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Isomorphism of chiral ammonium salts Ph(All)N$^+$Et(Me)X$^-\cdot$CHCl$_3$[†]

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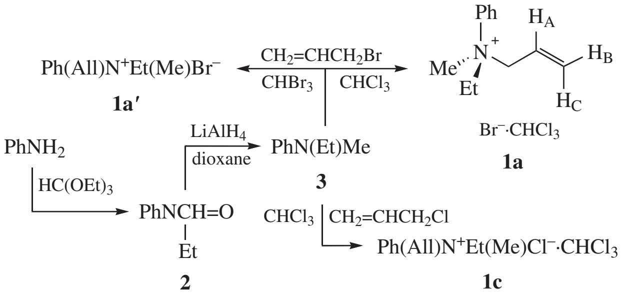
The title ammonium salts (X = Br, I) were synthesized, the identity of crystal structures for them (space groups $P2_12_12_1$, $Z = 4$) was found, spontaneous resolution of Ph(All)N$^+$Et(Me)Br$^-\cdot$CHCl$_3$ was performed, and the impossibility of replacement of the solvate molecule by CHBr$_3$ or CH$_2$Hal$_2$ (Hal = Cl, Br, I) was demonstrated by ^{1}H NMR and X-ray diffraction studies.

The crystal structure of Ph(All)N$^+$Et(Me)I$^-\cdot$CHCl$_3$ was studied previously.[1] Chiral ammonium salts are widely used as catalysts in asymmetric reactions,[2] as ionic liquids,[3] and in crystal engineering.[4] It seems reasonable to examine the usability of optically active salts Ph(All)N$^+$Et(Me)X$^-\cdot$CHCl$_3$ **1a–c** (**a** X = Br, **b** X = I, **c** X = Cl) in asymmetric allylation reactions. The salts of this type are known to racemize in solutions, and the rate of the process varies in the order: I > Br > Cl.[5] That is why salts **1a**,**c** and **1a′** were prepared and studied in terms of conglomerate formation (Scheme 1).[‡]

An X-ray diffraction (XRD) study[§] revealed that **1a** is isostructural to **1b**, it crystallizes in the same chiral space group $P2_12_12_1$. Furthermore, the refinement of Flack parameter [its value was 0.009(3)] indicated that the crystal is not a racemic



Scheme 1

twin and formally contains only one enantiomer. At the same time, the analysis of Fourier density synthesis demonstrated that

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[†] Asymmetric nitrogen, part 103.

[‡] ^{1}H NMR spectra were measured on a Bruker WM-400 spectrometer (400.13 MHz).

2: bp 112 °C (5 Torr). ^{1}H NMR (400 MHz, CDCl$_3$) δ: 1.14 (t, 3H, Me, ^3J 7.1 Hz), 3.84 (q, 2H, CH$_2$N, ^3J 7.1 Hz), 7.15, 7.28, 7.38 (m, 5H, Ph), 8.34 (s, 1H, HCO).

3: bp 52 °C (5 Torr). ^{1}H NMR (CDCl$_3$) δ: 1.17 (t, 3H, *Me*CH$_2$, ^3J 7.1 Hz), 2.95 (s, 3H, MeN), 3.44 (q, 2H, C*H*$_2$Me), 6.74, 6.77, 7.28 (m, Ph).

1a: yield 71%, mp 137.7 °C (in sealed capillary). ^{1}H NMR (CD$_3$CN) δ: 1.05 (t, 3H, *Me*CH$_2$N, ^3J 7.1 Hz), 3.48 (s, 3H, MeN), 4.03 (m, 2H, C*H*$_2$Me, ABX$_3$ spectrum, $\Delta\nu_{AB}$ 79 Hz, $^2J_{AB}$ –14.0 Hz, $^3J_{AX} = {}^3J_{BX} = 7.1$ Hz), 4.58 (m, 2H, C*H*$_2$CH, ABX spectrum, $\Delta\nu_{AB}$ 52 Hz, $^2J_{AB}$ –13.0 Hz, $^3J_{AX}$ 4.8 Hz, $^3J_{BX}$ 6.4 Hz), 5.50 (d, 1H, H$_C$, $^3J_{CA}$ 16.5 Hz), 5.57 (m, 1H, H$_A$, $^3J_{AC}$ 16.5 Hz, $^3J_{AB}$ 10.1 Hz, $^3J_{H_ACCH_2N}$ 4.8 and 6.4 Hz), 5.62 (d, 1H, H$_B$, $^3J_{BC}$ 10.1 Hz), 7.58, 7.64, 7.77 (5H, Ph), 7.71 [s, 1H, CHCl$_3$ (for CHCl$_3$ in pure CD$_3$CN, 7.58 ppm)].

Suitable for XRD study crystals were grown from the mixture CHCl$_3$–isooctane at –21 °C. For crystals 10 and 6 mg there was found $[\alpha]_D$ +31.0 and +26.2 (*c* 0.15, CHCl$_3$), for next crystals 11 mg $[\alpha]_D$ +16.2 (*c* 0.27, MeOH) and 6 mg $[\alpha]_D$ +26.2 (*c* 0.15, CHCl$_3$) and 6 mg $[\alpha]_D$ –12.7 (*c* 0.15, MeOH). The absolute configuration (*S*)-(+) and (*R*)-(–) **1a** is obviously the same as for **1b**, due to identity of the chiral cations.[1]

1a′ was prepared by crystallization from a mixture of THF/MeCN (2:1) and twofold excess of CHBr$_3$, mp in sealed capillary 132–135 °C (decomp.). ^{1}H NMR (CDCl$_3$) δ: 1.06 (t, 3H, *Me*CH$_2$N, ^3J 7.1 Hz), 3.72, (s, 3H, MeN), 4.56 (2H, C*H*$_2$Me, ABX$_3$ spectrum, ^2J –14.1 Hz, ^3J 7.1 Hz), 5.18 (2H, NC*H*$_2$CH, ABX spectrum, ^2J –12.7 Hz, ^3J 5.8 and 8.1 Hz), 5.37 (dd, 1H, H$_A$, $^3J_{AC}$ 16.1 Hz, $^3J_{AB}$ 10.1 Hz), 5.44 (dd, 1H, H$_B$, $^3J_{BA}$ 10.1 Hz, $^3J_{BC}$ 1.3 Hz), 5.78 (dd, 1H, H$_C$, ^3J 16.1 Hz, ^2J 1.3 Hz), 7.48 (t, 1H), 7.59 (t, 2H), 7.88 (d, 2H, Ph). For CHBr$_3$ in CDCl$_3$ δ: 6.83 (s, HC).

1c: yield 21%, strongly hygroscopic solid, the ^{1}H NMR spectrum in CD$_3$CN is the same as for **1a**. By crystallization from mixtures CHCl$_3$ with hydrocarbons (hexane, pentane, isooctane) and with ethyl acetate crystals suitable for XRD study were not prepared.

[§] Crystals of **1a** (C$_{12}$H$_{18}$N, CHCl$_3$, Br, $M = 375.55$) are orthorhombic, space group $P2_12_12_1$, at 100 K: $a = 9.730(2)$, $b = 12.372(3)$ and $c = 13.365(3)$ Å, $V = 1608.9(6)$ Å^3, $Z = 4$ ($Z' = 1$), $d_{calc} = 1.550$ g cm^{-3}, μ(MoKα) = 30.37 cm^{-1}, $F(000) = 760$. Intensities of 101238 reflections were measured with a Bruker SMART APEX2 CCD diffractometer [λ(MoKα) = 0.71072 Å, ω-scans, $2\theta < 90°$] and 12963 independent reflections [$R_{int} = 0.0396$] were used in further refinement.

Crystals of **1a′** (C$_{12}$H$_{18}$BrN, $M = 256.18$) are orthorhombic, space group *Pbcn*, at 100 K: $a = 10.8510(14)$, $b = 12.4726(13)$ and $c = 18.9661(17)$ Å, $V = 2566.9(5)$ Å^3, $Z = 8$ ($Z' = 1$), $d_{calc} = 1.326$ g cm^{-3}, μ(MoKα) = 31.69 cm^{-1}, $F(000) = 1056$. Intensities of 19464 reflections were measured with a Bruker SMART APEX2 CCD diffractometer [λ(MoKα) = 0.71072 Å, ω-scans, $2\theta < 66°$] and 5063 independent reflections [$R_{int} = 0.0616$] were used in further refinement.

The substantial redundancy in data allows empirical absorption correction to be applied using multiple measurements of equivalent reflections with SADABS Bruker program. The structures were solved by direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Upon the refinement of occupancies for two enantiomers the number of restrains, *i.e.* the DFIX instructions for C–C bond lengths of allyl group and ADP for carbon atoms were applied. Hydrogen atoms for main component in **1a** were located from the Fourier synthesis of the electron density and refined in the isotropic approximation. For **1a** the refinement converged to $wR_2 = 0.0595$ and GOF = 1.017 for all independent reflections [$R_1 = 0.0310$ was calculated against F for 10636 observed reflections with $I > 2\sigma(I)$]. For **1a′** the refinement converged to $wR_2 = 0.1065$ and GOF = 0.975 for all independent reflections [$R_1 = 0.0404$ was calculated against F for 2749 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0.

CCDC 685726 and 713421 contain 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. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.

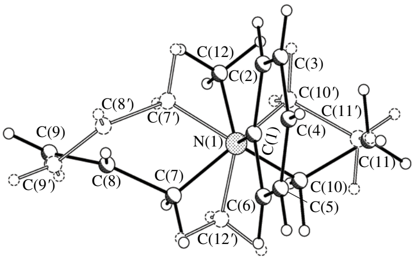

Figure 1 Superposition of two enantiomers in the crystal of **1a**. The minor enantiomer with occupancy equal to 0.121(2) is shown by dashed lines.

some residual density is located around N(1) that can be interpreted as the presence of the opposite enantiomer. Taking into account that the residual density does not exceed 1.0 eÅ^{-3}, we additionally collected the dataset with $2\theta \le 90°$ to increase the resolution. The refinement of occupancies led to the value for minor enantiomer as low as 0.121(2) (Figure 1).

This makes us to reinvestigate the previously published data for iodide **1b**. Unfortunately, the resolution of available dataset was restricted to $2\theta \le 60°$ and, although the maxima of residual density (0.56 eÅ^{-3}), which can be interpreted as a methyl group, was located in the vicinity of N(1) atom, it was impossible to refine correctly the occupancy of the opposite enantiomer. Thus, we can conclude that, unlike in the bromide salt, the occupancy for minor enantiomer in the iodide is much lower or even close to zero.

The crystal packing in **1a** is similar to that in the previously studied iodide salt. However, there are some distinct differences, which are mainly reflected in the variation of interactions between the halide anion and the $CHCl_3$ solvate molecule. Indeed, in both crystals X···Cl contacts assembles the anion and $CHCl_3$ molecule and the X···H–C interactions lead to the formation of a 3D framework with the chiral ammonium located in the resulted pores.

Although these associates are similar, only Br(1)···H and Br(1)···Cl(1) interactions are shortened [2.53 and 3.447(1) Å] in comparison with iodide [2.81 and 3.599(2) Å] for account of the van der Waals radii difference[7] (0.17 Å), while Br(1)···Cl(2) interaction becomes even longer [from 3.899(1) to 3.961(2) Å] (Figure 2). Apparently, such a variation of $X^-\cdots CHCl_3$ interactions distance plays a crucial role in cation–anion binding and, consequently, is reflected in the degree of enantiomer resolution.

Despite the minor enantiomer geometry was determined less accurately, we can conclude that it participates in the formation of C–H···Cl interactions between the allyl group and the solvate molecule, while for the major enantiomer such interactions are absent.

A possibility to replace the solvate molecule $CHCl_3$ by $CHBr_3$ was examined with bromide **1a′**. Its synthesis and crystallization in the presence of $CHBr_3$ leads to bromide **1a′** crystals, where the absence of $CHBr_3$ was confirmed by NMR and XRD studies. In contrast to **1a** and **1b**, bromide **1a′** crystallizes as a racemate (space group *Pbcn*, $Z = 8$). Nevertheless, the same type of disorder was found in **1a′** (Figure 3). The occupancies of two enantiomers are 0.76 and 0.24. The only type of interionic interactions in the crystal of **1a′** is C–H···Br contacts. The shortest contacts are observed for the ordered phenyl ring (H···Br *ca.* 2.8 Å), while the interactions for disordered part are slightly weaker.

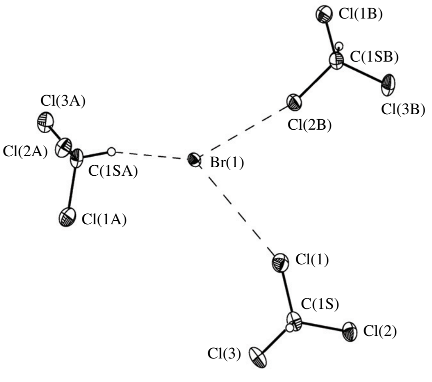

Figure 2 The scheme illustrating the bromide···$CHCl_3$ interactions in the crystal of **1a**.

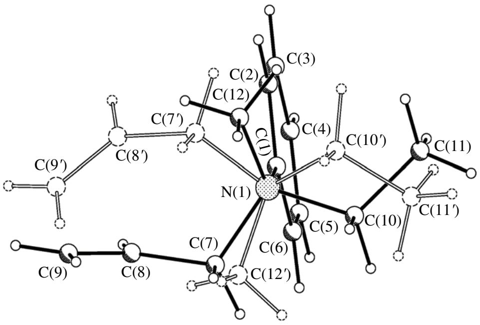

Figure 3 Superposition of two enantiomers in the crystal of **1a′**. The minor enantiomer with occupancy equal to 0.239(4) is shown by dashed lines.

Thus, a new example of isomorphism in chiral ammonium salts **1a**,**b** was found and their spontaneous resolution was carried out. Earlier, the same phenomenon was described for salts Ph(Me)N$^+$Bn(All)X$^-$ at X = Br, I.[8] The available information clearly shows that $CHCl_3\cdots X$ (X = Br, I) interactions play the major role in the formation of chiral crystal packing. At the same time, on the basis of energy of cation–anion X···H–C contacts, as well as the shape of the molecule, one cannot adequately distinguish between the two enantiomers upon crystallization.

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