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

Christoph Holst, Dieter Schollmeyer, and Herbert Meier

Institute of Organic Chemistry, University of Mainz, Duesbergweg 10-14, 55099 Mainz, Germany

Reprint requests to Prof. Dr. H. Meier. Fax: +49 (0)6131-3925396. E-mail: hmeier@mail.uni-mainz.de

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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 CDCl₃ 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 $\mathbf{1}$ 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 $\mathbf{1}$ 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 C₆₀ [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].



Results and Discussion

Rubin's aldehyde (4) is usually obtained from mesitylene in five reaction steps [1,2]. Scheme 1 re-



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

veals 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 FeSO₄ afforded the trialdehyde **4** in 72 % yield (Scheme 1).

Table 1 contains the ¹H and ¹³C NMR data of **3** and **4**. In contrast to **4**, compound **3** consists in CDCl₃ 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 (CDCl₃, T = -15 °C) is 1:1.15.

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Fig. 1. ¹H NMR spectra of **3** in C₂D₂Cl₄: 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 ¹H NMR spectra of **3a**, **b** at 365 K (85 °C) and 260 K (-13 °C) in C₂D₂Cl₄ and the corresponding coalescence phenomenon in the temperaturedependent measurements. Three signals of **3b** with the frequencies v_1 , v_3 and v_4 and one signal of **3a** with the frequency v_2 are involved in the coalescence. Therefore the free activation energy ΔG^{\neq} for the exchange process can be estimated according to Eq. 1:

$$\Delta G^{\neq} = \mathbf{R}T_{\rm c} \left(22.96 + \ln \frac{3T_{\rm C}}{3v_2 - (v_1 + v_3 + v_4)} \right) (1)$$

At the coalescence temperature $T_c = 340 \pm 5$ K, the free activation energy ΔG^{\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 ¹³C NMR data of **3a** and **3b** measured in CDCl₃ at 20 °C.

	3a		3	3b	
	¹³ C	^{1}H	¹³ C	^{1}H	
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 ¹³C 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 CHCl₂ 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 $Br \cdots Cl$ in **3a** are generally much smaller.

Distances Br ··· Cl Molecule A Molecule B Molecule C

Table 2. Distances d (Å) of the Br atoms from the mean plane

of the benzene ring and distances between the Br and the

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

Cl atoms of 3a^a.

¹H and ¹³C 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), AlCl₃ (0.50 g, 3.75 mmol) and 10 mL of dry CHCl₃ were

Table 3. D	etails of the	X-ray crystal	structure ana	lysis of 3a .

	-
Formula	C9H3Br3Cl6
Mr	563.54
Crystal size, mm ³	0.1 imes 0.2 imes 0.3
Crystal habit	block
Crystal system	hexagonal
Space group	P65
<i>a</i> , Å	16.4172(3)
<i>c</i> , Å	30.2406(6)
V, Å ³	7058.6(4)
Ζ	18
Т, К	173
$D_{\text{calcd}}, \text{Mg m}^{-3}$	2.39
<i>F</i> (000), e	4752
μ (Mo K_{α}), mm ⁻¹	8.7
Abs. corr.; T_{\min} / T_{\max}	multiscan; 0.07 / 0.15
hkl range	$-20/21,\pm 21,\pm 39$
θ range, deg	1.4-27.8
Refl. measd. / unique / Rint	99752 / 11214 / 0.0843
Refl. with $I \ge 2\sigma(I)$	6859
Param. refined / restraints	487 / 1
$R(F) / wR(F^2)^a [I \ge 2\sigma(I)]$	0.0481 / 0.1225
Weighting scheme A ^b	0.068
$\operatorname{GoF}(F^2)^{\mathrm{c}}$	0.889
x(Flack)	0.010(9)
$\Delta \rho_{\rm fin}$ (max / min), e Å ⁻³	2.56 / -1.22

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

stirred in a sealed tube at 120 °C for 16 h. The cold reaction mixture was poured into 10 mL of H₂O and treated with 20 mL of CHCl₃. The organic layer was dried (Na₂SO₄), concentrated and purified by column chromatography (40×2 cm SiO₂, petroleum ether, b. p. 40–70 °C). Crystallization from petroleum ether (b. p. 40–70 °C) yielded **3a** as colorless crystals (985 mg, 55 %)

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which melted at 205–206 °C. – IR (KBr): v (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]⁺ (Br₂Cl₆ isotope pattern). – C₉H₃Br₃Cl₆ (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 Fe₂SO₄ · 7H₂O (20 mg, 0.072 mmol) in 5 mL of conc. H₂SO₄ 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 H₂O (2 × 30 mL) and purified by flash chromatography (7 × 7 cm SiO₂, CH₂Cl₂). Recrystallization form methanol yielded 255 mg (72%) of a colorless powder, m. p. 250 °C (decomp.). – IR (KBr): v (cm⁻¹) = 3392, 2894, 1702, 1537, 1401, 1335, 993, 945. – FD MS: m/z (%) = 402//400/398/396 (35/89/100/25) [M]⁺ (Br₃ isotope pattern). – C₉H₃Br₃O₃ (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 Mo K_{α} radiation ($\lambda = 0.71073$ 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.

The effects of the three activation barriers are superimposed by a temperature effect on the chemical shifts; the resulting singlet at 365 K lies at lower field than all four singlets at 260 K. All effects together prevented us from a more exact evaluation by a line shape analysis.

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