Achiral and α-Amino Acid Derived Dicationic Imidazoliophanes

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1. General experimental information

Column chromatography was carried out with SiO$_2$ 60 (particle size 0.040-0.063 mm, 230-400 mesh; Merck) and commercially available solvents. Thin layer chromatography (TLC) was conducted on aluminium sheets coated with SiO$_2$ 60 F$_{254}$ obtained from Merck, with visualisation by UV lamp (254 or 360 nm). Melting points (mp) were measured on a Büchi B-540 melting-point apparatus in open capillaries and are uncorrected. $^1$H- and $^{13}$C-NMR spectra were recorded at 360/400/500 MHz and 90/100/125 MHz, respectively, with Bruker AMX 360, Avance 400 or Avance 500 instruments at 25°C. Chemical shifts are reported in ppm relative to TMS. Residual solvent signals in the $^1$H- and $^{13}$C-NMR spectra were used as an internal reference (CDCl$_3$: $\delta = 7.25$ and 77.23 ppm, CD$_3$OD: $\delta = 3.31$ and 49.15 ppm). Coupling constants (J) are given in Hz. The apparent resonance multiplicity is described as s (singlet), br s (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), ABq (A-B quartet) and m (multiplet). Additional NMR techniques such as $^{13}$C-APT, $^1$H-$^1$H COSY, $^1$H-$^{13}$C HMBC and $^1$H-$^{13}$C HMQC were used for regular signal assignment. The phenyl, pyridine, imidazole and imidazolium protons and carbons are marked as Ar, Py and Im, respectively. Occasionally, $^1$H- and $^{13}$C-NMR spectra showed broad signals or two set of signals without estimated spin-spin interactions as a result of hindered rotation in carbamate function. In CD$_3$OD solution, a rapid H-D exchange of C2-H of the imidazole was observed for the target imidazoliophanes and 6. Optical rotation values were measured on a Perkin-Elmer 341 instrument, concentration $c$ is given in g/100 mL MeOH. The enantiomeric purity was verified by measuring $^1$H-NMR spectra with (R)-Mosher acid. The mass spectra were measured on a LC-MS Micromass Quattro Micro API (Waters) instrument with a direct input (ESI+, 0.5 mL stream MeOH, mass range 200-1100 Da and MassLynx software were used). Reagents and solvents were purchased from Aldrich or Penta and used without further purification. Starting imidazoles 1a-d, 2 and 13 were synthesised according to the literature.$^{1-3}$

Dry acetone was freshly prepared prior to use.
2. General synthetic procedures

2.1. Synthesis of imidazoles 4b/5b.

To a solution of imidazole 1b (273 mg, 1.0 mmol) in acetonitrile (10 mL), NaOH (0.5 mL, 25%, aq.) was added and the reaction mixture was stirred for 20 min. A solution of 2-bromomethylpyridine in CH₂Cl₂ (10 mL) obtained by the neutralization of 2-bromomethylpyridine hydrochloride (208 mg, 1.0 mmol) with Na₂CO₃ (aq.) and extraction into CH₂Cl₂ (10 mL) was added and the reaction mixture was stirred 24 hours at 25 °C. The reaction was monitored on TLC (SiO₂; hexane/EtOAc/MeOH/NH₄OH, 3:5:1:0.1). The solvent was evaporated in vacuo, H₂O (5 mL) was added and the reaction mixture was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were dried (Na₂SO₄) and the solvent evaporated. The crude product was purified by two consecutive column chromatographic separations. The first separation (R₁) afforded a pure mixture of both regioisomers that were separated on a second column (R₂).

(S)-Benzyl 2-methyl-1-[1-(pyridin-2-ylmethyl)-1H-imidazol-4-yl]propylcarbamate (4b)

Yield 200 mg (55%), white solid, mp 112-114 °C, R₁ = 0.50 (silica gel; hexane/EtOAc/MeOH/NH₄OH = 3/5/1/0.1), R₂ = 0.12 (silica gel; EtOAc/hexane = 3/1), [α]D²² = −27.0 (c 0.5, MeOH).

¹H NMR (360 MHz, CDCl₃) δ: 0.82 (3H, t, J = 6.6 Hz, (CH₃)₂CH), 0.91 (3H, t, J = 6.5 Hz, (CH₃)₂CH), 2.10-2.16 (1H, m, (CH₃)₂C₄H), 4.48 (1H, t, J = 8.1 Hz, CHNH), 5.05 (2H, ABq, J = 12.3 Hz, CH₂Ph), 5.09-5.13 (2H, m, CH₂Py), 5.72 (1H, d, J = 9.0 Hz, CHNH), 6.78 (1H, s, 5-Him), 6.88 (1H, d, J = 7.5 Hz, Py), 7.20 (1H, t, J = 6.9 Hz, Py), 7.25-7.29 (5H, m, Ar), 7.49 (1H, s, 2-Him), 7.62 (1H, t, J = 7.5 Hz, Py), 8.56 (1H, d, J = 3.9 Hz, Py).

¹³C NMR (90 MHz, CDCl₃) δ: 18.8 a 19.3 ((CH₃)₂CH), 33.0 ((CH₃)₂CH), 52.6 (CH₂Py), 55.1 (CHNH), 66.7 (OCH₂Ph), 116.5 (5-Cim), 121.2 (Py), 123.2 (Py), 128.1 (Ar), 128.2 (Ar), 128.6 (Ar), 136.9 (Ar), 137.5 (Py), 137.5 (2-Cim), 142.4 (4-Cim), 149.8 (Py), 156.2 (Py), 156.3 (CO).

MS (ESI, m/z): 365 [M⁺], 387 [M⁺+Na], 751 [2M⁺+Na].
Elemental analysis Found: C, 69.04; H, 6.77; N, 15.09. Calc. for C₂₁H₂₄N₄O₂: C, 69.21; H, 6.64; N, 15.37(%).

(5)-Benzyl 2-methyl-1-[1-(pyridin-2-ylmethyl)-1H-imidazol-5-yl]propylcarbamate (5b)

Yield 69 mg (19%), yellowish oil, R₁₁ = 0.50 (silica gel; hexane/EtOAc/MeOH/NH₄OH = 3/5/1/0.1), R₁₂ = 0.06 (silica gel; EtOAc/hexane = 3/1), [α]_D²² = −22.0 (c 0.5, MeOH).

¹H NMR (500 MHz, CDCl₃) δ: 0.82 (3H, t, J = 6.3 Hz, (CH₃)₂CH), 0.98 (3H, t, J = 6.2 Hz, (CH₃)₂CH), 2.06-2.08 (1H, m, (CH₃)₂C), 4.53 (1H, t, J = 8.6 Hz, CHNH), 5.00 (2H, ABq, J = 12.2 Hz, CH₂Ph), 5.17 (1H, d, J = 9.0 Hz, CHNH), 5.27 (2H, ABq, J = 15.8 Hz, CH₂Py), 6.96-6.98 (2H, m, Py a 4-H), 7.17 (1H, t, J = 6.5 Hz, Py), 7.26-7.33 (5H, m, Ar), 7.53-7.59 (2H, m, Py a 2-H), 8.52-8.53 (1H, m, Py).

¹³C NMR (125 MHz, CDCl₃) δ: 18.8 a 20.2 ((CH₃)₂CH), 32.4 ((CH₃)₂CH), 50.3 (CH₂Py), 51.7 (CHNH), 66.8 (OCH₂Ph), 121.3 (4-C), 122.9 (Py), 126.9 (Py), 128.0 (Ar), 128.1 (Ar), 128.5 (Ar), 136.3 (Ar), 137.1 (5-C), 137.1 (Py), 138.0 (2-C), 149.7 (Py), 155.8 (Py), 155.9 (CO).

MS (ESI, m/z): 365 [M⁺], 387 [M⁺+Na], 751 [2M⁺+Na].

Elemental analysis Found: C, 68.92; H, 6.69; N, 15.20. Calc. for C₂₁H₂₄N₄O₂: C, 69.21; H, 6.64; N, 15.37(%).

2.2. Synthesis of bridged dicationic imidazoles 6a,c,d.

To a solution of 2 (0.3 mmol) in dry acetone (20 mL), 1,3-bis(bromomethyl)benzene or 2,6-bis(bromomethyl)pyridine (0.15 mmol) was added at once and the reaction mixture was heated at reflux under argon atmosphere for the indicated time. After the reaction completion as monitored on TLC (silica gel, hexane/EtOAc/MeOH/NH₄OH = 3/5/1/0.1), the solvent was evaporated in vacuo, the residue was taken up into EtOAc/MeOH (20:1), treated with CH₂Cl₂/hexane (1:1) to precipitate the crude product which was filtered off. This procedure was repeated three times and the product was dried in vacuum.
Compound 6a

The title compound was synthesized from 2a and 1,3-bis(bromomethyl)benzene following the general procedure.

Yield 87 mg (67%), off-white solid, mp 103-107 °C, [α]_D^{22} = –9.7 (c 1.0, MeOH).

^1H NMR (400 MHz, CD_3OD) δ: 1.18 (6H, t, J = 7.2 Hz, 2xCH_3(CH_2)), 1.46-1.52 (6H, m, 2xCH_3(CH)), 3.49 (2H, q, J = 7.2 Hz, CH_3CH_2), 3.61-3.64 (2H, m, CH_3CH_2), 3.87-5.08 (6H, m, 2xPhCH_2CO a 2xCHNH), 5.46-5.62 (8H, m, 2xPhCH_2N a 2xOCH_2N), 7.29-7.60 (14H, m, ArH), 7.81 (2H, s, 2x5-H_im), 9.04-9.37 (2H, 2xs, 2x2-H_im).

^13C NMR (90 MHz, CD_3OD) δ: 15.3 a 15.6 (2xCH_3(CH_2)), 20.1 (2xCH_3(CH)), 42.7 a 44.1 (2xCH_3(CH_2)), 51.9 (2xCHNH), 53.5 a 53.9 (2xPhCH_2N), 67.0 a 67.9 (2xPhCH_2CO), 78.7 a 80.6 (2xOCH_2N), 119.9 (Ar), 121.3 a 122.1 (2x4-C_im), 128.9 a 129.0 (Ar), 129.3 (Ar), 129.7 (Ar), 130.6 (Ar), 131.5 (Ar), 135.9 a 136.1 (Ar), 136.7 a 136.9 (Ar), 138.2 (Ar), 138.9 (Ar), 157.7 a 158.2 (CO).

MS (ESI, m/z): 789-791 (1:1) [M⁺-Br].

Elemental analysis Found: C, 55.46; H, 5.97; Br, 18.06; N, 9.35; Calc. for C_{40}H_{50}Br_2N_6O_6: C, 55.18; H, 5.79; Br, 18.35; N, 9.65(%)..

Compound 6c

The title compound was synthesized from 2c and 2,6-bis(bromomethyl)pyridine following the general procedure.

Yield 73 mg (51%), off-white solid, mp 85-90 °C, [α]_D^{22} = –32.0 (c 0.2, MeOH).

^1H NMR (400 MHz, CD_3OD) δ: 0.82-0.88 (12H, m, 2x(CH_3)_2CH), 1.16-1.25 (6H, m, 2xCH_3(CH_2)), 1.57-1.61 (4H, m, 2x(CH_3)_2CHCH_2), 1.81-1.88 (2H, m, 2x(CH_3)_2CH), 3.49 (2H, q,
$J = 6.8 \text{ Hz, CH}_3\text{CH}_2$, 3.63-3.65 (2H, m, CH$_3$CH$_2$), 4.42-4.55 (6H, m, 2xCHNH), 4.96-5.06 (4H, m, 2xOCH$_2$Ph), 5.52-5.68 (8H, m, 2xPyCH$_2$N a 2xOCH$_2$N), 7.30-7.48 (13H, m, ArH), 7.78-7.82 (2H, m, 2x5-H$_{\text{im}}$), 9.35 (2H, s, 2-H$_{\text{im}}$).

$^{13}$C NMR (90 MHz, CD$_3$OD) δ: 15.3 a 15.6 (2xCH$_3$CH$_2$), 21.9 a 23.4 (4x(CH$_3$)$_2$CH), 25.9 (2x(CH$_3$)$_2$CHCH$_2$), 34.1 (2x(CH$_3$)$_2$CHCH$_2$), 43.6 (2xCH$_3$CH$_2$), 45.0 (2xCHNH), 52.3 a 52.8 (2xPyCH$_2$N), 67.0 a 67.9 (2xPhCH$_2$CO), 80.5 a 80.6 (2xOCH$_2$N), 120.8 (Ar), 123.7 (Ar), 128.9 a 129.0 (Ar), 129.3 (Ar), 129.6 a 129.7 (Ar), 138.2 (Ar), 139.0 (Ar), 140.1 (Ar), 140.7 (Ar), 154.8 (Py), 158.1 (2xCO).

MS (ESI, m/z): 874-876 (1:1) [M$^+$-Br].

Elemental analysis Found: C, 56.73; H, 6.59; Br, 16.43; N, 10.02. Calc. for C$_{45}$H$_{61}$Br$_2$N$_7$O$_6$: C, 56.55; H, 6.43; Br, 16.72; N, 10.26(%).

**Compound 6d**

The title compound was synthesized from 2d and 2,6-bis(bromomethyl)pyridine following the general procedure.

Yield 90 mg (59%), off-white solid, mp 87-92 °C, $[\alpha]_D^{22} = -21.5$ (c 0.2, MeOH).

$^1$H NMR (400 MHz, CD$_3$OD) δ: 1.17-1.19 (6H, m, 2xCH$_3$CH$_2$), 3.12-3.20 (4H, m, 2xCHC$_2$H$_2$), 3.49 (2H, q, $J = 6.8$ Hz, CH$_3$CH$_2$), 3.58-3.60 (2H, m, CH$_3$CH$_2$), 4.84-5.09 (6H, m, 2xPhCH$_2$CO a 2xCHNH), 5.40-5.68 (8H, m, 2xPyCH$_2$N a 2xOCH$_2$N), 7.10-7.47 (20H, m, ArH), 7.45-7.88 (3H, m, ArH), 7.90 (2H, s, 2x5-H$_{\text{im}}$), 9.30-9.35 (2H, 2xs, 2x2-H$_{\text{im}}$).

$^{13}$C NMR (100 MHz, CD$_3$OD) δ: 15.2 a 15.6 (2xCH$_3$CH$_2$), 34.1 (2xCH$_3$CH$_2$), 40.3 a 40.6 (2xPhCH$_2$CH), 48.2 a 48.3 (2xCHNH), 52.3 a 52.7 (2xPyCH$_2$N), 66.9 a 67.7 (2xPhCH$_2$CO), 80.5 a 80.6 (2xOCH$_2$N), 121.1 a 121.4 (Ar), 122.7 a 123.4 (Ar), 123.8 a 124.7 (Ar), 128.1 a 128.2 (Ar), 128.8 (Ar), 129.2 (Ar), 129.6 (Ar), 129.7 (Ar), 129.8 (Ar), 130.5 a 130.6 (Ar), 137.9 a 138.1 (Ar), 139.6 (Ar), 140.0 a 140.7 (Ar), 154.0 a 154.5 (Py), 157.8 a 158.9 (2xCO).

MS (ESI, m/z): 942-944 (1:1) [M$^+$-Br].

Elemental analysis Found: C, 60.24; H, 5.77; Br, 15.22; N, 9.25. Calc. for C$_{51}$H$_{57}$Br$_2$N$_7$O$_6$: C, 59.83; H, 5.61; Br, 15.61; N, 9.58(%).
3. Characterization of precyclophanes 12a-e and 14-15

2-[[4-(1-(1S)-Benzyloxycarbonylamino-2-methylpropyl)-1H-imidazol-1-yl]methyl]-6-[[5-(1-(1S)-benzyloxycarbonylamino-2-methylpropyl)-1H-imidazol-1-yl]methyl]pyridine (12a).

The title compound was synthesized from 1a and 2,6-bis(bromomethyl)pyridine following the general procedure. Yield 56 mg (19%), pale yellow oil, $R_{f1} = 0.40$ (silica gel; hexane/EtOAc/MeOH/NH$_3$OH = 3/5/1/0.1), $R_{f2} = 0.26$ (silica gel; acetone/MeOH = 10/1), $[\alpha]_D^{22} = -10.4$ (c 0.5, MeOH).

$^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.45 (3H, d, $J = 6.6$ Hz, $CH_3^a$CH), 1.49 (3H, d, $J = 6.6$ Hz, $CH_3^b$CH), 4.81-4.86 (2H, m, $CH_2^{a,b}$NH), 4.93-5.07 (6H, m, $CH_2^{a,b}$Ph and $CH_2^a$Py), 5.17 (2H, ABq, $J = 16.2$ Hz, $CH_2^b$Py), 5.38-5.40 (1H, m, CHN$^H_a$), 5.70-5.73 (1H, m, CHN$^H_b$), 6.64 (1H, s, 5-$H_{im}^a$), 6.80 (1H, d, $J = 7.6$ Hz, Py), 6.90-6.97 (2H, m, Py and 4-$H_{im}^b$), 7.21-7.33 (11H, m, Ar and 2-$H_{im}^b$), 7.49 (1H, s, 2-$H_{im}^a$), 7.52 (1H, t, $J = 7.5$ Hz, Py).

$^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 20.3 ($CH_3^b$CH), 21.6 ($CH_3^a$CH), 41.7 ($CH^b$), 45.3 ($CH^a$), 49.7 (Py$CH_2^b$), 52.1 (Py$CH_2^a$), 66.6 (Ph$CH_2^a$), 66.9 (Ph$CH_2^b$), 115.6 (5-$C_{im}^a$), 120.4 (Py), 120.6 (Py), 127.0 (4-$C_{im}^b$), 128.1 (Ar), 128.2 (Ar), 128.2 (Ar), 128.4 (Ar), 128.6 (Ar), 128.7 (Ar), 133.0 (5-$C_{im}^b$), 136.3 (Ar), 136.9 (Ar), 137.4 (Ar), 137.5 (2-$C_{im}^a$), 138.5 (Py), 139.3 (2-$C_{im}^b$), 144.7 (4-$C_{im}^a$), 155.5 (Py), 155.9 (Py), 156.1 (CO), 156.2 (CO).

MS (ESI, $m/z$): 594 (M$^+$), 616 (M+Na$^+$).

Elemental analysis Found: C, 66.37; H, 6.14; N, 16.25. Calc. for C$_{33}$H$_{35}$N$_7$O$_4$: C, 66.76; H, 5.94; N, 16.52(%).

2-[[4-(1-(1S)-Benzyloxycarbonylamino-2-methylpropyl)-1H-imidazol-1-yl]methyl]-6-[[5-(1-(1S)-benzyloxycarbonylamino-2-methylpropyl)-1H-imidazol-1-yl]methyl]pyridine (12b).
The title compound was synthesized from 1b and 2,6-bis(bromomethyl)pyridine following the general procedure.

Yield 71 mg (22%), pale yellow oil, Rf1 = 0.42 (silica gel; hexane/EtOAc/MeOH/NH₄OH = 3/5/1/0.1), Rf2 = 0.05 (silica gel; acetone/hexane = 2/1), [α]D²² = −22.6 (c 0.5, MeOH).

1H-NMR (360 MHz, CDCl₃): 0.81 (3H, d, J = 5.8 Hz, (CH₃)a₂CH), 0.84 (3H, d, J = 6.2 Hz, (CH₃)b₂CH), 0.93 (3H, d, J = 5.7 Hz, (CH₃)b₂CH), 0.97 (3H, d, J = 6.1 Hz, (CH₃)b₂CH), 2.01-2.06 (1H, m, (CH₃)₂CHₐ), 2.13-2.17 (1H, m, (CH₃)₂CHₐ), 4.48-4.52 (2H, m, CHₐₕNH), 4.91-5.16 (9H, m, CH₂aPy and CH₂aₕbPh and CHNHₕ), 5.24 (2H, ABq, J = 16.5 Hz, CH₂bPy), 5.84 (1H, d, J = 8.6 Hz, CHNHₕ), 6.69 (1H, s, 5-Himₐ), 6.82 (1H, d, J = 6.5 Hz, Py), 6.97-6.99 (2H, m, 4-Himₐ and Py), 7.26-7.31 (10H, m, Ar), 7.45 (1H, s, 2-Himₐ), 7.55-7.56 (2H, m, 4-Himₐ and Py).

13C-NMR (125 MHz, CDCl₃): 18.7 ((CH₃)a₂CH), 19.1 ((CH₃)b₂CH), 19.4 ((CH₃)b₂CH), 20.4 ((CH₃)b₂CH), 32.7 ((CH₃)₂CHₕ), 33.0 ((CH₃)₂CHₕ), 50.1 (PyCH₂b), 51.9 (CHₕ), 52.2 (PyCH₂a), 55.1 (CHₕ), 66.7 (PhCH₂a), 67.0 (PhCH₂b), 116.7 (5-Cimₐ), 120.4 (Py), 120.8 (Py), 126.9 (4-Cimₐ), 128.1 (Ar), 128.2 (Ar), 128.2 (Ar), 128.4 (Ar), 128.6 (Ar), 128.7 (Ar), 132.5 (5-Cimₐ), 136.4 (Ar), 137.0 (Ar), 137.3 (2-Cimₐ), 138.5 (Py), 138.8 (2-Cimₐ), 142.4 (4-Cimₐ), 156.0 (Py), 156.1 (Py), 156.3 (CO), 156.5 (CO).

MS (ESI, m/z): 650 (M)+, 672 (M+Na)+.

Elemental analysis Found: C, 68.12; H, 7.02; N, 14.74. Calc. for C₃₇H₄₃N₇O₄: C, 68.39; H, 6.67; N, 15.09 (%).

2-[[4-(1-(1S)-Benzyloxycarbonylamino-3-methylbutyl)-1H-imidazol-1-yl]methyl]-6-[[5-(1-(1S)-benzyloxycarbonylamino-3-methylbutyl)-1H-imidazol-1-yl]methyl]pyridine (12c).

The title compound was synthesized from 1c and 2,6-bis(bromomethyl)pyridine following the general procedure.

Yield 54 mg (16%), white solid, Rf1 = 0.33 (silica gel; hexane/EtOAc/MeOH/NH₄OH = 3/5/1/0.1), Rf2 = 0.30 (silica gel; acetone/MeOH = 10/1), mp 54-57 °C, [α]D²² = −37.6 (c 0.5, MeOH).

1H-NMR (500 MHz, CDCl₃): 0.78-0.91 (12H, m, (CH₃)₂b₂CH), 1.54-1.57 (2H, m, (CH₃)₂CHₕb), 1.66-1.70 (4H, m, (CH₃)₂CHCH₂aₕb), 4.75-4.76 (1H, m, CHₕNH), 4.80-4.82 (1H,
m, CHF<sub>b</sub>NH), 4.90-5.10 (6H, m, CH<sub>a</sub><sup>b</sup>Ph and CH<sub>a</sub><sup>b</sup>Py), 5.18 (1H, m, CHNHN<sub>b</sub>), 5.23 (2H, ABq, J = 16.5 Hz, CH<sub>b</sub><sup>b</sup>Py), 5.64 (1H, d, J = 8.5 Hz, CHNHN<sub>b</sub>), 6.69 (1H, s, 5-H<sub>im</sub><sup>a</sup>), 6.77 (2H, d, J = 7.0 Hz, Py), 6.95-6.98 (2H, m, 4-H<sub>im</sub><sup>b</sup>+Py), 7.22-7.29 (10H, m, Ar), 7.37 (1H, s, 2-H<sub>im</sub><sup>b</sup>), 7.47-7.55 (2H, m, Ar and 2-H<sub>im</sub><sup>a</sup>).

<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>) δ: 22.4 (CH<sub>a</sub><sup>b</sup>)<sub>2</sub>CH), 22.6 (CH<sub>b</sub><sup>b</sup>)<sub>2</sub>CH), 22.7 (CH<sub>a</sub><sup>b</sup>)<sub>2</sub>CH), 22.8 (CH<sub>b</sub><sup>b</sup>)<sub>2</sub>CH), 25.0 (CH<sub>a</sub><sup>b</sup>)<sub>2</sub>CH<sup>ab</sup>, 43.8 (CH<sup>b</sup>NH), 44.0 (CH<sub>a</sub><sup>b</sup>)<sub>2</sub>CHCH<sub>b</sub><sup>b</sup>, 44.8 (CH<sup>b</sup>NH), 47.8 (CH<sub>a</sub><sup>b</sup>)<sub>2</sub>CHCH<sub>a</sub><sup>a</sup>, 49.8 (PhCH<sub>b</sub><sup>b</sup>), 52.2 (PhCH<sub>a</sub><sup>a</sup>), 66.6 (PyCH<sub>b</sub><sup>b</sup>), 66.9 (PyCH<sub>b</sub><sup>b</sup>), 116.1 (5-C<sub>im</sub><sup>a</sup>), 120.4 (Py), 120.6 (Py), 127.1 (4-C<sub>im</sub><sup>b</sup>), 128.1 (Ar), 128.1 (Ar), 128.2 (Ar), 128.4 (Ar), 128.6 (Ar), 128.7 (Ar), 132.8 (5-C<sub>im</sub><sup>b</sup>), 136.3 (Ar), 136.9 (Ar), 137.5 (Py), 137.7 (2-C<sub>im</sub><sup>a</sup>), 138.4 (Py), 139.2 (2-C<sub>im</sub><sup>b</sup>), 144.0 (4-C<sub>im</sub><sup>a</sup>), 155.7 (Py), 156.1 (Py), 156.1 (CO), 156.3 (CO).

MS (ESI, m/z): 678 (M)+, 700 (M+Na)+.

Elemental analysis Found: C, 68.72; H, 7.04; N, 14.20. Calc. for C<sub>39</sub>H<sub>47</sub>N<sub>7</sub>O<sub>4</sub>: C, 69.10; H, 6.99; N, 14.46(%).

2-[[4-(1-(1S)-Benzyloxycarbonylamino-2-phenylethyl)-1H-imidazol-1-yl)methyl]-6-[[5-(1-(1S)-benzyloxycarbonylamino-2-phenylethyl)-1H-imidazol-1-yl)methyl]pyridine (12d).

The title compound was synthesized from 1d and 2,6-bis(bromomethyl)pyridine following the general procedure.

Yield 119 mg (32%), white solid, R<sub>f1</sub> = 0.47 (silica gel; hexane/EtOAc/MeOH/NH<sub>4</sub>OH = 3/5/1/0.1), R<sub>f2</sub> = 0.38 (silica gel; acetone/MeOH = 10/1), mp 72-75 °C, [α]<sub>D</sub><sup>22</sup> = -43.8 (c 0.5, MeOH).

<sup>1</sup>H-NMR (500 MHz, CD<sub>3</sub>OD) δ: 2.93-2.94 (1H, dd, J = 13.5 Hz, J = 8.6 Hz, PhCH<sub>a</sub><sup>b</sup>CH), 3.05-3.06 (2H, m, PhCH<sub>a</sub><sup>b</sup><sup>ab</sup>CH), 3.12-3.14 (1H, dd, J = 13.5 Hz, J = 7.4 Hz, PhCH<sub>b</sub><sup>b</sup>CH), 4.81 (2H, ABq, J = 12.5 Hz, PhCH<sub>b</sub><sup>b</sup>O), 4.89-4.95 (2H, m, CH<sup>b</sup>NH<sub>a</sub>), 4.95-5.10 (4H, m, PhCH<sub>b</sub><sup>b</sup>O and CH<sub>a</sub><sup>b</sup>Py), 5.20 (2H, ABq, J = 16.5 Hz, CH<sub>b</sub><sup>b</sup>Py), 6.81 (1H, d, J = 7.5 Hz, Py), 6.82 (1H, d, J = 7.5 Hz, Py), 7.02-7.04 (3H, m, 4-H<sub>im</sub><sup>b</sup> and Py), 7.06-7.24 (18H, m, Ar), 7.53 (1H, t, J = 7.7 Hz, Py), 7.63 (1H, s, 2-H<sub>im</sub><sup>b</sup>), 7.65 (1H, s, 2-H<sub>im</sub><sup>a</sup>).
**13C-NMR** (125 MHz, CD3OD) δ: 41.7 (PhCH\textsubscript{2}aCH), 42.5 (PhCH\textsubscript{2}bCH), 48.6 (CH\textsuperscript{b}NH), 50.8 (CH\textsubscript{2}aPy), 52.7 (CH\textsuperscript{a}NH), 53.0 (CH\textsubscript{2}aPy), 67.4 (PhCH\textsubscript{2}a,bCO), 118.1 (5-C\textsubscript{im}\textsuperscript{a}), 121.7 (Py), 121.9 (Py), 127.4 (4-C\textsubscript{im}\textsuperscript{b}), 127.7 (Ar), 128.7 (Ar), 128.8 (Ar), 128.9 (Ar), 129.0 (Ar), 129.3 (Ar), 129.4 (Ar), 129.5 (Ar), 130.5 (Ar), 130.6 (Ar), 134.4 (5-C\textsubscript{im}\textsuperscript{b}), 138.2 (Ar), 138.4 (Ar), 138.9 (2-C\textsubscript{im}\textsuperscript{a}), 139.1 (Ar), 139.8 (Ar), 139.8 (Py), 140.1 (2-C\textsubscript{im}\textsuperscript{b}), 143.9 (4-C\textsubscript{im}\textsuperscript{a}), 157.5 (Py), 157.6 (Py), 157.8 (CO), 158.0 (CO), one signal is missing.

**MS** (ESI, m/z): 746 (M\textsuperscript{+}), 768 (M\textsuperscript{+}+Na).

Elemental analysis Found: C, 72.30; H, 5.87; N, 13.29. Cald. for C\textsubscript{45}H\textsubscript{43}N\textsubscript{7}O\textsubscript{4}: C, 72.46; H, 5.81; N, 13.15(%).

1-[4-(1-(1S)-benzyloxycarbonylaminoethyl)-1H-imidazol-1-yl]-3-[5-(1-(S)-benzyloxycarbonylaminoethyl)-1H-imidazol-1-yl]benzene (12e).  

![Chemical Structure](image)

The title compound was synthesized from 1a and 1,3-bis(bromomethyl)benzene following the general procedure.

Yield 92 mg (31%), pale yellow oil, \( R_f = 0.38 \) (silica gel; hexane/EtOAc/MeOH/NH\textsubscript{4}OH = 3/5/1/0.1), \( R_f = 0.03 \) (silica gel; acetone/hexane = 2/1), \([\alpha]_D\textsuperscript{22} = -4.4 \) (c 0.5, MeOH).

**1H-NMR** (500 MHz, CDCl\textsubscript{3}) δ: 1.44-1.47 (6H, m, CH\textsubscript{3}a,bCH), 4.79-4.81 (2H, m, CH\textsubscript{2}a,bNH), 4.91-4.93 (2H, m, CH\textsubscript{2}aNim), 5.04 (4H, ABq, \( J = 12.1 \) Hz, CH\textsubscript{2}aPh), 5.09-5.14 (5H, m, CH\textsubscript{2}aNim and CH\textsubscript{2}aPh and CHNH\textsubscript{b}), 5.59 (1H, d, \( J = 6.0 \) Hz, CHNH\textsubscript{a}), 6.67 (2H, m, 5-H\textsubscript{im}\textsuperscript{a} and Ar), 7.00 (1H, s, 5-H\textsubscript{im}\textsuperscript{b}), 7.02 (2H, m, Ar), 7.24-7.32 (10H, m, Ar), 7.38 (1H, s, 2-H\textsubscript{im}\textsuperscript{a}), 7.48 (1H, s, 2-H\textsubscript{im}\textsuperscript{b}).

**13C-NMR** (125 MHz, CDCl\textsubscript{3}) δ: 20.4 (CH\textsubscript{3}bCH), 21.4 (CH\textsubscript{3}aCH), 41.4 (CH\textsuperscript{b}), 45.0 (CH\textsuperscript{a}), 48.4 (NimCH\textsubscript{2}b), 50.6 (NimCH\textsubscript{2}a), 66.6 (PhCH\textsubscript{2}), 67.0 (PhCH\textsubscript{2}), 115.4 (5-C\textsubscript{im}\textsuperscript{a}), 125.5 (Ar), 125.7 (Ar), 126.7 (Ar), 127.0 (5-C\textsubscript{im}\textsuperscript{b}), 128.2 (Ar), 128.3 (Ar), 128.4 (Ar), 128.6 (Ar), 128.7 (Ar), 131.1 (Ar), 133.4 (4-C\textsubscript{im}\textsuperscript{b}), 136.0 (Ar), 136.4 (Ar), 136.9 (Ar), 137.1 (Ar), 137.1 (2-C\textsubscript{im}\textsuperscript{a}), 137.6 (Ar), 138.9 (2-C\textsubscript{im}\textsuperscript{b}), 144.7 (4-C\textsubscript{im}\textsuperscript{a}), 155.4 (CO), 155.9 (CO).

**MS** (ESI, m/z): 593 (M\textsuperscript{+}), 616 (M\textsuperscript{+}+Na).

Elemental analysis Found: C, 68.61; H, 6.44; N, 13.83. Calc. for C\textsubscript{34}H\textsubscript{36}N\textsubscript{6}O\textsubscript{4}: C, 68.90; H, 6.12; N, 14.18(%).
1,3-Bis[(4,5-diphenyl-1H-imidazole-1-yl)methyl]benzene (14).

![Chemical structure of 14](image)

The title compound was synthesized from 4,5-diphenylimidazole 13 and 1,3-bis(bromomethyl)benzene following the general procedure.

Yield 175 mg (65%), white solid, \(R_f = 0.64\) (silica gel; hexane/EtOAc/MeOH/NH\(_4\)OH = 3/5/1/0.1), mp 83-84 °C (lit. 155-157 °C).

\(^1\)H-NMR (360 MHz, CDCl\(_3\)) \(\delta\): 4.86 (4H, s, CH\(_2\)N), 6.48 (1H, s, Ar), 6.83 (2H, d, \(J = 7.5\) Hz, Ar), 7.10-7.19 (11H, m, Ar), 7.30-7.35 (6H, m, Ar), 7.45 (4H, d, \(J = 7.1\) Hz, Ar), 7.57 (2H, s, 2-H\(_{im}\)).

\(^13\)C-NMR (90 MHz, CDCl\(_3\)) \(\delta\): 48.7 (CH\(_2\)N), 125.7 (Ar), 126.6 (Ar), 126.7 (Ar), 128.3 (Ar), 128.9 (Ar), 129.0 (Ar), 129.1 (Ar), 129.2 (Ar), 129.5 (Ar), 130.6 (Ar), 131.1 (Ar), 134.5 (Ar), 137.2 (Ar), 137.5 (Ar), 138.6 (Ar).

MS (ESI, \(m/z\)): 543 (M\(^+\)), 565 (M+Na\(^+\)), 1085 (2M+1\(^+\)), 1107 (2M+Na\(^+\)).

Elemental analysis Found: C, 83.76; H, 5.95; N, 10.29. Calc. for C\(_{38}\)H\(_{30}\)N\(_4\): C, 84.10; H, 5.57; N, 10.32 (%).

2,6-Bis[(4,5-diphenyl-1H-imidazole-1-yl)methyl]pyridine (15).

![Chemical structure of 15](image)

The title compound was synthesized from 4,5-diphenylimidazole 13 and 2,6-bis(bromomethyl)pyridine following the general procedure.

Yield 167 mg (61%), white solid, \(R_f = 0.35\) (silica gel; hexane/EtOAc/MeOH/NH\(_4\)OH = 3/5/1/0.1), mp 94-95 °C.

\(^1\)H-NMR (360 MHz, CDCl\(_3\)) \(\delta\): 4.98 (4H, s, 2xCH\(_2\)N), 6.65 (2H, d, \(J = 7.7\) Hz, Ar), 7.11-7.19 (10H, m, Ar), 7.30-7.33 (6H, m, Ar), 7.48 (5H, d, \(J = 6.1\) Hz, Ar), 7.67 (2H, s, 2-H\(_{im}\)).
$^{13}$C-NMR (90 MHz, CDCl$_3$) δ: 50.2 (2xCH$_2$N), 120.3 (2xPy), 126.6 (Ar), 126.7 (Ar), 128.3 (Ar), 128.8 (Ar), 128.9 (Ar), 129.1 (Ar), 130.4 (Ar), 131.0 (Ar), 134.5 (Ar), 137.6 (Ar), 138.1 (Py), 138.4 (Ar), 156.5 (2xPy).

MS (ESI, m/z): 544 (M)$^+$, 566 (M+Na)$^+$, 1087 (2M+1)$^+$, 1109 (2M+Na)$^+$.

Elemental analysis Found: C, 81.32; H, 5.77; N, 12.91. Calc. for C$_{37}$H$_{29}$N$_5$: C, 81.74; H, 5.38; N, 12.88(%).
4. Crystallography

The X-ray measurements were carried out on a Bruker Kappa CCD diffractometer equipped with graphite monochromator (MoKα radiation, λ = 0.71073 Å) and an Oxford Cryostream low-temperature device. Unit cell dimensions were obtained by least-squares refinement of all measured reflexions (HKL, Scalepack\textsuperscript{3}). All structures were solved by direct methods (SIR97\textsuperscript{6}, SHELX-97\textsuperscript{7}). Non-hydrogen atoms were refined anisotropically by full-matrix least-squares analysis. Hydrogen positions have been calculated and included in the final structure factor calculation. All ellipsoids in the ORTEP\textsuperscript{8} plots are at the 50% level.

*Crystal data of 9*

\[2(C_7H_9N_3)^+ \cdot 2(Br^-) \cdot 2(CH_3O)\]
\[C_{46}H_{44}Br_2N_6O_2\]
Mr = 872.706
Triclinic
P\{1\}
a = 9.65230 (10)Å
b = 13.6217 (2)Å
c = 16.4095 (3)Å
α = 84.2073 (6)°
β = 84.1515 (6)°
γ = 70.8095 (7)°
V = 2021.81 (5)Å\textsuperscript{3}
Z = 2

Density measured by: not measured
Cell parameters from 22011 refl.
T = 223 K
Cube
0.46 x 0.38 x 0.15 mm
Colourless
Crystal source: F. Bures

*Data collection*

KappaCCD CCD diffractometer
Absorption correction: integration
Tmin = 0.519 , Tmax = 0.757
38299 measured reflections
9262 independent reflections
7362 observed reflections

Criterion: >2sigma(I)
Rint = 0.062
θmax = 27.48 °
h = -12 → 12
k = -17 → 17
l = -21 → 21

*Refinement*

Refinement on F\textsuperscript{2}
fullmatrix least squares refinement
R(all) = 0.0620
R(gt) = 0.0454
wR(ref) = 0.1482
wR(gt)= 0.1339
S(ref) = 1.049
9262 reflections
515 parameters
4 restraints
H positions constr
Calculated weights 1/[(σ\textsuperscript{2}(I_o)+(I_o+I_c)\textsuperscript{2}/900]
Figure 1. ORTEP drawing showing both symmetry independent molecules in the crystal structure of 9 at 223 K. Ellipsoids are shown at 50% probability level.
5. Representative NMR spectra

Figure 2. $^1$H- and $^{13}$C-NMR spectra of precyclophane 14.
Figure 3. $^1$H- and APT $^{13}$C-NMR spectra of precyclophane 11a.
Figure 4. \(^1\text{H}-^1\text{H}\) COSY and \(^1\text{H}-^{13}\text{C}\) HMQC NMR spectra of precyclophane 11a.
Figure 5. $^1$H-$^{13}$C HMBC NMR spectrum of precyclophane 11a.
Figure 6. $^1$H- and APT $^{13}$C-NMR NMR spectra of precyclophane 12a.
Figure 7. $^1$H-$^1$H COSY and $^1$H-$^{13}$C HMOC NMR spectra of precyclophane 12a.
Figure 8. $^1$H-$^{13}$C HMBC NMR spectrum of precyclophane 12a.
Figure 9. $^1$H- and $^{13}$C-NMR spectra of imidazoliophane 7.
Figure 10. 1H- and APT 13C-NMR spectra of imidazoliophane 10a.
Figure 11. $^1$H-$^{13}$C COSY and $^1$H-$^{13}$C HMQC NMR spectra of imidazoliophane 10a.

Figure 12. $^1$H-$^{13}$C HMBC NMR spectrum of imidazoliophane 10a.
6. References

7. Sheldrick, G.M. *Acta Cryst.* **2008**, *A64*, 112.