Synthesis of tetrachloroisophthalic and -terephthalic aldehydes and stable bis(nitrile oxides) based on them

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A new route for the synthesis of 2,4,5,6-tetrachloroisophthalic and 2,3,5,6-tetrachloroterephthalic aldehydes from the corresponding tetrachlorobenzenes was developed. The method involves dichloromethylation of the initial compounds with chloroform in the presence of aluminum chloride and subsequent hydrolysis of the resulting 1,3-bis(dichloromethyl)-2,4,5,6-tetrachlorobenzene and 1,4-bis(dichloromethyl)-2,3,5,6-tetrachlorobenzene. Stable 2,4,5,6-tetrachlorobenzene-1,3-dicarbonitrile oxide and 2,3,5,6-tetrachlorobenzene-1,4-dicarbonitrile oxide were obtained for the first time from the above aldehydes *via* the corresponding oximes. The products were characterized by IR and ^{13}C NMR spectra, and were converted into substituted 1,3- and 1,4-phenylenebis(isoxazolines) using 1,3-dipolar cycloaddition with styrene.

Key words: 2,4,5,6-tetrachloroisophthalic aldehyde, 2,3,5,6-tetrachloroterephthalic aldehyde; electrophilic dichloromethylation of tetrachlorobenzenes; 1,3-bis(dichloromethyl)-2,4,5,6-tetrachlorobenzene, 1,4-bis(dichloromethyl)-2,3,5,6-tetrachlorobenzene; stable 2,4,5,6-tetrachlorobenzene-1,3-dicarbonitrile oxide and 2,3,5,6-tetrachlorobenzene-1,4-dicarbonitrile oxide, synthesis; 1,3-dipolar cycloaddition.

Nitrile oxides are active 1,3-dipoles that react readily with compounds containing multiple bonds and various functional groups.[1—4] This feature provides the possibility of using bis(nitrile oxides) as effective low-temperature curing agents for unsaturated rubbers. The use of bis(nitrile oxides) of the general formula ONC—X—CNO (X is phenylene, biphenylene, naphthylene, or phenanthrylene) as curing agents for unsaturated polymers, for example, polybutadiene, has been patented.[5] Previously, a method of synthesis of stable aromatic bis(nitrile oxides), in which the nitrile oxide functions are shielded by two methyl or ethyl groups located in the *ortho*-positions, was developed in our laboratory.[6]

Aldehydes act as the most important key compounds in the synthesis of nitrile oxides, including aromatic nitrile oxides, because synthetic schemes include most frequently oximation of an aldehyde and transformation of the aldoxime into a nitrile oxide. Preparation of dialdehydes, which are precursors of bis(nitrile oxides), is an especially complicated task. In particular, introduction of the first aldehyde group deactivates the aromatic ring and hampers further formylation; therefore the development of multistage procedures is required. One of the solutions of this problem, which allows one to prepare sterically shielded aromatic dialdehydes[7] and to bypass the deactivating effect of the formyl group, is transformation of the latter into a dichloromethyl group; after that, the second aldehyde group can easily be introduced. The subsequent hydrolysis leads to the desired dialdehyde.

The purpose of this work is to synthesize stable bis(nitrile oxides), the CNO groups in the molecules of which are shielded by Cl atoms, *viz.*, 2,4,5,6-tetrachloroisophthalobis(nitrile oxide) (**1**) and 2,3,5,6-tetrachloroterephthalobis(nitrile oxide) (**2**). Note that the complete replacement of the hydrogen atoms in the benzene ring by chlorine atoms ensures the unusually high stability of a related compound, pentachlorobenzonitrile oxide.[8] The sequence of transformations, which was planned and accomplished, is presented in Scheme 1.

At first glance, it would seem that 2,4,5,6-tetrachloroisophthalic (**3**) and 2,3,5,6-tetrachloroterephthalic (**4**) dialdehydes, needed as the starting compounds, can be obtained most easily *via* the long-known chlorination of *m*- and *p*-xylenes giving 1,3-bis(dichloromethyl)-2,4,5,6-tetrachlorobenzene (**5**) and 1,4-bis(dichloromethyl)-2,3,5,6-tetrachlorobenzene (**6**) followed by hydrolysis. However, the methods reported for the chlorination of xylenes[9—11] afford mixtures containing products of more extensive chlorination together with compounds chlorinated to a lesser degree than is needed. Consequently, the target octachlorides **5** and **6** are obtained in a yield of no more than 45%. Furthermore, the melting points reported for pairs of isomeric octachlorides and those for the dialdehydes synthesized from them are fairly close to one another and, accord-

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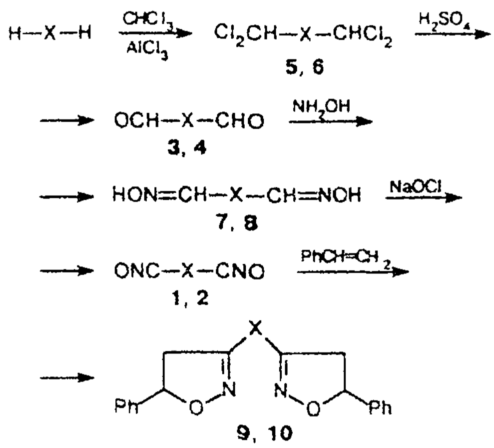
Scheme 1

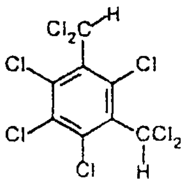


1, 3, 5, 7, 9: X = 2,3,4,6-Cl_4C_6

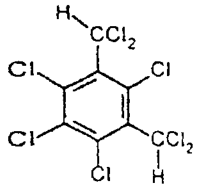
2, 4, 6, 8, 10: X = 2,3,5,6-Cl_4C_6

ing to some sources, they even coincide. In the absence of any other characteristics of the compounds and in view of the fact that the difference between the boiling points of the initial *m*- and *p*-xylenes is minor, doubts are cast upon the individuality of the products. Therefore, to prepare dialdehydes **3** and **4**, we have chosen the method[12,13] involving dichloromethylation of tetrachlorobenzenes with chloroform in the presence of anhydrous $AlCl_3$ and subsequent hydrolysis of the dichloromethyl group to give an aldehyde group. This procedure makes it possible to introduce two dichloromethyl groups, since, as noted above, the first introduced group deactivates the ring only weakly and virtually does not hamper further electrophilic substitution.

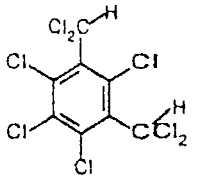
Note that the yield and characteristics of products synthesized previously[12,13] are well reproducible, but the melting point of octachloride **5** differs markedly from the value reported for the product obtained by chlorination of *m*-xylene; the octachloride was isolated[12] upon dichloromethylation of 1,2,3,5-tetrachlorobenzene, m.p. 108—110 °C; previously,[11] it was described with a melting point of 94—96 °C. The melting points of samples of octachloride **6**, synthesized by various methods, are almost identical (126—128[11] and 127—129 °C,[13] respectively). The ^1H NMR spectra of octachlorides **5** and **6**, recorded at room temperature, exhibit two broadened signals each, which is due to hindered rotation of the $CHCl_2$ groups. Without dwelling on a detailed interpretation of the spectra, we note that the ^1H NMR spectrum of octachloride **5** obtained at −41 °C in deuterotoluene has been reported,[14] and the signals corresponding to three rotation isomers have been assigned. The energetically favorable rotamer **A** containing nonequivalent $CHCl_2$ groups is responsible for two singlets, while "symmetrical" rotamers **B** and **C** account for one singlet each (for the sake of clarity, we showed only the C—H bonds, which are coplanar to the benzene ring, and did not show the C—Cl bonds of the $CHCl_2$ groups, one of which is located above the plane of the benzene ring, while the other is below this plane). As the temperature increases, the signals are broadened and then coalesce, so that at 70 °C, the spectrum exhibits only two broad signals.[14]



A



B



C

The unique ability of the above-mentioned tetrachlorobenzenes to undergo dichloromethylation is probably due to the presence of weak electron-withdrawing substituents in the aromatic ring and to the steric effect created by the two Cl atoms in the *ortho*-positions and by the Cl atoms in the other positions "buttressing" them (*cf.* Ref. 8). The electron-withdrawing substituents prevent the dichloromethyl derivatives from forming benzyl-type cations, which could act as electrophiles toward molecules of unreacted initial compound and thus lead to undesirable "cross-linking," giving diarylchloromethane and triarylmethane derivatives. The steric shielding plays a similar role, *i.e.*, it also prevents "cross-linking". The low stability of the benzyl cations under consideration is also confirmed by the data on hydrolysis of the dichloromethyl group. In fact, to carry out the hydrolysis of bis-dichloromethyl derivatives of tetrachlorobenzenes **5** and **6**, these compounds must be kept in concentrated H_2SO_4 at 130—150 °C for 5—6 h.[9,15] However, hydrolysis of a dichloromethyl group in an activated aromatic ring occurs under milder conditions. For example, dichloromethyl-substituted di-, tri-, and tetramethylbenzaldehydes are hydrolyzed upon boiling in a mixture of ethanol and butanol with concentrated HCl for 1 h.[7] It is significant that the melting points of both octachlorides **5** and **6** (see above) and the products of their hydrolysis that we obtained differ noticeably from those reported previously; 2,4,5,6-tetrachloroisophthalic aldehyde (**3**) has a melting point of 177—178 °C (see Ref. 10: m.p. 197 °C), and 2,3,5,6-tetrachloroterephthalic aldehyde (**4**) has a melting point of 182—183.5 °C (see Ref. 9: m.p. 195 °C). Moreover, after recrystallization of a crude product, its melting point decreases.

The transformation of dialdehydes **3** and **4** into the corresponding dialdoximes **7** and **8** presented no problems. The dialdoximes that we obtained are high-melting crystalline substances, poorly soluble in most organic solvents.

Nitrile oxides **1** and **2** were synthesized by the oxidation of aldoximes **7** and **8** with a solution of sodium hypochlorite. Purification of stable nitrile oxides presents a separate problem. Their recrystallization is inefficient, since at ~100 °C, these nitrile oxides isomerize to isocyanates. Therefore, researchers usually restrict themselves to reprecipitation. The nitrile oxides **1** and **2** obtained by us have not been described in the literature and can be of interest as reagents for cross-linking (curing) or modification of rubbers, in particular, due to their good solubility in many organic solvents. The ability of bis(nitrile oxides) **1** and **2** to undergo 1,3-dipolar cycloaddition was proved by converting them into cycloadducts with styrene **9** and **10**. The reaction proceeds when a mixture of nitrile oxide with styrene is kept in a solvent at room temperature for 24 h. Isoxazolines formed in virtually quantitative yields are high-melting crystalline substances.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 radiospectrometer, and IR spectra were obtained on a Perkin-Elmer 577 instrument (for suspensions in Vaseline oil).

1,3-Bis(dichloromethyl)-2,4,5,6-tetrachlorobenzene (5) was prepared according to a known procedure,[12] by refluxing a mixture of 1,2,3,5-tetrachlorobenzene[16] (9.77 g, 0.045 mol) and anhydrous $AlCl_3$ (13 g, 0.098 mol) in 200 mL of dry $CHCl_3$ for 14 h. Yield 14.1 g (82%), m.p. 109—110 °C (from hexane). ^{1}H NMR ($CDCl_3$) δ: 7.61 and 7.72 in a ratio of ~3 : 1 (br.s, 2 H, $CHCl_2$).

1,4-Bis(dichloromethyl)-2,3,5,6-tetrachlorobenzene (6)[13] was prepared in a similar way from 1,2,4,5-tetrachlorobenzene[17] (15.8 g, 0.073 mol) and anhydrous $AlCl_3$ (21 g, 0.158 mol) in 200 mL of dry $CHCl_3$. Yield 24.3 g (87%), m.p. 125—127 °C (hexane). ^{1}H NMR ($CDCl_3$), δ: 7.61 and 7.63 in a ratio of ~1 : 1 (br.s, 2 H, $CHCl_2$).

2,4,5,6-Tetrachloroisophthalic aldehyde (3) was prepared by a previously described procedure[9] from 1,3-bis(dichloromethyl)-2,4,5,6-tetrachlorobenzene **5** (13.3 g, 0.035 mol) and $FeSO_4$ (1 g, 0.0066 mol) in 100 mL of concentrated H_2SO_4 (150 °C, 5 h). Then the mixture was cooled and poured on ice, and the resulting precipitate was filtered off, thoroughly washed with water on the filter, and recrystallized from 50% MeCOOH. Yield 6.45 g (68%), m.p. 177—178 °C. ^{1}H NMR ($CDCl_3$), δ: 10.36 (s, 2 H, CHO). ^{13}C NMR ($CDCl_3$), δ: 187.0 (CHO); 138.3, 134.2, 132.3, and 129.2 (C arom.). Found (%): C, 35.36; H, 0.79; Cl, 52.24. $C_8H_2Cl_4O_2$. Calculated (%): C, 35.34; H, 0.74; Cl, 52.15.

2,3,5,6-Tetrachloroterephthalic aldehyde (4)[10] was prepared in a similar way from 1,4-bis(dichloromethyl)-2,3,5,6-tetrachlorobenzene **6** (21 g, 0.055 mol) and $FeSO_4$ (1 g, 0.0066 mol) in 110 mL of concentrated H_2SO_4. Crystallization from MeCOOH gave 9.0 g (60%) of the aldehyde, m.p. 182—183.5 °C. ^{1}H NMR ($CDCl_3$), δ: 10.34 (s, 2 H, CHO). ^{13}C NMR ($CDCl_3$), δ: 186.9 (CHO); 136.2 and 133.5 (C arom.). Found (%): C, 35.53; H, 0.84; Cl, 51.87. $C_8H_2Cl_4O_2$. Calculated (%): C, 35.34; H, 0.74; Cl, 52.15.

2,4,5,6-Tetrachloroisophthlalic aldoxime (7). A solution of hydroxylamine hydrochloride (2.92 g, 0.042 mol) and sodium acetate (3.44 g, 0.042 mol) in 15 mL of water was added to a boiling solution of aldehyde **3** (3.9 g, 0.014 mol) in 50 mL of EtOH. The resulting mixture was refluxed for 2 h. The precipitate of oxime **7** that formed after cooling (3.18 g, m.p. 211—212 °C) was filtered off. The addition of water to the filtrate gave 0.78 g of a precipitate, whose crystallization from aqueous EtOH gave an additional 0.6 g of oxime **7**, m.p. 212.0—212.5 °C. Overall yield 89%. ^{1}H NMR (DMSO-d_6), δ: 8.20 (s, 2 H, CH); 11.90 (s, 1 H, OH); (CD_3OD), δ: 8.35 (s, 2 H, CH). ^{13}C NMR (CD_3OD), δ: 146.0 (CH); 136.3, 135.3, 133.7, and 133.0 (C arom). Found (%): C, 32.14; H, 1.20; Cl, 46.91; N, 9.09. $C_8H_4Cl_4N_2O_2$. Calculated (%): C, 31.82; H, 1.34; Cl, 46.97; N, 9.28.

2,3,5,6-Tetrachloroterephthalic aldoxime (8). A solution of hydroxylamine hydrochloride (6.05 g, 0.087 mol) and sodium acetate (7.15 g, 0.087 mol) in 30 mL of water was added to a suspension of aldehyde **4** (7.9 g, 0.029 mol) in 100 mL of EtOH. The heterogeneous mixture thus formed was refluxed for 2 h. After cooling, the precipitate was filtered off and crystallized from EtOH to give 8.4 g (95%) of oxime **8**, m.p. 269—270 °C. ^{1}H NMR (DMSO-d_6), δ: 8.25 (s, 2 H, CH); 11.95 (s, 2 H, NOH). ^{13}C NMR (DMSO-d_6), δ: 144.2 (CHNOH); 132.0 and 131.9 (C arom). Found (%): C, 32.16; H, 1.36; Cl, 47.20; N, 9.46. $C_8H_4Cl_4N_2O_2$. Calculated (%): C, 31.82; H, 1.34; Cl, 46.97; N, 9.28.

2,4,5,6-Tetrachlorobenzene-1,3-dicarbonitrile oxide (1). A 13% solution of sodium hypochlorite (27.5 mL, 0.048 mol) (prepared by passing chlorine through an aqueous solution of NaOH; the concentration was determined by titration) was added dropwise with intense stirring to a suspension of oxime **7** (3.6 g, 0.012 mol) in 100 mL of CH_2Cl_2. The resulting mixture was stirred for 1.5 h, and during this period, the oxime entirely dissolved. Then the organic layer was separated, the aqueous solution was extracted with CH_2Cl_2 (3×20 mL), and the combined organic extracts were washed with water and dried with $MgSO_4$. The solvent was evaporated, and the residue was crystallized from a chloroform—ethanol mixture (3 : 2, v/v) to give 3.3 g (93%) of nitrile oxide **1**, m.p. 280—281 °C. ^{13}C NMR ($CDCl_3$), δ: 142.0, 139.4, and 133.7 (C—Cl); 115.6 ($\underline{C}$—CNO); 29.6 (CNO). IR, ν/cm^{-1}: 2300 (CN). Found (%): C, 32.49; Cl, 48.11; N, 9.48. $C_8Cl_4N_2O_2$. Calculated (%): C, 32.25; Cl, 47.60; N, 9.40.

2,3,5,6-Tetrachlorobenzene-1,4-dicarbonitrile oxide (2) was prepared in a similar way from oxime **8** (3 g, 0.01 mol) and 13% solution of sodium hypochlorite (23 mL, 0.04 mol) and recrystallized from a chloroform—ethanol mixture (3 : 1, v/v). Yield 2.38 g (80%), m.p. 285—286 °C. IR, ν/cm^{-1}: 2300 (CN). Found (%): C, 32.40; Cl, 47.75; N, 9.59. $C_8Cl_4N_2O_2$. Calculated (%): C, 32.25; Cl, 47.60; N, 9.40.

Tetrachloro-*m*-phenylenebis(5-phenyl-4,5-dihydroisoxazole) (9). A solution of nitrile oxide **1** (0.3 g, 0.001 mol) and styrene (0.23 mL, 0.002 mol) in 10 mL of chloroform was allowed to stand at ~20 °C for 24 h. Then the solvent was evaporated, and the remaining oil was crystallized by adding a small amount of hexane to give 0.48 g (94%) of adduct **9**, m.p. 153—154 °C. ^{1}H NMR ($CDCl_3$), δ: 7.35 (m, 10 H, Ph); 5.85 (dd, 2 H, C$\underline{H}$—Ph, J = 11 and 8 Hz); 3.70 (dd, 2 H, CH_2, J = 17 and 11 Hz); 3.25 (dd, 2 H, CH_2, J = 17 and 11 Hz) Found (%): C, 56.71; H, 3.43; Cl, 28.36; N, 5.59. $C_{24}H_{16}Cl_4N_2O_2$. Calculated (%): C, 56.94; H, 3.19; Cl, 28.01; N, 6.32.

Tetrachloro-*p*-phenylenebis(5-phenyl-4,5-dihydroisoxazole) (10) was prepared in a similar way from nitrile oxide **2** (0.2 g, 0.67 mmol) and styrene (0.16 mL, 1.34 mol) in 5 mL of $CHCl_3$. Yield 0.31 g (91%), m.p. 160—166 °C. ^1H NMR ($CDCl_3$), δ: 7.50 (m, 10 H, Ph); 5.90 (dd, 2 H, $C\underline{H}$—Ph, J = 11 and 8 Hz); 3.75 (dd, 2 H, CH_2, J = 17 and 11 Hz); 3.25 (dd, 2 H, CH_2, J = 17 and 11 Hz). ^{13}C NMR ($CDCl_3$), δ: 153.0 (C=N); 140.0 ($C(Ph)_{ipso}$); 132.8 and 132.4 (C_6Cl_4); 128.9 ($C(Ph)_m$); 128.5 ($C(Ph)_p$); 126.1 ($C(Ph)_o$); 83.5 ($\underline{C}H$—Ph); 44.8 (CH_2). Found (%): C, 56.27; H, 3.48; Cl, 27.67; N, 5.50. $C_{24}H_{16}Cl_4N_2O_2$. Calculated (%): C, 56.94; H, 3.19; Cl, 28.01; N, 6.32.

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References

1. C. Grundmann and P. Grunanger, *The Nitrile Oxides*, Springer-Verlag, Berlin, 1971, 242 pp.
2. *1,3-Dipolar Cycloaddition Chemistry*, Ed. A. Padwa, Wiley, New York, 1984, **1**, 817; **2**, 704.
3. K. B. G. Torssell, *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*, Verlagsgeselschaft, Weinheim, 1988, 322.
4. M. M. Krayushkin, *Zh. Vsesoyuz. Khim. Obshch. im. D. I. Mendeleeva*, 1991, **36**, 463 [*Mendeleev Chem. J.*, 1991, **36** (Engl. Transl.)].
5. US Pat. 3390204 (Hercules); *Chem. Abstrs.* 1968, **69**, 36900g.
6. D. V. Tsyganov, A. P. Yakubov, L. I. Belen'kii, and M. M. Krayushkin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 1398 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 1238 (Engl. Transl.)].
7. A. P. Yakubov, D. V. Tsyganov, L. I. Belen'kii, and M. M. Krayushkin, *Tetrahedron*, 1993, **49**, 3397.
8. B. J. Wakefield and D. J. Wright, *J. Chem. Soc., C*, 1970, 1165.
9. Ger. Pat. 243749 (Bayer); *Chem. Zbl.*, 1912, I, 763; Frdl. X, 219.
10. Ger. Pat. 360414 (Cassella); *Chem. Zbl.*, 1923, II, 406; Frdl. XIV, 378.
11. P. G. Harvey, F. Smith, M. Stacey, and J. C. Tatlow, *J. Appl. Chem.*, 1954, **4**, 319.
12. J. Veciana, C. Rovira, M. J. Crespo, O. Armut, V. M. Domingo, and F. Palacio, *J. Am. Chem. Soc.*, 1991, **113**, 2552.
13. J. Castaner and J. Riera, *J. Org. Chem.*, 1991, **56**, 5445.
14. J. Peeling, B. W. Goodwin, T. Schaefer, and C. Wong, *Can. J. Chem.*, 1971, **49**, 1489.
15. US Pat. 3146086, 1964; *RZhKhim.*, 1966, 6N, 489P (in Russian).
16. H. U. Hodgson and A. P. Mahadevan, *J. Chem. Soc.*, 1947, 173.
17. A. P. Terent'ev and L. A. Yanovskaya, *Reaktsii i metody issledovaniya organicheskikh soedinenii* [*Reactions and Methods for Investigation of Organic Compounds*], 1957, **6**, 102 (in Russian).

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