Synthesis and Structure of 1-Ethyl-2,4,5-triphenyl-1*H*-imidazole (Ethyl-Lophine)

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Ethyl-Lophine, 1-ethyl-2,4,5-triphenyl-1*H*-imidazole, $C_{23}H_{20}N_2$, was synthesized as a precursor for large organic cations in ionic liquids using an improved microwave-assisted method. The title compound and a precursor compound were characterized by NMR, IR, and DSC thermal measurements, as well as elemental analyses. The crystal structure of ethyl-lophine was determined by single-crystal X-ray structure analysis (triclinic, $P\bar{1}$, $a = 10.1137(3)$, $b = 12.4935(4)$, $c = 14.6351(4)$ Å, $\alpha = 98.182(2)^\circ$, $\beta = 90.694(2)^\circ$, $\gamma = 102.666(2)^\circ$, $Z = 4$, $wR2 = 0.1030$ for 611 refined parameters).

Key words: Ionic Liquid, Imidazole, X-Ray Structure, Synthesis

Introduction

Ionic liquids (ILs) have been receiving much attention during the last 10 years from both industry and academia [1 – 3]. Ionic liquids are salts with melting points below 100 °C that can exhibit intrinsically useful properties, such as wide liquid ranges (up to 400 °C), negligible vapor pressures, large electrochemical windows, and high electrical conductivities [4]. Such compounds are being applied as solvents for chemical processes [5 – 7], for liquid-liquid extractions [8], for electrodepositions [9, 10], for spectroscopic studies [9 – 15], as electrolytes in solar cells [16, 17], and as components in hybrid materials [18]. One of the unique features of ionic liquids is the tunability of their chemical and physical properties by selection of an appropriate anion/cation combination. Widely used are combinations of small inorganic or organic anions with large organic cations like *N*-alkylpyridinum, tetraalkylammonium, tetraalkyl- or tetraarylphosphonium, and especially the cations resulting from the alkylation/arylation of *N*-alkylimidazole. Examples of such imidazole derivatives with alkyl and aryl substituents include 2,4-di-*t*-butyl-2-(1-methyl-4,5-diphenyl-1*H*-imidazol-2-yl)phenol [19], 1-methyl-2-(2-nitrophenyl)-4,5-diphenyl-1*H*-imidazole [20] and 2,2′-(1,4-phenylene)bis(4,5-diphenyl-1-methyl-1*H*-imidazole) [21].

In this paper we report the synthesis and single-crystal X-ray structure of 1-ethyl-2,4,5-triphenyl-1*H*-imidazole (ethyl-lophine), which was studied as a cation precursor with respect to the influence of large substituents on melting points and other physical properties of ILs [22 – 26].

Results and Discussion

Synthesis

Lophine and derivatives of lophine have been known already for a long time [27 – 30]. The imidazole ring system as an important part of lophine is a component of for example histidine. Therefore lophine and its derivatives are of high biological and pharmaceutical importance; see for example [31]. Because of this high importance several conventional, solvent-based procedures for the synthesis of 2,4,5-trisubstituted 1*H*-imidazole have been developed [32 – 34, and references cited therein]. Recent developments have aimed

at high-yield "green" procedures, trying to avoid organic solvents by using microwave irradiation [24]. We have now used this method for the synthesis of 2,4,5-triphenyl-1*H*-imidazole and obtained the product in 87 % yield. Besides avoiding organic solvents, a further advantage of this method are the short reaction times of only *ca.* 5 minutes. Spectroscopic and analytical data are given in the experimental section. Using the two-phase reaction system CH_2Cl_2/H_2O, lophine and bromoethane were reacted to give ethyl-lophine using tetradodecylammonium bromide as phase transfer reagent [25]. Again, the product was obtained after work-up in high yield (92 %). This modified two-step procedure is the most convenient method to obtain ethyl-lophine in multi-gram scales in high yields. One-step procedures are not preferred for the synthesis of ethyl-lophine on multi-gram scales, because of their longer reaction times, smaller scales (milligrams) or the use of catalysts [35, 36].

Crystal structure

Already in the late 19th century there has been an excited discussion about the constitution of lophine and its derivatives [29, 30]. Until now, crystal structures of more than 30 derivatives are known, and recently the crystal structure of the parent compound lophine has been reported [37]. The single-crystal X-ray structure of 1-ethyl-2,4,5-triphenyl-1*H*-imidazole has now been established by X-ray diffraction analysis. Suitable crystals were grown by slow evaporation of the solvent from saturated solutions of the compound in *n*-hexane at room temperature. Crystal data and parameters of the structure determination are given in Table 1, and selected bond lengths in Table 2. Crystals of the title compound are built up from isolated neutral molecules. Ethyl-lophine crystallizes in the centrosymmetric triclinic space group $P\bar{1}$ with 4 molecules in the unit cell. All atoms are located on general positions. Therefore, the molecules possess no higher symmetry. The asymmetric unit consists of two symmetry-independent molecules, **1** and **2**. The molecular structures are shown in Fig. 1 as displacement ellipsoid plots with the atom numbering scheme included. The packing of the molecules in the unit cell is shown in Fig. 2. Figure 3 shows the least-squares superposition of the two symmetry-independent molecules. It is clear, that the molecular structure of **1** and **2** is close to identical. Selected interatomic distances are given in Table 2. They are all found within the expected range of respective bond lengths.

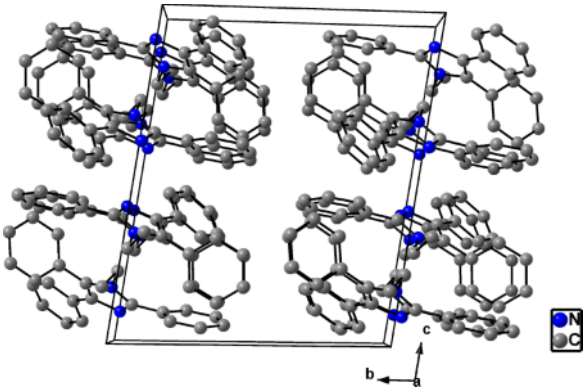

Fig. 2 (color online). Packing of 1-ethyl-2,4,5-triphenyl-1*H*-imidazole molecules in the unit cell; view along the [100] direction.

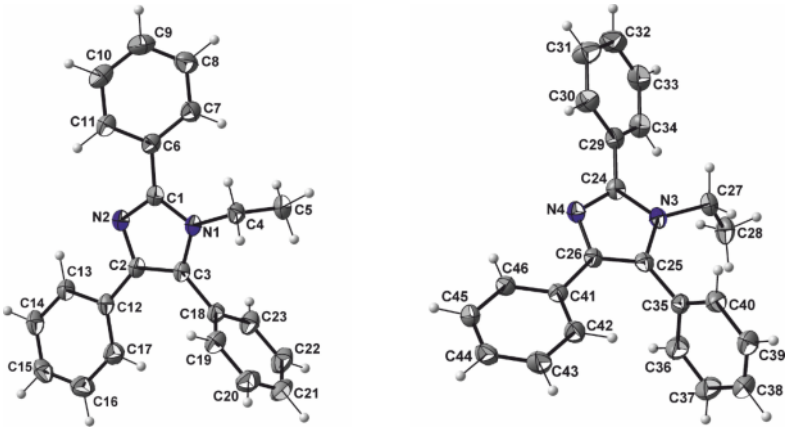

Fig. 1 (color online). Molecular structure of the two symmetry-independent molecules in crystals of 1-ethyl-2,4,5-triphenyl-1*H*-imidazole with atom numbering scheme. Atomic displacement ellipsoids are shown at the 50 % probability level.

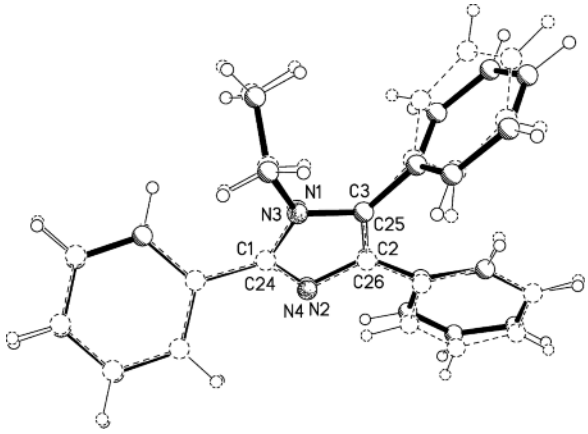

Fig. 3. Best-fit superposition of the two symmetry-independent molecules in crystals of 1-ethyl-2,4,5-triphenyl-1*H*-imidazole.

Table 1. Crystal structure data for 1-ethyl-2,4,5-triphenyl-1*H*-imidazole.

Formula	$C_{23}H_{20}N_2$
Fw, g·mol^{-1}	324.42
T, K	173(2)
Crystal system	triclinic
Space group	$P\bar{1}$, no. 2
a, Å	10.1137(3)
b, Å	12.4935(4)
c, Å	14.6351(4)
α, deg	98.182(2)
β, deg	90.694(2)
γ, deg	102.666(2)
V, Å^3; Z	1784.06(9); 4
D_{calcd}, g·cm^{-3}	1.21
μ(Mo K_α), mm^{-1}	0.1
2θ range, deg	4.8 to 52.6
Refl. collected / unique / R_{int}	27 170 / 7117 / 0.025
Refined parameters	611
$R1$ / $wR2$ [$I > 2\sigma(I)$][a,b]	0.0374 / 0.0913
$R1$ / $wR2$ (all data)[a,b]	0.0509 / 0.1030
A / B[b]	0.0452 / 0.5425
GoF[c] on F^2	1.034
Residual density, e Å^{-3}	0.032 / –0.196

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; [b] $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $w = [\sigma^2(F_o^2) + (AP)^2 + BP]^{-1}$, where $P = (\mathrm{Max}(F_o^2, 0) + 2F_c^2)/3$; [c] $\mathrm{GoF} = [\Sigma w(F_o^2 - F_c^2)^2/(n_{obs} - n_{param})]^{1/2}$.

Experimental Section

Analysis and spectroscopic measurements

^{1}H NMR, and ^{13}C NMR spectra were recorded on a Bruker ARX 300 spectrometer. Spectra were calibrated with respect to the solvent signal ([D$_6$]DMSO: $\delta_H = 2.50$, $\delta_C = 39.5$ ppm; $CDCl_3$: $\delta_H = 7.25$, $\delta_C = 77.0$ pm). MIR spectra (500 – 4000 cm^{-1}) were recorded by using ATR technique on a Thermo Nicolet 380 FT-IR spectrometer. Elemental analyses for C, H, and N were obtained with a Flash EA 1112 NC Analyzer from CE Instruments. Melting points were determined by DSC measurements using a Mettler Toledo DSC823^e in the range of 0 – 200 °C with a heating rate of 10 K · min^{-1} (Ar atmosphere, Al crucible). All melting points are peak temperatures. For microwave-assisted synthesis a CEM MarsXpress device was used.

Table 2. Selected bond lengths (Å) for 1-ethyl-2,4,5-triphenyl-*H*-imidazole with estimated standard deviations in parentheses.

Molecule **1**		Molecule **2**	
Atoms	Distance (Å)	Atoms	Distance (Å)
	N–C (imidazole ring)		
N1–C1	1.371(2)	N3–C24	1.371(2)
N1–C3	1.382(2)	N3–C25	1.382(2)
N2–C1	1.326(2)	N4–C24	1.326(2)
N2–C2	1.382(2)	N4–C26	1.380(2)
	C–C (imidazole ring)		
C2–C3	1.382(2)	C25–C26	1.380(2)
	exocyclic N–C		
N1–C4	1.479(2)	N3–C27	1.475(2)
	exocyclic C–C		
C1–C6	1.474(2)	C24–C29	1.476(2)
C2–C12	1.477(2)	C26–C41	1.478(2)
C3–C18	1.486(2)	C25–C35	1.481(2)
	average C–C (phenyl)		
	1.390		1.389
	C–C (ethyl)		
C4–C5	1.520(2)	C27–C28	1.519(2)

Materials

Benzil (Aldrich, > 98 %), benzaldehyde (Aldrich, > 99.5 %), NH_4OAc (Aldrich, > 98 %), KOH (VWR, > 86 %), and tetradodecylammonium bromide (TDDABr, Aldrich, > 99 %) were used without further purification. Bromoethane (Aldrich, > 99 %) was distilled over CaH_2 prior to use. 2,4,5-Triphenyl-1*H*-imidazole (lophine) and 1-ethyl-2,4,5-triphenyl-*H*-imidazole (ethyl-lophine) were synthesized by modified known procedures [24, 25].

Synthesis of 2,4,5-triphenyl-1H-imidazole – lophine

Benzil (4.2 g, 20.0 mmol), NH_4OAc (5.4 g, 70.0 mmol) and freshly distilled benzaldehyde (2.2 g, 20.0 mmol) were mixed in a PTFE vessel and heated in a microwave oven over a period of 5 min at 800 W ($T_{max} = 120$ °C). The resulting solid was suspended in methanol, transferred to a mortar and well ground. The powder was finally recrystallized from methanol/acetone (2 : 1, 150 mL), yielding a slightly yellow solid. Yield: 5.4 g (87 %), m. p. 273 – 275 °C (lit. [24]

276 – 277 °C). – Elemental analysis for $C_{21}H_{16}N_2$ (296.372) (%): calcd. C 85.10, H 5.55, N 9.34; found C 85.11, H 5.44, N 9.45. – ^{1}H NMR ([D$_6$]DMSO): $\delta = 7.27 - 8.06$ (m, 15H, phenyl), 12.48 (s, 1H, N*H*) ppm. – ^{13}C NMR ([D$_6$]DMSO): δ = 125.0 – 131.0 (C_{phenyl}), 135.0, 137.0 (NH–*C*=*C*–N), 145.4 (NH–*C*=N) ppm. – IR (cm^{-1}): $\nu = 3164$, 3079, 3059, 3040, 2988, 2966, 2869, 2866, 2810, 2784, 2731, 1602, 1588, 1504, 1489, 1462, 1446, 1442, 1412, 1397, 1129, 1071, 966, 917, 843, 777, 766, 736, 713, 706, 698, 691, 674, 606.

Synthesis of 1,3-diethyl-2,4,5-triphenyl-1H-imidazole – ethyl-lophine

Lophine (1.0 g, 3.4 mmol) and TDDABr (0.3 g, 0.4 mmol) were dissolved in 100 mL dichloromethane. To this solution an aqueous potassium hydroxide solution was added (10.0 g of KOH in 250 mL water), and the resulting red two-phase system was brought to reflux under vigorous stirring. Then bromoethane (50 mL) was added in one portion, and the emulsion was refluxed for further 5 h (the red color disappeared after 4 h). After cooling to room temperature, 250 mL diethyl ether was added, and the phases were separated. The organic phase was washed three times with small portions of water (50 – 100 mL) and dried over $MgSO_4$. The solution was evaporated to dryness, and the resulting yellow residue was recrystallized from *n*-hexane, yielding ethyl-lophine as an off-white powder. Yield 1.0 g (92 %). m. p. 120 °C (lit. [26]: 120 °C). – Elemental analysis for $C_{23}H_{20}N_2$ (324.425) (%): calcd. C 84.75, H 6.84, N 8.36; found C 85.15, H 6.21, N 8.63. – ^{1}H NMR ($CDCl_3$): δ = 1.03 (t, 3H, -C*H*$_3$), 3.97 (q, 2H, -C*H*$_2$-), 7.13 – 7.75 (m, 15H, phenyl) ppm. – ^{13}C NMR ($CDCl_3$): δ = 16.2 (-*C*H$_3$), 39.6 (-*C*H$_2$-), 129.3, 131.5, 131.6 (*ipso*-C_{phenyl}), 126.1 – 131.0 (*ortho*-, *meta*-, *para*-C_{phenyl}), 134.6, 137.7 (N–*C* = *C*–N), 147.3 (N–*C*=N) ppm. – IR (cm^{-1}): ν = 3060, 2997, 2975, 2934, 1599, 1499, 1478, 1469, 1442, 1394, 1378, 1355, 1324, 1309, 1269, 1233, 1177, 1154, 1129, 1087, 1071, 1025, 1001, 957, 912, 849, 808, 769, 741, 719, 693, 672, 644, 628, 615, 537.

X-Ray structure analysis

A transparent, colorless crystal of 1-ethyl-2,4,5-triphenyl-*H*-imidazole was mounted on the tips of a thin glass fiber for the single-crystal X-ray diffraction measurements. Data were collected on a Bruker-Nonius Apex X8 diffractometer equipped with a CCD detector. Measurements were done using monochromatic MoK_α radiation ($\lambda = 0.71073$ Å). Preliminary data of the unit cell were obtained from the positions of the reflections on three sets of 12 frames, each measured in three different directions of the reciprocal space. After completion of the data measurements the intensities were corrected for Lorentz, polarization and absorption effects using the Bruker-Nonius software [38, 39]. The structure solution (Direct Methods) and refinement was done with the aid of the SHELXS/L-97 program package [40 – 42]. All non-hydrogen atoms were refined anisotropically. The positions of the hydrogen atoms were taken from difference electron density maps and refined isotropically. Crystal data, data collection, and refinement parameters are collected in Table 1.

CCDC 765921 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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