An Efficient Synthesis of Rubin's Aldehyde and its Precursor 1,3,5-Tribromo-2,4,6-tris(dichloromethyl)benzene

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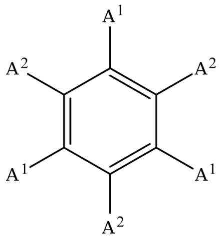
2,4,6-Tribromobenzene-1,3,5-tricarboxaldehyde (**4**) can be efficiently prepared in two reaction steps from 1,3,5-tribromobenzene. The intermediate 1,3,5-tribromo-2,4,6-tris(dichloromethyl)benzene (**3**) crystallizes from petroleum ether in its C_{3h} structure. However, in $CDCl_3$ solution it exists at room temperature in two isomeric forms: **3a** (C_{3h}) and **3b** (C_s) (1 : 1.15). The intramolecular Br···Cl distances are much smaller than the sum of the van der Waals radii. Therefore, the exocyclic C–C bonds show a hindered rotation.

Key words: Polyfunctional Aromatics, Hexasubstituted Benzenes, Hindered Rotation

Introduction

Benzene derivatives **1** with three functional groups A^1 in 1,3,5-position and three other functional groups A^2 in 2,4,6-position are very valuable starting compounds for orthogonal synthetic strategies. A great variety of hexasubstituted benzene derivatives can be prepared on the basis of compounds **1** with different functionalities.

Rubin's aldehyde [1, 2], namely 2,4,6-tribromobenzene-1,3,5-tricarboxaldehyde (2,4,6-tribromotrimesinaldehyde, A^1 = CHO, A^2 = Br) served for example as a precursor of hexaethynylbenzenes and other [6]star compounds [1 – 3], polycyclic aromatics [2], fullerene C_{60} [3], graphyne [3], and polycentric metal complexes [4]. We are interested in Rubin's aldehyde as a precursor of conjugated star-shaped or dendritic oligomers [5, 6].



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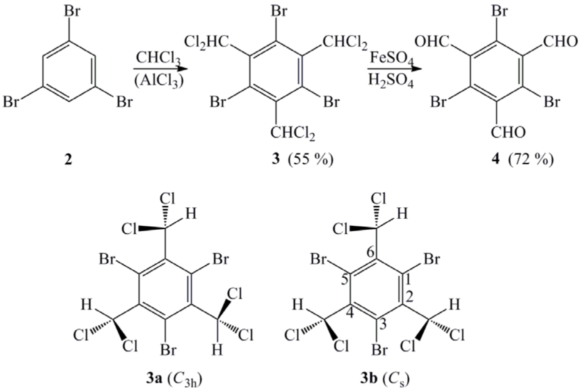
Results and Discussion

Rubin's aldehyde (**4**) is usually obtained from mesitylene in five reaction steps [1, 2]. Scheme 1 reveals that we succeeded to prepare **4** in two steps from commercially available 1,3,5-tribromobenzene (**2**). The Friedel-Crafts alkylation of **2** with chloroform yielded 1,3,5-tribromo-2,4,6-tris(dichloromethyl)benzene (**3**) in a yield of 55 %. Subsequent hydrolysis of **3** with conc. H_2SO_4 in the presence of $FeSO_4$ afforded the trialdehyde **4** in 72 % yield (Scheme 1).



Scheme 1. Preparation of Rubin's aldehyde (**4**).

Table 1 contains the ^1H and ^{13}C NMR data of **3** and **4**. In contrast to **4**, compound **3** consists in $CDCl_3$ solution at room temperature of two isomers, namely **3a**, showing C_{3h} symmetry, and the less symmetrical rotamer **3b** (C_s). Obviously, the rotation of the dichloromethyl groups is hindered by the neighboring Br substituents. The statistical ratio **3a** : **3b** amounts to 1 : 3, the measured ratio ($CDCl_3$, T = −15 °C) is 1 : 1.15.

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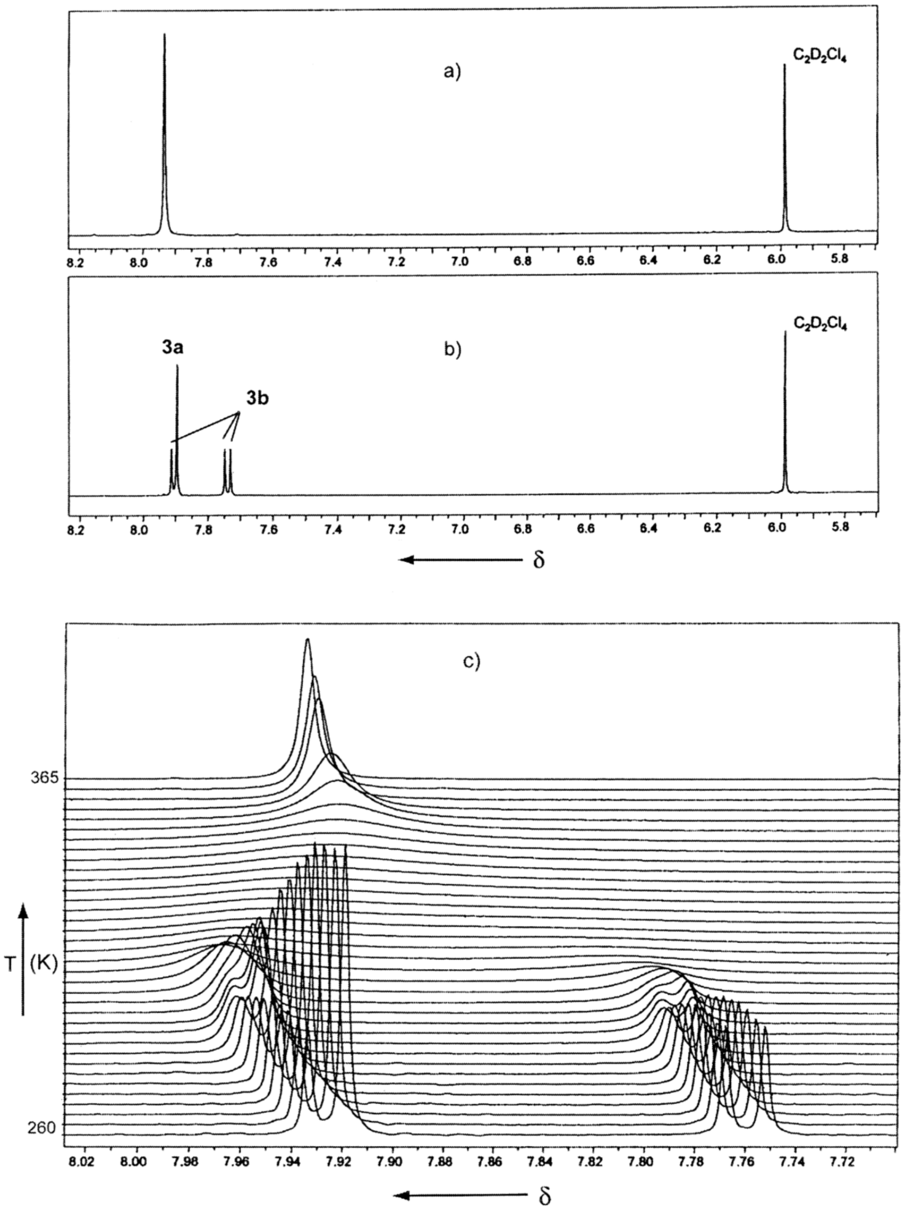

Fig. 1. ^{1}H NMR spectra of **3** in $C_2D_2Cl_4$: a) measurement at 365 K, b) measurement at 260 K, c) coalescence measurement in the aromatic region (δ values related to TMS as internal standard).

Semiempirical calculations (PC Model V 7.00, MestRe-C2.3) gave a small enthalpy difference of 0.3 kcal mol^{-1} in favor of **3a**. The statistical entropy term R ln3 reverts the rotamer distribution.

Fig. 1 shows the ^{1}H NMR spectra of **3a**, **b** at 365 K (85 °C) and 260 K (−13 °C) in $C_2D_2Cl_4$ and the corresponding coalescence phenomenon in the temperature-dependent measurements. Three signals of **3b** with the frequencies ν_1, ν_3 and ν_4 and one signal of **3a** with the frequency ν_2 are involved in the coalescence. Therefore the free activation energy $\Delta G^{\neq}$ for the exchange process can be estimated according to Eq. 1:

$$\Delta G^{\neq} = \mathrm{R}T_\mathrm{c}\left(22.96 + \ln\frac{3T_\mathrm{C}}{3\nu_2 - (\nu_1 + \nu_3 + \nu_4)}\right) \quad (1)$$

At the coalescence temperature $T_\mathrm{c} = 340 \pm 5$ K, the free activation energy $\Delta G^{\neq}$ amounts to 16.7 ± 0.3 kcal mol^{-1} [7]. This result agrees very well with the barrier of 16.3 ± 0.4 kcal mol^{-1} which was obtained for 1,3,5-trichloro-2,4,6-tris(dichloromethyl)-

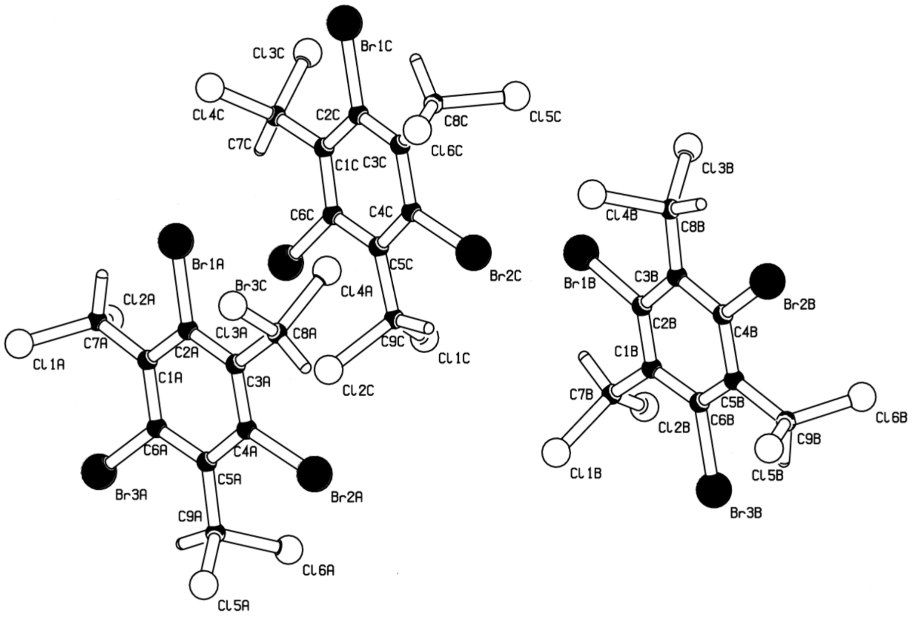

Fig. 2. Part of the crystal structure of **3a** which contains three slightly different molecules in the asymmetric unit.

Table 1. ^1H and ^{13}C NMR data of **3a** and **3b** measured in $CDCl_3$ at 20 °C.

	3a		**3b**	
	^{13}C	^1H	^{13}C	^1H
C-1	127.0		125.3	
C-2	138.3		135.9	
C-3	127.0		129.8	
C-4	138.3		140.2	
C-5	127.0		127.4	
C-6	138.3		130.0	
2-$CHCl_2$, 6-$CHCl_2$	71.1	7.94	71.7, 71.8	7.77, 7.78
4-$CHCl_2$	71.1	7.94	71.0	7.95

benzene [8]. Trialdehyde **4** has a much lower barrier for the rotation of the formyl groups. Thus, it gives at room temperature only one set of ^1H and ^{13}C signals, each.

Crystallization of **3** from a solution in petroleum ether (b.p. 40 – 70 °C) yielded selectively the more symmetric form **3a** (Fig. 2). The asymmetric unit contains three slightly different molecules **3a** (A, B, C). The most interesting geometrical parameters concern the distances between the Br atoms and the neighboring Cl atoms of the prochiral $CHCl_2$ groups. The deviation of the Br atoms from the plane of the benzene ring is very small (Table 2). The geminal Cl atoms are below and above the benzene ring plane in an equivalent distance.

The sum of the van der Waals radii of Br and Cl amounts to $1.80 + 1.95 = 3.75$ Å. Table 2 reveals that the distances Br···Cl in **3a** are generally much smaller.

Table 2. Distances *d* (Å) of the Br atoms from the mean plane of the benzene ring and distances between the Br and the Cl atoms of **3a**[a].

Distances Br···Cl	Molecule A	Molecule B	Molecule C
d (Br-1)	−0.03(1)	−0.09(1)	−0.05(3)
Br-1···Cl-3	3.308(2)	3.345(3)	3.249(3)
Br-1···Cl-4	3.317(3)	3.345(3)	3.359(3)
d (Br-2)	−0.09(1)	0.11(2)	−0.12(1)
Br-2···Cl-5	3.342(2)	3.443(4)	3.346(3)
Br-2···Cl-6	3.306(2)	3.460(4)	3.345(3)
d (Br-3)	0.17(1)	0.01 (1)	0.14(1)
Br-3···Cl-1	3.296(3)	3.501(3)	3.309(3)
Br-3···Cl-2	3.346(3)	3.473(6)	3.324(2)

[a] The crystallographic atom numbering chosen does not correspond to the IUPAC nomenclature.

The rotation around the exocyclic C–C single bonds is considerably hindered, since its transition state has an even shorter Br···Cl distance.

Experimental Section

^1H and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer. Field-desorption MS measurements were performed with a Finnigan MAT 95 spectrometer. A Perkin Elmer Spectrum 6X was used for recording the IR spectra. Elemental analyses were performed in the microanalytical laboratory of the Chemistry Department of the University of Mainz.

*1,3,5-Tribromo-2,4,6-tris(dichloromethyl)benzene (**3a**)*

1,3,5-Tribromobenzene (**2**) (1.00 g, 3.18 mmol), $AlCl_3$ (0.50 g, 3.75 mmol) and 10 mL of dry $CHCl_3$ were

Table 3. Details of the X-ray crystal structure analysis of **3a**.

Formula	$C_9H_3Br_3Cl_6$
M_r	563.54
Crystal size, mm^3	$0.1 \times 0.2 \times 0.3$
Crystal habit	block
Crystal system	hexagonal
Space group	$P6_5$
a, Å	16.4172(3)
c, Å	30.2406(6)
V, Å^3	7058.6(4)
Z	18
T, K	173
D_{calcd}, Mg m^{-3}	2.39
$F(000)$, e	4752
μ(MoK_α), mm^{-1}	8.7
Abs. corr.; T_{min} / T_{max}	multiscan; 0.07 / 0.15
hkl range	−20/21, ±21, ±39
θ range, deg	1.4 – 27.8
Refl. measd. / unique / R_{int}	99752 / 11214 / 0.0843
Refl. with $I \geq 2\sigma(I)$	6859
Param. refined / restraints	487 / 1
$R(F)$ / $wR(F^2)$[a] $[I \geq 2\sigma(I)]$	0.0481 / 0.1225
Weighting scheme A[b]	0.068
GoF (F^2)[c]	0.889
x(Flack)	0.010(9)
$\Delta\rho_{\text{fin}}$ (max / min), e Å^{-3}	2.56 / −1.22

[a] $R1 = \|F_o| - |F_c\|/\Sigma|F_o|$; [b] $wR2 = [\Sigma w(F_o{}^2 - F_c{}^2)^2/\Sigma w(F_o{}^2)^2]^{1/2}$, $w = [\sigma^2(F_o{}^2) + (AP)^2]^{-1}$, where $P = (\text{Max}(F_o{}^2,0) + 2F_c{}^2)/3$, and A is a constant adjusted by the program; [c] $\text{GoF} = [\Sigma w(F_o{}^2 - F_c{}^2)^2/(n_{\text{obs}} - n_{\text{param}})]^{1/2}$.

stirred in a sealed tube at 120 °C for 16 h. The cold reaction mixture was poured into 10 mL of H_2O and treated with 20 mL of $CHCl_3$. The organic layer was dried (Na_2SO_4), concentrated and purified by column chromatography (40 × 2 cm SiO_2, petroleum ether, b. p. 40 – 70 °C). Crystallization from petroleum ether (b. p. 40 – 70 °C) yielded **3a** as colorless crystals (985 mg, 55 %) which melted at 205 – 206 °C. – IR (KBr): ν (cm^{-1}) = 3037, 1516, 1362, 1257, 1222, 990, 784, 704. – FD MS: m/z (%) = 568/566/564/562/560 (30/81/100/85/44) $[M]^+$ (Br_2Cl_6 isotope pattern). – $C_9H_3Br_3Cl_6$ (563.56): calcd. C 19.18, H 0.54; found C 19.10, H 0.71.

2,4,6-Tribromobenzene-1,3,5-tricarboxaldehyde (4)

To $Fe_2SO_4 \cdot 7H_2O$ (20 mg, 0.072 mmol) in 5 mL of conc. H_2SO_4 500 mg (0.887 mmol) of **3** was added. The mixture was vigorously stirred and heated to 130 °C. The evolved HCl gas was piped into 2 M aqueous NaOH. After 4 h the mixture was cooled to 0 °C and treated with 20 mL of ice water. The formed precipitate was washed with H_2O (2 × 30 mL) and purified by flash chromatography (7 × 7 cm SiO_2, CH_2Cl_2). Recrystallization form methanol yielded 255 mg (72 %) of a colorless powder, m. p. 250 °C (decomp.). – IR (KBr): ν (cm^{-1}) = 3392, 2894, 1702, 1537, 1401, 1335, 993, 945. – FD MS: m/z (%) = 402//400/398/396 (35/89/100/25) $[M]^+$ (Br_3 isotope pattern). – $C_9H_3Br_3O_3$ (398.84): calcd. C 27.10, H 0.76; found C 26.88, H 0.93.

Crystal structure analysis

Some details of the crystal structure analysis of **3a** are summarized in Table 3. The intensity data were collected on a Bruker APEX II diffractometer with graphite-monochromatized MoK_α radiation (λ = 0.71073 Å) using ω and φ scans (0.5° scan width). Reflections were corrected for background, absorption, Lorentz and polarization effects. The structure was solved by Direct Methods (SIR92 [9]) and refined using SHELXL-97 [10].

CCDC 815312 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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