(methoxycarbonyl)cycloheptatrienide with chlorine and bromine gave high yields of the corresponding chloro- and bromohepta(methoxycarbonyl)cycloheptatrienes; the fluoro derivative was obtained by the exchange reaction of the corresponding bromide with silver fluoride. In contrast to the mentioned halides, the iodo derivative has proved unstable. Thermolysis of bromohepta(methoxycarbonyl)cycloheptatriene was studied, as well as its conversion to the azido and methoxy derivatives upon treatment with NaN₃ or methanol.

Key words: potassium hepta(methoxycarbonyl)cycloheptatrienide, hepta(methoxycarbonyl)cycloheptatriene halides, nucleophilic substitution, thermolysis.

In recent years, we have been interested in the exploring a possibility of a conjugation effect in the cycloheptatriene system, whose electron density is substantially decreased because of the presence of seven electron-withdrawing ester substituents. In this system, the only hydrogen atom exhibits a high acidity, whereas a formed anion is very stable. In this case, in a counterpoise to the antiaromatic character of the cycloheptatrienyl anion, the delocalization effect of the negative charge over the ester groups is a stabilizing factor. In fact, the X-ray diffraction data show that in the hepta(methoxycarbonyl)cycloheptatrienyl anion (1), the seven-membered ring is somewhat flattened, the nearest to the anionic center double bonds are elongated and the single bonds are shortened, that indicates a partial conjugation of the carbocycle five C atoms with a delocalization of the negative charge over the oxygen atoms of the ester groups.¹ In this case, one of the double bonds is not involved in the conjugation system and considerably deviates from the plane of the five-carbon part of the ring. At the same time, ¹H and ¹³C NMR data show that in solutions no any differences in the C-CO₂CH₃ fragments are observed, that indicates a rapid averaging dynamics of these fragments in anion 1. In this connection, anion 1 not only can react as C- or O-nucleophile^{1,2} with electrophiles, but also might exhibit electrophilic properties, which, for example, are observed in the reactions with primary amines.^{3,4} In most cases, these transformations are accompanied by considerable changes in the carbon skeleton.

In comparison with hepta(methoxycarbonyl)cycloheptatriene (HMCH, H[1]), the same system but with an alternative distribution of electron density is of a certain interest. Such an approach, in particular, could have been realized in the case of the replacement of the proton with a halogen atom. In this case, it becomes possible to generate substituted tropylium cation and to endow molecule with a new type of reactivity.

It is known⁵ that penta(methoxycarbonyl)cyclopentadiene anion can be easily involved in the reaction with molecular bromine and chlorine, with the compounds obtained serving as halogenation agents (they oxidize the iodide anion and halogenate phenols), that indicates a strong polarization of the C-Hal bond. It appears that K[1] similarly easy reacts with molecular halogens. The reaction was carried out by the addition of an acetonitrile solutions of bromine or iodine to the acetonitrile solution of K[1], whereas chlorine gas was purged through the solution in the case of chloro derivative. Judging from the disappearance of a characteristic crimson color of the anion, the reaction at 20 °C is completed virtually instantly and in the case of chlorine and bromine leads to the corresponding halo derivatives 2a,b as colorless crystalline compounds in virtually quantitative yields (Scheme 1).

The structure of halides **2a,b** was confirmed by X-ray diffraction data (Fig. 1). In both compounds, a slight elongation of the C(1)–C(2) and C(1)–C(7) bonds (d = 0.1523-0.1527 nm) as compared to HMCH was observed,¹ with the C–Cl and the C–Br bond distances being 0.1802 and 0.1965 nm, respectively, which is somewhat longer than in the halohydrocarbons (0.1782 and 0.1938 nm, respectively).

Fluoride 2c was synthesized by the exchange reaction: silver fluoride was added to a solution of bromide 2b in acetonitrile and after precipitation of insoluble silver bromide (~4 h), fluoride 2c was obtained in quantitative yield (see Scheme 1).

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 $E = CO_2Me$; X = Cl(a), Br(b)



Fig. 1. General view of molecules **2a** (*a*) and **2b** (*b*) in representation of atoms by thermal ellipsoids.

An interesting fact was found when analyzing the ¹H and ¹³C NMR spectra of these compounds. At room temperature, a considerable broadening was observed for some signals of the methoxy groups in the ¹H NMR spectra of compounds **2a** and **2b**. When the sample is heated to 50 °C or cooled to -20 °C, these signals in the ¹H NMR spectrum become narrower (Fig. 2). Most likely, this fact can be explained by two dynamic processes observed at different temperatures: a retardation of the rotation of the ester groups and the migration of the halogen atom over the atoms of the seven-membered ring, similarly to that observed in the case of thiophenylcycloheptatrienes.⁶

Similar pattern was also observed in the ¹³C NMR spectra. Thus, at room temperature for both chloro- (2a) and bromo-substituted HMCH (2b), the signals for the quaternary carbon atoms of the seven-membered ring are strongly broadened and virtually cannot be seen. Upon heating of **2b** to 50 °C, a single narrow signal is clearly observed in the region of olefin C atoms at δ 136. Conversely, upon cooling of the sample to -30 °C all three expected signals appear in the ¹³C NMR spectrum. In this case, the signals at δ 126 and 144, which at 50 °C are barely seen because of the strong broadening, become narrow enough, while the signal at δ 136 considerably broadens. Besides, at -30 °C a second set of all the signals appears in the ¹H and ¹³C NMR spectra, that, apparently, corresponds to the registration of both possible conformers due to the hindered inversion of the nonplanar configuration of the seven-membered ring. The ratio of these signals is ~5: 1 and does not change upon reduction of the sample temperature to $-60 \,^{\circ}\text{C}$.

In the case of iodine, all the attempts to obtain the product similar to halides 2a-c were unsuccessful, with methyl benzenehexacarboxilate (3) being the only isolable reaction product.⁷ The cycloheptatrienyl derivative was not detected even by low-temperature NMR spectroscopy; when the reaction was carried out at -30 °C, only the signal for benzenehexacarboxylate 3 was clearly detected in the ¹H NMR spectra and no other informative signals were observed.

It appears that a similar process takes place also upon reflux of bromide 2b in benzene for several hours. Under these conditions, it decomposes with the formation of benzenehexacarboxylate 3, however, we failed to intercept a residual fragment of molecule 2b, which formally corresponds to the carbene particle :CBrCO₂Me, using different unsaturated compounds (styrene, methyl acrylate). Apparently, the formation of benzenehexacarboxylate results from the disintegration of unstable hepta(methoxycarbonyl)tropylium formed from compound 2b at elevated temperatures.

The reaction of bromide 2b with primary amines (benzylamine, 2-ethoxyethylamine) gave benzenehexacarboxylate 3 and HMCH itself as the identified reac-

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Fig. 2. ¹H NMR spectra of chloro derivative 2a in CDCl₃ at different temperatures: $-30 \circ C(a)$, $-10 \circ C(b)$, $25 \circ C(c)$, $50 \circ C(d)$.

tion products. The formation of the latter indicates that bromide **2b** can also serve as a brominating agent, as it takes place in the case of 1-bromo-1,2,3,4,5-penta-(methoxycarbonyl)cyclopenta-2,4-diene.⁵ Nonetheless, we accomplished a formal nucleophilic substitution of bromine in compound **2b** with retention of the seven-membered ring in the reaction of bromide **2b** with sodium azide in methanol. In this case, we detected both the primary reaction products, which were the corresponding azide **4**, and its decomposition products, benzenehexacarboxylate **3** and methyl cyanoformate slowly formed even at room temperature (Scheme 2). Because of the low stability of the azide, we failed to isolate it in the pure form, however, the ¹H and ¹³C NMR spectra and mass spectrometric data clearly indicated its formation.

The observed decomposition of azide 4 differs from the behavior of the suggested 1-azido-1,2,3,4,5-penta-(methoxycarbonyl)cyclopentadiene, which decomposed at room temperature with the liberation of nitrogen accompanied by the 1,2-shift of the methoxycarbonyl substituent from carbon atom to the nitrogen atom with to form the corresponding *N*-methoxycarbonyliminocyclopentadiene.⁸

The substitution of bromine in compound **2b** with a methoxy group takes place upon reflux in methanol. Besides the formation of methoxy derivative **5**, the



Scheme 2

reaction gives benzenehexacarboxylate **3** and HMCH approximately in the equal ratio and in up to 50% overall yield (see Scheme 2). At room temperature, all the methoxy groups in the ¹H NMR spectrum of compound **5** are found as three broad signals with the ratio of integral intensities of 1:6:1. Upon cooling of the sample to -30 °C, the signals become narrower and the central signal "splits" into three singlet signals of equal intensities.

Unfortunately, our attempts to increase the yield of compound 5 failed. Though running the reaction in 85% aqueous methanol significantly shortened the reaction time (from 20 h for anhydrous methanol to 4 h), the yield of compound 5 in this case was no more than 30%. This can be explained either by the formation of unstable hydroxy derivative of HMCH, or by the decomposition of 5 upon treatment with HBr and traces of water. Relatively low yield of compound 5 was also observed when the reaction was carried out in anhydrous methanol; in this case, the amount of the product in the reaction mixture stopped to increase from a certain moment, only consumption of the starting bromide 2b and increase in the amount benzenehexacarboxylate 3 and HMCH were observed. Our attempts to neutralize the forming HBr with bases, for example, K₂CO₃ or tertiary amines, were also unsuccessful. The side reactions considerably dominated when ethanol or propanol were used, in this case only benzenehexacarboxylate 3 and HMCH were mainly detected in the reaction mixture even for the low conversions of the starting bromide 2b.

All the synthesized halocycloheptatrienes 2a-c are colorless compounds, which distinguishes them from the penta(methoxycarbonyl)cyclopentadiene halides, which in solution have electron absorption spectra identical to the spectrum of penta(methoxycarbonyl)cyclopentadienyl anion. The absence in 2a-c of strong crimson color characteristic of anion 1 and their specific behavior in the reactions with nucleophiles indicate that these compounds are prone to a heterolytic cleavage of the C—Hal bond with elimination of the halide anion and an instantaneous transformation of the formed unstable hepta(methoxy-carbonyl)tropylium.

Experimental

¹H and ¹³C NMR spectra were recorded on Bruker AMX 400 (400.1 and 100.6 MHz) and Bruker AVANCE II 300 spectrometers (300 and 75.5 MHz) for solutions in CDCl₃ or (CD₃)₂SO containing 0.05% of Me₄Si as an internal standard. Mass spectra were recorded on a Finnigan MAT INCOS-50 instrument (EI, 70 eV, direct injection); high resolution mass spectra (ESI-HRMS) were obtained on a Bruker micrOTOF II instrument. Thin-layer chromatography was performed on Silicagel 60 plates (Merck). Single crystal X-ray diffraction studies of compounds **2a** and **2b** were carried out on a Bruker 1K SMART CCD automated diffractometer (Mo-Kα radiation) at 100 K. Crystals of both compounds are monoclinic, space group *P*21/*c*. Parameters for compound **2a**: a = 8.9473(8) Å, b = 34.699(3) Å, c = 7.9931(7) Å, V = 2413.5(4) Å³, $d_{calc} = 1.466$ g cm⁻³; for compound **2b**: a = 9.0035(9) Å, b = 34.687(4) Å, c = 7.9689(8) Å, V = 2416.3(4) Å³, $d_{calc} = 1.587$ g cm⁻³. Atomic coordinates and full crystallographic informations were deposited with the Cambridge Structural Database (CCDC 1023830 and CCDC 1023828 for **2a** and **2b**, respectively). Hepta(methoxycarbonyl)cycloheptatriene (HMCH) and potassium hepta(methoxycarbonyl)cycloheptatrienide K[1] were synthesized according to the described procedures.¹ Solvents of the reagent grade (>99.5%) were used without additional purification.

7-Chloro-1,2,3,4,5,6,7-hepta(methoxycarbonyl)cyclohepta-1,3,5-triene (2a). Chlorine gas was passed through a solution of compound K[1] (0.54 g, 1 mmol) in acetonitrile (10 mL) until a crimson color disappeared. The solvent was evaporated in vacuo, the residue was treated with AcOEt (5 mL) and the mixture was passed through a layer of silica gel (about 1 cm), which was additionally washed with AcOEt (3 mL). After evaporation of the solvent, 2a (0.52 g, 98%) was obtained as colorless crystals, m.p. 170-171 °C (decomp.). Found (%): C, 47.22; H, 4.00. $C_{21}H_{21}ClO_{14}$. Calculated (%): C, 47.34; H, 3.97. MS (EI), m/z $(I_{\rm rel} (\%))$: 501 (15), 503 (6) $[M - OMe]^+$; 473 (98), 475 (48) $[M - CO_2Me]^+$; 453 (65); 395 (48); 59 (100) $[CO_2Me]^+$. ¹H NMR (CDCl₃, 50 °C), δ: 3.75 (s, 3 H, OMe); 3.77, 3.81, 3.86 (all s, 6 H each, 6 OMe). ¹³C NMR (CDCl₃, 50 °C), δ: 53.0 (2 OMe); 53.2 (4 OMe); 54.7 (OMe); 66.7 (br, C(7)); 127.8 (br, =C); 136.0 (=C); 145.4 (br, =C); 162.9, 163.5, 164.4 (6 COO); 165.0 (COO). ¹H NMR (CDCl₃, -30 °C), δ: major conformer: 3.65 (s, 3 H, OMe); 3.68, 3.75, 3.84 (all s, 6 H each, 6 OMe); minor conformer: 3.71, 3.73, 3.76 (all s, 6 H each, 6 OMe); 3.77 (s, 3 H, OMe). ¹³C NMR (CDCl₃, $-30 \,^{\circ}$ C), δ : major conformer: 53.4 (2 OMe); 53.7 (4 OMe); 55.2 (OMe); 66.6 (br, C(7)); 126.3 (=C); 135.5 (br, =C); 144.4 (=C); 163.0, 163.5, 164.2 (6 COO); 165.5 (COO); minor conformer: 51.8, 53.7, 53.8 (6 OMe); 54.7 (OMe); 66.6 (C(7)); 132.4 (=C); 135.5 (br, =C); 136.4 (=C); 163.7, 164.2, 164.6 (6 COO); 166.3 (COO).

7-Bromo-1,2,3,4,5,6,7-hepta(methoxycarbonyl)cyclohepta-1,3,5-triene (2b). A solution of bromine (0.16 g, 1 mmol) in acetonitrile (1 mL) was added to a solution of K[1] (0.54 g, 1 mmol) in acetonitrile (10 mL) and the mixture was stirred for 10 min at 20 °C. The solvent was evaporated in vacuo, the residue was treated with AcOEt (5 mL), and the mixture was passed through a short layer of silica gel, which was additionally washed with AcOEt (3 mL). After evaporation of the solvent, bromide 2b (0.57 g, 98%) was obtained as yellowish crystals, m.p. 162–164 °C (decomp.). Found (%): C, 43.50; H, 3.61. C₂₁H₂₁BrO₁₄. Calculated (%): C, 43.69; H, 3.67. MS (EI), *m/z* (*I*_{rel} (%)): 545 (3), 547 (3) [M - OMe]⁺; 517 (28), 519 (29) [M - CO₂Me]⁺; 497 (32); 453 (68); 395 (93); 59 (100) [CO₂Me]⁺. ¹H NMR (CDCl₃, 50 °C), δ: 3.67 (s, 3 H, OMe); 3.70, 3.74, 3.78 (all s, 6 H each, 6 OMe). ¹³C NMR (CDCl₃, 50 °C), δ: 52.0 (br, C(7)); 53.0 (2 OMe); 53.2 (4 OMe); 54.6 (OMe); 128.1 (br, =C); 136.3 (=C); 143.5 (br, =C); 163.5 (4 COO); 164.4 (2 COO); 165.8 (COO). ¹H NMR (CDCl₃, -30 °C), δ : major conformer: 3.75 (s, 3 H, OMe); 3.79, 3.85, 3.95 (all s, 6 H each, 6 OMe); minor conformer: 3.82, 3.84, 3.87 (all s, 6 H each, 6 OMe); 3.89 (s, 3 H, OMe). ¹³C NMR (CDCl₃, -30 °C), δ : major conformer: 51.0 (br, C(7)); 53.3 (2 OMe); 53.6 (4 OMe); 55.1 (OMe); 126.4 (=C); 135.6 (br, =C); 144.3 (=C); 163.1, 163.5, 164.2 (6 COO); 165.5 (COO); minor conformer: 51.0 (C(7)); 51.9 (2 OMe); 53.7 (4 OMe); 54.7 (OMe); 132.5 (=C); 135.6 (br, =C); 136.5 (=C); 163.7 (4 COO); 164.6 (2 COO); 166.2 (COO).

7-Fluoro-1,2,3,4,5,6,7-hepta(methoxycarbonyl)cyclohepta-1,3,5-triene (2c). Silver fluoride (0.15 g, 1.2 mmol) was added to a solution of bromide **2b** (0.58 g, 1 mmol) in acetonitrile (30 mL). The mixture was stirred for 4 h, the solvent was evaporated in vacuo. The residue was treated with chloroform (10 mL) and the mixture was passed through a short layer of silica gel, which was additionally washed with CHCl₃ (3 mL). After evaporation of the solvent, fluoride 2c (0.50 g, 97%) was obtained as a waxlike mass. MS (EI), m/z (I_{rel} (%)): 485 (12) [M - OMe]⁺; 457 (100) $[M - CO_2Me]^+$; 429 (32); 395 (30); 355 (28); 59 (55) $[CO_2Me]^+$. HRMS (ESI): found: m/z 539.0817; $C_{21}H_{21}FO_{14}$; calculated: 539.0808 [M+Na]. ¹H NMR (CDCl₃, 27 °C), δ: 3.75 (s, 3 H, OMe); 3.76, 3.79, 3.86 (all s, 6 H each, 6 OMe). ¹³C NMR (CDCl₃, 27 °C), δ: 53.4 (6 OMe); 54.6 (OMe); 90.8 (br.d, C(7), ${}^{1}J_{C,F} = 192$ Hz); 126.6 (br, =C); 136.0 (=C); 142.4 (br, =C); 161.8, 163.2, 164.3 (6 COO); 163.3 (br, COO). ¹⁹F NMR (CDCl₃), δ: -165.4.

7-Azido-1,2,3,4,5,6,7-hepta(methoxycarbonyl)cyclohepta-1,3,5-triene (4). A solution of bromide 2b (0.10 g, 0.17 mmol) and sodium azide (0.017 g, 0.26 mmol) in MeOH (5 mL) was stirred for 3 h at 20 °C. A precipitate formed was filtered off and dried *in vacuo* at 0 °C to obtain azide 4 (0.052 g, 60%) as colorless crystals, slowly decomposing at room temperature, that is characterized by the appearance and a gradual increase in the content of benzenehexacarboxylate 3. HRMS (ESI): found: m/z562.0923; C₂₁H₂₁N₃O₁₄; calculated: 562.0916 [M+Na]⁺. IR (KBr), v/cm⁻¹: 2130, 1738. ¹H NMR (DMSO-d₆), δ : 3.74, 3.76 (both s, 9 H and 12 H, 7 OMe). ¹³C NMR (DMSO-d₆), δ : 53.2 (6 OMe); 54.2 (OMe); 73.6 (C(7)); 130.5, 135.5, 139.5 (all br, =C); 161.5, 162.8, 163.3 (6 COO); 165.3 (br, COO). ¹⁴N NMR (DMSO-d₆), δ : -138.2 (br.s).

7-Methoxy-1,2,3,4,5,6,7-hepta(methoxycarbonyl)cyclohepta-1,3,5-triene (5). A solution of bromide 2b (0.29 g, 0.5 mmol) in methanol (20 mL) was refluxed under argon for 20 h. The solvent was evaporated *in vacuo* and the residue was subjected to chromatography on a column with SiO₂ (eluent CHCl₃—AcOEt, 4 : 1). The fraction containing compound 5 was dissolved in diethyl ether and washed with 50% aqueous solution of NaOH to remove HMCH left after chromatography. After evaporation of ether, compound **5** (0.14 g, 52%) was obtained as a yellow oil. HRMS (ESI): found: m/z 551.1009; $C_{22}H_{24}O_{15}$; calculated: 551.1007 [M+Na]⁺. ¹H NMR (CDCl₃, 25 °C), δ : 3.31 (br.s, 3 H, OMe); 3.75 (br.s, 18 H, 6 OMe); 3.84 (br.s, 3 H, OMe). ¹³C NMR (CDCl₃, 25 °C), δ : 53.4, 53.5, 53.7 (6 OMe); 54.2 (CO₂<u>Me</u> at C(7)); 56.7 (OMe); 81.4 (br, C(7)); 128.2 (br, =C); 132.2 (C=); 134.0 (br, =C); 164.3, 165.0, 165.1 ((6 COO); 167.3 (COO at C(7)).

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References

- Yu. V. Tomilov, D. N. Platonov, R. F. Salikov, G. P. Okonnishnikova, *Tetrahedron*, 2008, 64, 10201.
- 2. Yu. V. Tomilov, D. N. Platonov, E. V. Shulishov, G. P. Okonnishnikova, *Tetrahedron*, 2013, **69**, 6855.
- 3. Yu. V. Tomilov, D. N. Platonov, G. P. Okonnishnikova, *Tetrahedron Lett.*, 2009, **50**, 5605.
- D. N. Platonov, G. P. Okonnishnikova, Yu. V. Tomilov, Mendeleev Commun., 2010, 20, 83.
- R. C. Cookson, J. B. Henstock, J. Hudec, B. R. D. Whitear, J. Chem. Soc. (C), 1967, 1986.
- V. I. Minkin, I. E. Mikhailov, G. A. Dushenko, O. E. Kompan, A. Zschunke, *Russ. Chem. Bull.* (*Int. Ed.*) 1998, 47, 884 [*Izv. Akad. Nauk, Ser. Khim.*, 1998, 913].
- S. Brun, M. Parera, A. Pla-Quintana, A. Roglans, T. Leon, T. Achard, J. Sol, X. Verdaguer, A. Riera, *Tetrahedron*, 2010, 66, 9032.
- I. E. Mikhailov, G. A. Dushenko, V. I. Minkin, *Russ. J. Org. Chem. (Engl. Transl.)*, 1993, **29**, 887 [*Zh. Org. Khim.*, 1993, **29**, 1072].

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