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Synthesis and structural studies of *tris*-2-chlorobenzylamine and *tris*-2-bromobenzylamine

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The *tris*-2-chloro and 2-bromotribenzylamines are prepared from aqueous ammonia and 2-chlorobenzyl chloride and 2-bromobenzyl bromide, respectively, in ethanol. Recrystallization yielded colorless cubes of each product. The crystal structures are each solved in space group $P\bar{1}$, and are isostructural. The *tris*-2-chloro compound, **1**, has $a = 7.4226(5)$ Å, $b = 9.0825(7)$ Å, $c = 14.529(1)$ Å, $\alpha = 78.279(1)^\circ$, $\beta = 82.389(1)^\circ$, $\gamma = 84.661(1)^\circ$, and $V = 948.41(12)$ Å^3 with $Z = 2$, and $d_{\mathrm{calc}} = 1.368$ Mg/m^3. The *tris*-2-bromo analog, **2**, has $a = 7.6569(11)$ Å, $b = 9.0922(13)$ Å, $c = 14.614(2)$ Å, $\alpha = 79.286(2)^\circ$, $\beta = 81.777(2)^\circ$, $\gamma = 85.401(2)^\circ$, and $V = 987.9(2)$ Å^3 with $Z = 2$, and $d_{\mathrm{calc}} = 1.762$ Mg/m^3. Lithium–halogen exchange experiments conducted in tetrahydrofuran at -78°C using *n*-butyl lithium revealed that no exchange occurred for the *tris*-2-chloro compound, but did occur for the *tris*-2-bromo analog to yield tribenzylamine upon quench and work-up.

KEY WORDS: Tribenzylamine; triclinic; 2-chloro; 2-bromo; lithium–halogen exchange.

Introduction

Tetradentate tripodal ligands have shown tremendous scope in the synthesis of transition-metal complexes, especially in the bioinorganic genre. Perhaps the most extensively studied examples are those comprising *tris*-(2-pyridylmethyl)amine,[1] (referred to herein as tpa, Fig. 1), which has been widely exploited in complexes of copper[2] and iron.[3]

We are interested in exploring the organometallic chemistry of complexes of the *tris*-phenylide analog (Fig. 1) of tpa; we rationalized that this trianionic ligand should be accessible from *in situ* lithium–halogen exchange of *tris*-2-chlorobenzylamine and its 2-bromo counterpart. The synthesis of the latter was first reported over 100 years ago,[4] and recently found utility in the preparation of tripodal benzenethiols.[5] The former, perhaps surprisingly, has no record in the literature. The ensuing report gives high-yielding syntheses of *tris*-2-chlorobenzylamine and *tris*-2-bromobenzylamine, the crystal structures of both compounds, routine characterizations, and the results of lithium–halogen exchange endeavors.

Experimental

Materials and methods

The reagents 2-chlorobenzylamine (95%), 2-chlorobenzyl chloride (98%), and 2-bromobenzyl bromide (98%) were purchased from the Aldrich

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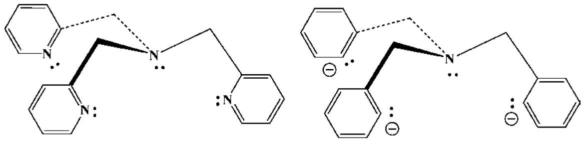

Fig. 1. Representations of tpa and its *tris*-phenylide counterpart.

Chemical Company. The triethylamine and aqueous ammonia were purchased from the Fisher Company. All solvents were reagent grade and were used without further purification. Melting points were recorded using an electrothermal EM-6 apparatus, and were not corrected. Nuclear magnetic resonance spectra were recorded using a Jeol Eclipse 400 MHz spectrometer. Mass spectrometry measurements were recorded on a Finnigan Mat GCQ instrument. Elemental analyses were determined using an Exeter Analytical CE440 SHA Elemental Analyzer.

Synthesis of tris-2-chlorobenzylamine (1)

The combination of 2-chlorobenzylamine (1.49 g, 10.0 mmol) with 2-chlorobenzyl chloride (3.29 g, 20.0 mmol) and triethylamine (2.02 g, 20 mmol) in acetonitrile (20 mL) in a 100 mL round-bottom flask yielded a colorless solution. After heating and stirring at reflux for 36 h, the clear solution was allowed to cool to deposit white crystals; these were collected by filtration, washed with acetonitrile, and allowed to air-dry to yield 2.70 g (69%) of *tris*-2-chlorobenzylamine, **1**. The same product was also obtained from the combination of 2-chlorobenzyl chloride (4.83 g, 30.0 mmol) with 29% aqueous ammonia (2.64 g, 45.0 mmol) in ethanol at room temperature. A white solid precipitated during stirring over 24 h. The precipitate was collected by filtration, washed with ethanol, and allowed to air-dry to yield 1.67 g (43%) of white microcrystals. Recrystallization was effected from hot acetonitrile to yield colorless blocks. Melting point: 89–91°C. ^{1}H-NMR ($CDCl_3$, δ): 3.82 (s, 2H, N—CH_2), 7.15 (t, 1H, phenyl-H, $J = 7.5$ Hz), 7.22 (t, 1H, phenyl-H, $J = 7.5$ Hz), 7.31 (d, 1H, phenyl-H, $J = 8.0$ Hz), 7.65 (d, 1H, phenyl-H, $J = 7.5$ Hz). Mass spectrometry: (70 eV, electron impact) *m/z* 393, 391, 389, 280, 278, 264, 127, 125. Anal. Calcd for $C_{21}H_{18}NCl_3$: C, 64.55; H, 4.64; N, 3.58. Found: C, 64.28; H, 4.76; N, 3.64.

Synthesis of tris-2-bromobenzylamine (2)

The combination of 2-bromobenzyl bromide (5.29 g, 21.0 mmol) with 29% aqueous ammonia (1.76 g, 30.0 mmol) in ethanol at room temperature produced a white solid during stirring over 24 h. The precipitate was collected by filtration, washed with ethanol, and allowed to air-dry to yield 3.55 g (97%) of **2** as white microcrystals. Recrystallization was effected from hot acetonitrile to yield colorless blocks. Melting point: 122.0–122.5°C. ^{1}H-NMR ($CDCl_3$, δ): 3.79 (s, 2H, N—CH_2), 7.08 (t, 1H, phenyl-H, $J = 7.7$ Hz), 7.27 (t, 1H, phenyl-H, $J = 7.1$ Hz), 7.51 (d, 1H, phenyl-H, $J = 8.1$ Hz), 7.65 (d, 1H, phenyl-H, $J = 7.2$ Hz). Mass spectrometry: (70 eV, electron impact) *m/z* 527, 525, 523, 521, 370, 368, 366, 356, 354, 352, 171, 169. Anal. Calcd for $C_{21}H_{18}NBr_3$: C, 48.13; H, 3.46; N, 2.67. Found: C, 48.06; H, 3.43; N, 2.72.

Reactivity with n-*butyl lithium*

In a 50 mL round-bottom flask equipped with magnetic stirrer, 1.00 mmol of either **1** or **2** was dissolved in freshly distilled tetrahydrofuran (5.0 mL). Under nitrogen flow, the colorless solution was cooled to −78°C while stirring. After a few minutes, 1.2 mL of 2.5 M *n*-butyllithium in hexane (3.0 mmol) was injected by syringe and the solution turned peach-pink. After stirring for 10 min, the reaction was quenched by addition of water (0.20 mL, 11 mmol) to yield a colorless solution and white precipitate. After a few more minutes, the solution was filtered and the filtrate allowed to evaporate. The residual white solid from the reaction of **1** was recrystallized from acetonitrile to yield white crystals of starting material **1**; the residual white solid from the reaction of **2** was recrystallized from acetonitrile to yield white

Table 1. Crystal Data and Structure Refinement for *tris*-2-Chlorobenzylamine, **1**, and *tris*-2-Bromobenzylamine, **2**

	1	**2**
Empirical formula	$C_{21}H_{18}N\ Cl_3$	$C_{21}H_{18}N\ Br_3$
CCDC deposit number	CCDC-241081	CCDC-241082
Formula weight	390.71	524.09
Temperature (K)	173(2)	173(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
Unit cell dimensions		
a (Å)	7.4226(5)	7.6569(11)
b (Å)	9.0825(7)	9.0922(13)
c (Å)	14.529(1)	14.614(2)
α (°)	78.279(1)	79.286(2)
β (°)	82.389(1)	81.777(2)
γ (°)	84.661(1)	85.401(2)
Volume ($Å^3$)	948.41(12)	987.9(2)
Z	2	2
Density (calculated) (Mg/m^3)	1.368	1.762
Absorption coefficient (mm^{-1})	0.486	6.129
F(000)	404	512
Crystal color, morphology	Cube, Colorless	Cube, Colorless
Crystal size (mm)	0.25 × 0.25 × 0.21	0.25 × 0.25 × 0.25
Theta range for data collection (°)	1.44 to 25.10	2.28 to 27.51
Index ranges	$-8 \leq h \leq 8$ $-10 \leq k \leq 10$ $0 \leq l \leq 17$	$-9 \leq h \leq 9$ $-11 \leq k \leq 11$ $0 \leq l \leq 18$
Reflections collected	4750	10457
Independent reflections, *R* (int)	3236, 0.0234	4442, 0.0364
Observed reflections	2579	3535
Completeness to theta = 25.10°, 27.51°	95.5%	98.3%
Absorption correction	Multi-scan	Multi-scan
Max. and min. transmission	0.9048 and 0.8881	0.3095 and 0.3095
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	3236/0/226	4442/0/226
Goodness-of-fit on F^2	1.024	1.040
Final *R* indices [$I > 2\text{sigma}(I)$]	R1 = 0.0438, wR2 = 0.1146	R1 = 0.0347, wR2 = 0.0820
R indices (all data)	R1 = 0.0576, wR2 = 0.1221	R1 = 0.0496, wR2 = 0.0883
Largest diff. peak and hole ($e.Å^{-3}$)	0.268 and −0.340	0.646 and −0.759

crystals of tribenzylamine. The products of the lithium–halogen exchange experiments were determined based on comparative melting point and NMR measurements.

X-ray data collection, structure solution and refinement

Data collection for **1** was performed on a Siemens Smart Platform CCD diffractometer, and data collection for **2** was performed on a Bruker SMART CCD area detector diffractometer; both datasets were collected at 173 K, using Mo Kα radiation (graphite monochromator). Intensity data were corrected for absorption and decay using SADABS[6] for both **1** and **2**. The structures were solved using direct methods and refined using Bruker SHELXTL[7] for **1** and SHELXL V6.12[8] for **2**. Hydrogen atoms were placed in ideal positions and treated with a riding model. Table 1 contains complete details of data collection and refinement for both compounds.

Results and discussion

Compounds **1** and **2** were synthesized from 2-chlorobenzyl chloride and 2-bromobenzyl bromide, respectively, in ammoniacal ethanol solution; the substantially different yields (43%, **1**, vs. 97%, **2**) under these conditions perhaps reflect the greater susceptibility of 2-bromobenzyl bromide to nucleophilic attack, as well as the lesser solubility of **2** versus **1**. A better yield (69%) for **1** was achieved in acetonitrile solution from 2-chlorobenzyl chloride and 2-chlorobenzylamine. The recrystallized compounds gave elemental analyses for C, H, N, consistent with high purity of the bulk materials. Furthermore, the GC–MS data is consistent with the predominant formation of M-C_6H_5X, M-$C_6H_5XCH_2$, and $C_6H_5XCH_2$ cations (X = Cl, Br) during fragmentation of **1** and **2**.

The molecular compounds melted quite sharply; as might be expected, **2** melts at a higher temperature (122–123°C) than **1**, consistent with enhanced intermolecular forces resulting from the larger, more polarizable bromine vs. chlorine. Curiously, **1** melts at a slightly lower temperature (89–91°C) than the unsubstituted tribenzylamine (91–93°C). In the absence of hydrogen-bonds, normal dispersion forces would dictate that the more massive, substituted analog would melt at a significantly higher temperature, of course.

Not unexpectedly, the ^{1}H-NMR spectra of **1** and **2** are very similar in profile and chemical shift. The aromatic region for each is 7.00–7.70 δ, and a profile of two sets of doublets (at lower field) and two sets of triplets can be grossly assigned to the four unique protons of each phenyl ring; the magnetic equivalence of each of the three benzylic groups per compound is supported by the observation of a sharp singlet for the methylene protons which also concurs with an integration of 2:1 relative to each of the phenyl protons.

The structure of each compound is solved in the space group $P\bar{1}$—the space group being determined from systematic absences and intensity statistics. The compounds are isostructural; a complete list of crystal data and structure refinement parameters appears in Table 1. On going from **1** to **2**, the slight unit cell volume increase and calculated density difference naturally reflect the substitution of the three chlorine atoms by bromines; fractional atomic coordinates, of course, show very little difference for **1** vs. **2**. The atom-numbering scheme for **1** and **2** is given in Figs. 2 and 3, and important bond distances and angles are found in Table 2.

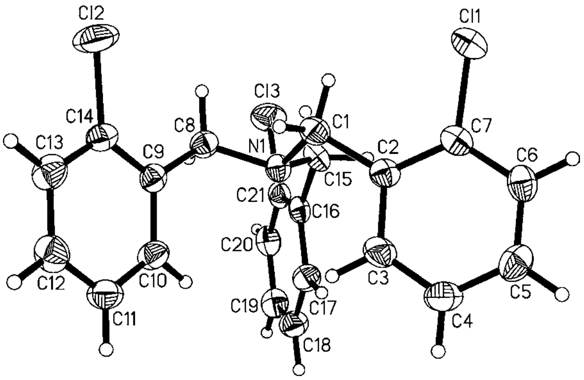

Fig. 2. Molecular structure showing atom-numbering scheme of *tris*-2-chlorobenzylamine, **1**, at 50% probability.

Inspection of the pertinent torsion angles reveals that each phenyl ring is an essentially planar unit, as would be expected; the rings are canted off perpendicular, however (as shown by the N1—C1—C2—C7 torsion angles of 132.5(2)° for **1** and 130.9(3)° for **2**, for example) to impart a propeller-shaped molecular geometry grossly

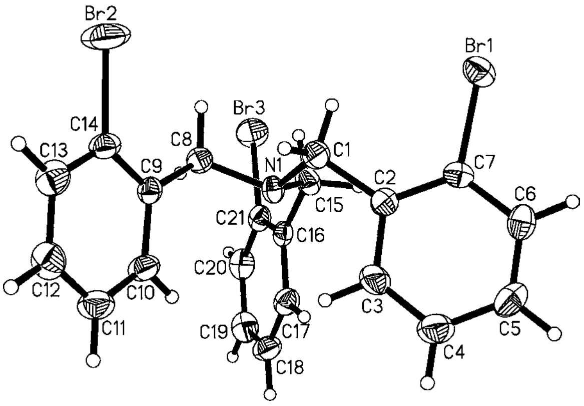

Fig. 3. Molecular structure showing atom-numbering scheme of *tris*-2-bromobenzylamine, **2**, at 50% probability.

Table 2. Selected Bond Lengths (Å) and Angles (°) for **1** and **2**

1		**2**	
N1—C1	1.465(3)	N1—C1	1.466(3)
N1—C15	1.467(3)	N1—C15	1.471(4)
N1—C8	1.462(3)	N1—C8	1.471(4)
C1—C2	1.505(3)	C1—C2	1.508(4)
C8—C9	1.510(3)	C8—C9	1.512(4)
C15—C16	1.510(3)	C15—C16	1.512(4)
C7—Cl1	1.749(2)	C7—Br1	1.908(3)
C14—Cl2	1.743(2)	C14—Br2	1.903(3)
C21—Cl3	1.742(2)	C21—Br3	1.907(3)
C1—N1—C15	110.92(17)	C1—N1—C15	111.2(2)
C1—N1—C8	110.96(18)	C1—N1—C8	111.1(2)
C15—N1—C8	111.12(17)	C15—N1—C8	110.8(2)
N1—C1—C2	110.87(18)	N1—C1—C2	110.6(2)
N1—C8—C9	110.54(18)	N1—C8—C9	110.4(2)
N1—C15—C16	111.52(17)	N1—C15—C16	110.9(2)

Note. Symmetry transformations used to generate equivalent atoms: #1 $-x + 1, -y + 1, -z + 1$.

consistent with the point group C_3. The mean C—C distance within the phenyl rings is 1.383(4) Å for **1**, and 1.386(4) Å for **2**, compared with 1.374(19) Å for tribenzylamine[9]; these slight differences are nevertheless consistent with the increased steric demands of Br vs. Cl vs. H. The mean sp^3–sp^2 C—C distances are 1.508(3) Å for **1**, and 1.510(4) Å for **2**, compared with 1.525(17) Å for tribenzylmine,[9] and the accepted value of 1.501 Å.[10]

The angles at the pyramidal nitrogen, C—N—C, give average values of 111.0(2)° for **1**, 111.0(2)° for **2**, and 110.0(9)° for tribenzylamine; again, the slightly larger angles for **1** and **2** might reasonably be considered to result from the greater steric demands of Br and Cl vs. H to slightly flatten the tetrahedron visualized from C1, C8, C15, and N. By the same token, the average N—C—C angle diminishes slightly for **2** (110.6(2)°) relative to **1** (111.0(2)°), and for tribenzylamine (111.5(11)°), is the largest of all.

For **1** and **2**, two of the three rings of each molecule appear to display stronger intermolecular stacking interactions than those of the third. Threefold crystal symmetry is also precluded in tribenzylamine (although in space group $P2_1/a$), where stronger stacking is displayed between phenyl rings along the *b* and *c* axes than along *a*.[9] Indeed, structure comparison reveals very little difference between **1** and **2**: analogous bonds and angles are essentially identical within calculated error limits, with the natural exception of the C—Cl vs. C—Br bonds. The difference here is ~0.16 Å, on average, which is consistent with the significant covalent radius difference between chlorine (0.97 Å) vs. bromine (1.14 Å).[11]

The combinations of **1** and **2** with *n*-butyllithium at −78°C revealed that the *tris*-chloro gave back itself, whereas the *tris*-bromo compound yielded tribenzylamine upon work-up. These observations are consistent with lithium–halogen exchange occurring only for the *tris*-bromo compound **2** under the reaction conditions used, probably a consequence of the longer carbon–bromine bonds rendering the bromine atoms more accessible to attack by the lithium reagent than their smaller chlorine counterparts in **1**. This result implicates the *in situ* formation of the desired *tris*-phenylide trianion at −78°C from the reaction of **2**, and bodes well for the eventual fulfillment of our objective to investigate organometallic complex analogs of tpa (Fig. 1).

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