# 52. Lipophilic Diamides as Ionophores for Alkali and Alkaline Earth Metal Cations

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*Summary*

A series of lipophilic *N, N, N', N'*-tetrasubstituted diamides were prepared and their selectivity in solvent polymeric membranes was studied. *cis-N, N, N', N'*-Tetraisobutylcyclohexane-1,2-dicarboxamide induces a selectivity in membranes for $Li^+$ over alkaline earth metal cations and other alkali metal cations by a factor of about 1000 and 100 respectively. The ionophore *N, N'*-diheptyl-*N, N'*-dimethylethylmalonamide is an attractive candidate for the use in microelectrodes for the determination of intracellular $Mg^{2+}$-activities.

**Introduction.** – Diamides without further donor atoms are known to interact with various cations [1] [2]. Their *N, N, N', N'*-tetrasubstituted lipophilic representatives behave as ionophores in liquid membranes [3]. Thus, the *N, N'*-diheptyl-*N, N'*-dimethylsuccinamide has been successfully used as ion-selective component in microelectrodes for the intracellular measurement of $Mg^{2+}$-activities [4]. Drastic selectivity changes have to be expected even for slight variations in the structure of the ligand [5–7]. There exist classical [5] [8] as well as quantum mechanical models [9] [10] for the prediction of certain aspects of the ion selectivity, but a clear-cut description of the behavior of ionophores in membranes is still impossible. We therefore prepared a series of *N, N, N', N'*-tetrasubstituted diamides and report here on their selectivity in membranes and their interaction with alkali and alkaline earth cations.

**Results and Discussion.** – The potentiometrically determined selectivity factors [11] induced in solvent polymeric membranes by some of the ligands studied *(Scheme)* are presented in *Figures 1* and *2*. The selectivity factors given as $K^{Pot}_{MgX}$ represent the membrane preference of the ion X relative to $Mg^{2+}$ [11]. In the absence of anionic sites, *e.g.* tetrakis(*p*-chlorophenyl)borate ($TpClPB^-$), most of the studied ligands do not drastically affect the selectivity of the membrane (columns 2(**1**), 3(**3**), 5(**6**) and 6(**7**) relative to column 1 in *Fig. 1*). A similar behavior was

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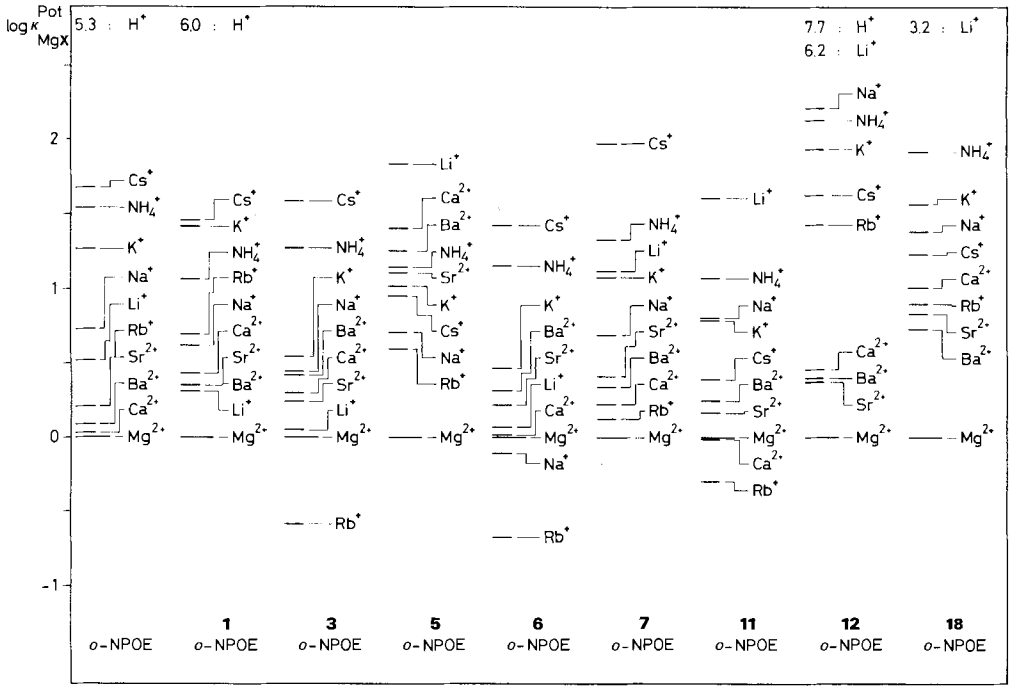
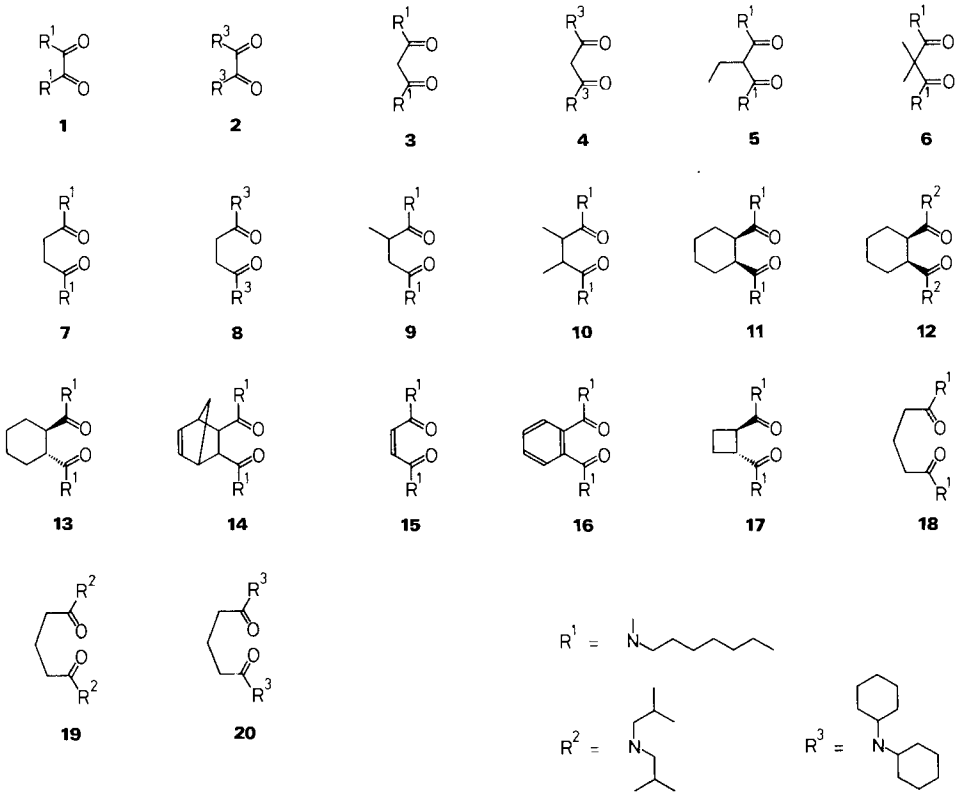



Fig. 1. *Selectivity factors, $\log K^{Pot}_{MgX}$, for solvent polymeric membranes with* o-*nitrophenyl octyl ether (*o-*NPOE) as membrane solvent.* Ligand-free membranes (column 1) are compared with membranes containing different lipophilic diamides as ion-selective ligands (separate solution method, 0.1 M solutions of the chlorides, 20–22 °C).

observed for the ligands **2**, **4**, **8**–**10**, **13**–**17**, **19** and **20**. Some ligands (**5**, **11**, **12**, **18**) induce however rather high $Li^+$-selectivity. Through appropriate substitution of the N-atoms in *cis*-1,2-cyclohexanedicarboxamide the ionophore **12** was obtained which yields $Li^+$-selective membranes that reject other alkali metal ions and alkaline earth metal cations by a factor of about 100 and 1000 respectively ($K^{Pot}_{LiX}$) [12]. Unfortunately, analogous changes of the substitution of glutaramide yielding the derivatives **18**–**20** did not lead to such large improvements in selectivity.

The incorporation of salts of lipophilic anions such as tetrakis(*p*-chlorophenyl)-borate into the membrane phase was proposed in order to reduce the interference by sample anions [13]. It was furthermore observed that some ligands behave as ionophores only in the presence of such lipophilic anionic sites (see *Fig. 1* and *2* in [14]). In many cases the membrane selectivities are spectacularly influenced by such lipophilic anions [15]. It is therefore worthwhile to study the selectivity behavior of neutral carrier membranes both in absence *(Fig. 1)* and in presence *(Fig. 2)* of lipophilic anionic sites. The membranes based on ligands **3** and **7** which exhibit behavior very similar to the ligand-free membrane in the absence of $TpClPB^-$ (see *Fig. 1*) indeed lead to drastic changes of the selectivities in presence of $TpClPB^-$ (see columns 3 and 6 relative to column 1 in *Fig. 2*).




Membranes based on malonamide and ethylmalonamide derivatives, **3** and **5**, respectively, exhibit somewhat improved selectivities for $Mg^{2+}$ as compared to the one based on the succinamide derivative **7** which has found application for intracellular $Mg^{2+}$-activity studies [4]. Because of the stronger rejection of $K^+$, membranes based on **5** are the most attractive candidates for this application. The dimethylmalonamide derivative **6** as well as the oxamide derivative **1** even in the presence of $TpClPB^-$ lead to membranes with almost the same selectivity sequence as the ligand-free membrane *(Fig. 2)*. In the case of ligand **12** $TpClPB^-$ causes a complete loss of the $Li^+$-selectivity (see *Fig. 1* and *2*).

The interaction of the $Li^+$-selective ionophore *cis-N, N, N', N'*-tetraisobutylcyclohexane-1,2-dicarboxamide (**12**) and of the $Mg^{2+}$-selective ionophore *N, N'*-diheptyl-*N, N'*-dimethylsuccinamide (**7**) with alkali and alkaline earth metal cations was corroborated by vapour pressure osmometry and $^{13}C$-NMR. spectroscopy.

The data presented in *Figure 3* and the fact that LiSCN is soluble only to 100 mol-% indicate that at least a (1:1)- and a (1:2)-$Li^+$/ionophore complex are formed in chloroform. A stability constant of $4.0 \pm 0.8$ kg $mol^{-1}$ for the (1:1)-complex has been determined by vapour pressure osmometry (ethanol, LiCl, 30° [16]). Similarly for the interaction of **7** with $Mg^{2+}$ only a stability constant of $1.5 \pm 0.4$ kg $mol^{-1}$ (ethanol, $MgCl_2$, 30°, [16]) for a (1:1)-complex could be

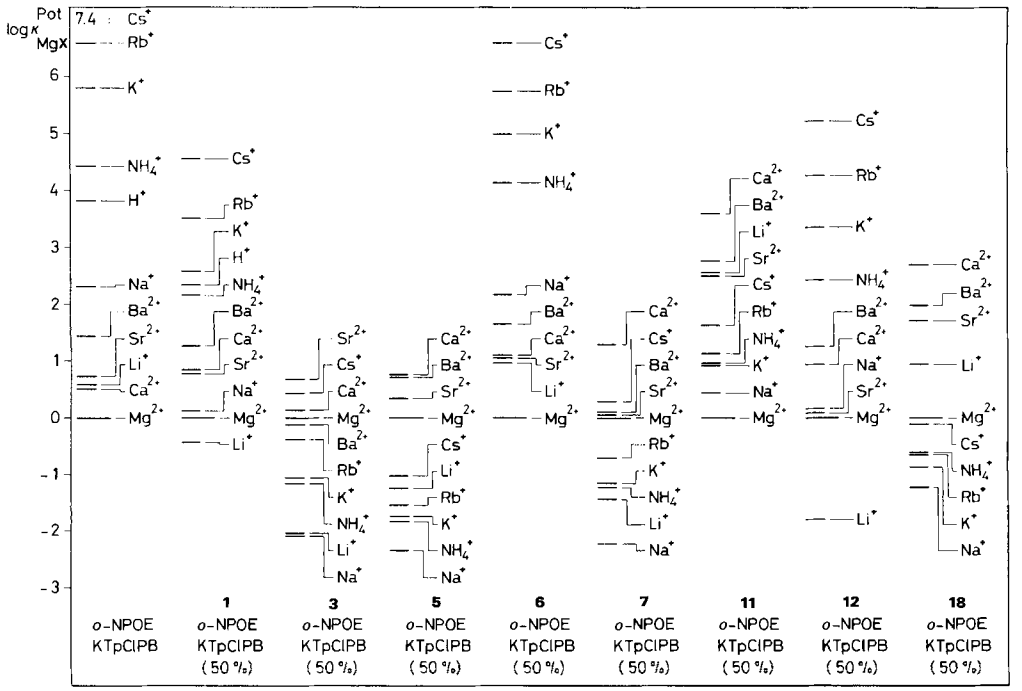



Fig. 2. *Selectivity factors, log* $K^{Pot}_{MgX}$*, for solvent polymeric membranes with o-nitrophenyl octyl ether (o-NPOE) as membrane solvent and incorporated lipophilic anionic sites (potassium tetrakis(p-chlorophenyl)borate (KTpClPB), mol-% given).* Ligand-free membranes (column 1) are compared with membranes containing different lipophilic diamides as ion-selective ligands (separate solution method, 0.1M solutions of the chlorides, 20–22°).

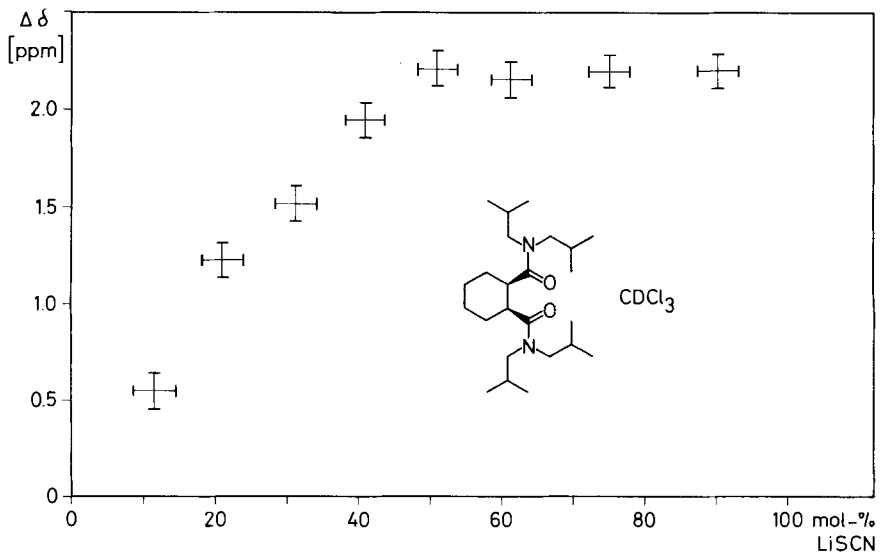



Fig. 3. *$^{13}$C-NMR. chemical shifts Δδ of the carbonyl C-atom of the diamide* **12** *induced by addition of LiSCN in $CDCl_3$*

determined reliably. There is, however, evidence for the existence of other complexes in chloroform solution [3]. If available stability constants in ethanol are used as criterion, ligand **12** is the weakest complexing agent investigated to date for use as highly selective ionophore in solvent polymeric membranes without lipophilic anionic sites.

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## Experimental Part

**EMF. measurements.** – The solvent polymeric membranes contained 1–2 wt.-% ligand, 33 wt.-% polyvinylchloride (PVC S704, *Lonza AG*, CH-3930 Visp) and 65–66 wt.-% *o*-nitrophenyl octyl ether (*o*-NPOE). The membrane preparation and the measuring technique have been described in detail elsewhere [17–19]. Throughout, cell assemblies of the type Hg; $Hg_2Cl_2$, KCl (satd.)/3M KCl/sample solution/solvent polymeric membrane/0.1M $MgCl_2$, AgCl; Ag were used. The activity coefficients used are described in [19].

**$^{13}$C-NMR. measurements.** – The $^{13}$C-NMR. spectra were recorded on a *Bruker Spectrospin* HFX-90/B-SC-FFT 12 spectrometer at 22.628 MHz. The chemical shifts are reported in $\delta$(ppm) relative to TMS as internal standard. To a solution of ligand **12** in $CDCl_3$, LiSCN was added stepwise up to the solubility limit of the salt. All samples were handled under $N_2$-atmosphere in a dry-box. The error bars in *Figure 3* correspond to uncertainties of $\pm 0.05$ ppm and $\pm 3$ mol-% LiSCN.

**Vapour pressure osmometry.** – Differential measurements were carried out at 30° in ethanol solutions of 0.13 mol kg$^{-1}$ and 0.018 mol kg$^{-1}$ in $MgCl_2$ and LiCl, respectively. The ligand concentrations varied from $2 \cdot 10^{-3}$ to $3 \cdot 10^{-2}$ mol kg$^{-1}$ in both experiments. For the computation of the formation constants and further details see [16].

**Preparation of the ligands.** – *General remarks.* For recording procedures of the spectra and abbreviations see [3]. The syntheses of ligands **2**, **3**, **4**, **7**, **8** and **20** were described earlier [20].

*General procedure for the preparation of ligands* **1**, **5**, **6**, **9**, **13**, *and* **16–19**. The acid chloride (1 mol-equiv.) was reacted with the amine (4 mol-equiv.) in toluene at RT. over night. The precipitated amine hydrochloride was filtered off and the solvent evaporated i.V. The residue was dissolved in diethyl ether and the organic phase washed with 0.2M HCl, 0.2M NaOH, and $H_2O$. The crude product was purified as described below.

*Preparation of* N,N′-*diheptyl*-N,N′-*dimethyloxamide* (**1**). The crude product (96%) was purified by flash chromatography (35 kPa) on silica gel with $CHCl_3$/ether 9:1 as eluent (yield: 60%). – IR. ($CHCl_3$): 1640. – $^1$H-NMR. ($CDCl_3$): 0.86 (*t*, 6 H, 2 C–$CH_3$); 1.1–1.9 (br., 20 H, 2($CH_2$)$_5$$CH_3$); 2.95 (*s*, 6 H, 2 N–$CH_3$); 3.35 (*m*, 4 H, 2 N–$CH_2$). – MS.: 312 (9, $M^+$), 227 (5), 156 (65), 128 (100), 57 (81), 43 (26), 41 (17).

$C_{18}H_{36}N_2O_2$ (312.49) Calc. C 69.18 H 11.61 N 8.96% Found C 68.92 H 11.41 N 8.84%

*Preparation of* N,N′-*diheptyl*-N,N′-*dimethylethylmalonamide* (**5**). The crude product (84%) was purified by flash chromatography (35 kPa) on silica gel with ethyl acetate/hexane 1:1. Destillation i.V. (0.05 Torr, 136–140°) gave ligand **5** (31%). – IR. ($CHCl_3$): 1640. – $^1$H-NMR. ($CDCl_3$): 0.86 (*t*, 6 H, 2($CH_2$)$_6$$CH_3$); 0.97 (*t*, 3 H, $CHCH_2CH_3$); 1.23 (br., 20 H, 2($CH_2$)$_5$); 1.91 (*m*, 2 H, $CHCH_2$); 2.88 and 2.94 (2*s*, 6 H, 2 N–$CH_3$); 3.1–3.6 (*m*, 5 H, 2 N–$CH_2$ and $CH_2CH$). – $^{13}$C-NMR. ($CDCl_3$): 12.9 (*qa*, $CHCH_2CH_3$); 14.1 (*qa*, 2($CH_2$)$_6$$CH_3$); 22.6 (*t*, 2 $CH_2CH_2CH_3$); 26.8, 27.1, 28.5, 29.1 (4*t*, $CH_2$); 31.8 (*t*, 2 $CH_2CH_2CH_3$); 33.4 and 35.1 (2 *qa*, 2 $CH_3N$); 48.3 and 49.5 (2*t*, 2 $CH_2N$); 51.2 (*d*, CH); 169.3 (*s*, 2 CO). – MS.: 354 (13, $M^+$), 226 (31), 199 (24), 198 (78), 156 (60), 128 (100), 57 (50), 44 (20), 43 (18).

$C_{21}H_{42}N_2O_2$ (354.58) Calc. C 71.14 H 11.94 N 7.90% Found C 71.19 H 12.25 N 7.87%

*Preparation of* N,N′-*diheptyl*-N,N′-*dimethyldimethylmalonamide* (**6**). The crude product (87%) was purified by flash chromatography (40 kPa) on silica gel with ethyl acetate/hexane 3:7. Destillation i.V. (0.09 Torr, 124–128°) gave ligand **6** (43%). – IR. ($CHCl_3$): 1620. – $^1$H-NMR. ($CDCl_3$): 0.87 (*t*, 6 H, 2 $CH_2CH_3$); 1.26 (br., 20 H, 2($CH_2$)$_5$); 1.35 (*s*, 6 H, 2 $CH_3C$); 2.82, 2.84 and 2.88 (3*s*, 6 H, 2 N–$CH_3$);

3.0–3.5 (*m*, 4 H, 2 $NCH_2$). – $^{13}$C-NMR. ($CDCl_3$): 14.1 (*qa*, 2 $CH_2CH_3$); 22.6 (*t*, 2 $CH_2CH_3$); 24.4 and 24.8 (2 *qa*, 2 C–$CH_3$); 26.8, 27.0, 28.3, 29.1 (4*t*, $CH_2$); 31.8 (*t*, 2 $CH_2CH_2CH_3$); 33.7 and 35.3 (2 *qa*, 2 N–$CH_3$); 48.7 (*s*, C); 49.4 (*t*, 2 N–$CH_2$); 173.2 (*s*, 2 CO). – MS.: 354 (50, $M^+$), 283 (87), 226 (48), 225 (51), 198 (24), 156 (56), 128 (100), 57 (76), 44 (17), 43 (22).

$C_{21}H_{42}N_2O_2$ (354.58) Calc. C 71.14 H 11.94 N 7.90% Found C 71.05 H 11.93 N 7.88%

*Preparation of* N,N′-*diheptyl*-N,N′-*dimethylmethylsuccinamide* (**9**). The crude product (19%) was purified by flash chromatography (35 kPa) on silica gel with ethyl acetate/hexane 1:1. Destillation i.V. (0.09 Torr, 122–126°) gave ligand **9** (6%). – IR. ($CHCl_3$): 1630. – $^1$H-NMR. ($CDCl_3$): 0.85 and 0.87 (2*t*, 6 H, 2 $CH_3CH_2$); 1.09 and 1.11 (2*d*, 3 H, $CH_3CH$); 1.24 (br., 20 H, 2$(CH_2)_5$); 2.84, 2.88, 2.95 and 3.06 (4*s*, 6 H, 2 N–$CH_3$); 2–3.6 (br., 7 H, 2 N–$CH_2$ and $CHCH_2$). – $^{13}$C-NMR. ($CDCl_3$): 14.1 (*qa*, 2 $CH_3CH_2$); 17.5 and 18.5 (2 *qa*, 2 $CH_3CH$); 22.6 (*t*, 2 $CH_2CH_3$); 26.8, 27.3, 27.4, 28.5, 28.8 and 29.1 (6*t*, $CH_2$); 31.8 (*t*, 2 $CH_2CH_2CH_3$); 32.3, 32.6, 33.4, 33.8 and 35.3 ($CH_2$ and 2 N–$CH_3$); 37.2, 37.4, 37.8 and 38.0 (4*d*, CH); 47.9, 50.0 and 50.2 (3*t*, 2 N–$CH_2$), 171.3, 175.9 and 176.1 (3*s*, 2 CO). – MS.: 354 (8, $M^+$), 226 (100), 198 (21), 156 (12), 128 (34), 57 (22), 44 (8), 43 (9).

$C_{21}H_{42}N_2O_2$ (354.58) Calc. C 71.14 H 11.94 N 7.90% Found C 70.67 H 11.75 N 7.88%

*Preparation of* trans-N,N′-*diheptyl*-N,N′-*dimethyl-1,2-cyclohexanedicarboxamide* (**13**). The crude product (95%) was purified by flash chromatography (35 kPa) on silica gel with ethyl acetate/hexane 1:1. Destillation i.V. (0.07 Torr, 137–140°) gave ligand **13** (29%). – IR. ($CHCl_3$): 1630. – $^1$H-NMR. ($CDCl_3$): 0.86 and 0.88 (2*t*, 6 H, 2 $CH_3CH_2$); 1–2 (br., 28 H, 2$(CH_2)_5CH_3$, 4 ring-$CH_2$); 2.82 and 3.02 (2*s*, 6 H, 2 N–$CH_3$); 2.6–3.8 (br., 6 H, 2 N–$CH_2$ and 2 CH). – $^{13}$C-NMR. ($CDCl_3$): 14.0 (*qa*, 2 $CH_3CH_2$); 22.6 (*t*, 2 $CH_2CH_3$), 25.7, 26.7, 26.8, 27.0, 27.4, 28.9, 29.1, 29.2 and 29.9 (9 *t*, $CH_2$); 31.9 (*t*, 2 $CH_2CH_2CH_3$); 33.8 and 35.4 (2 *qa*, 2 N–$CH_3$); 42.7, 42.8 and 43.0 (3 *d*, 2 CH); 47.9, 48.0 and 50.2 (3 *t*, 2 N–$CH_2$), 175.1 and 175.4 (2*s*, 2 CO). – MS.: 394 (1.5, $M^+$), 366 (6), 281 (2), 266 (67), 239 (14), 238 (23), 156 (19), 128 (100), 57 (29), 44 (11), 43 (9).

$C_{24}H_{46}N_2O_2$ (394.64) Calc. C 73.04 H 11.75 N 7.10% Found C 72.93 H 11.71 N 7.05%

*Preparation of* N,N′-*diheptyl*-N,N′-*dimethylphthalamide* (**16**). The crude product (88%) was purified by flash chromatography (35 kPa) on silica gel with ethyl acetate/hexane 1:1. Destillation i.V. (0.03 Torr, 135–138°) gave ligand **16** (48%). – IR. ($CHCl_3$): 1630; 1600. – $^1$H-NMR. ($CDCl_3$): 0.82 and 0.86 (2*t*, 6 H, 2 $CH_3CH_2$); 1–2 (br., 20 H, 2$(CH_2)_5CH_3$); 2.80 and 2.95 (2*s*, 6 H, 2 N–$CH_3$); 3.14 and 3.33 (2*t*, 4 H, 2 N–$CH_2$); 7.1–7.5 (*m*, 4 H, arom. H). – $^{13}$C-NMR. ($CDCl_3$): 14.0 (*qa*, $CH_3CH_2$); 22.6 (*t*, 2 $CH_2CH_3$); 26.4, 26.9, 28.0, 28.8, 29.1, 31.6 and 31.8 (7 *t*, $CH_2$); 32.3 and 37.1 (2 *qa*, 2 N–$CH_3$); 47.3 and 51.3 (2 *t*, 2 N–$CH_2$); 126.2, 126.5, 128.5 and 128.7 (4 *d*, phenyl CH); 134.9, 135.1 and 135.4 (3 *s*, C); 169.9 and 170.2 (2*s*, 2 CO). – MS.: 388 (16, $M^+$), 387 (17), 260 (84), 175 (16), 174 (16), 162 (55), 128 (100), 105 (13), 57 (27), 43 (16).

$C_{24}H_{40}N_2O_2$ (388.59) Calc. C 74.18 H 10.38 N 7.21% Found C 74.08 H 10.38 N 7.24%

*Preparation of* trans-N,N′-*diheptyl*-N,N′-*dimethyl-1,2-cyclobutanedicarboxamide* (**17**). The crude product (58%) was purified by flash chromatography (35 kPa) on silica gel with ethyl acetate/hexane 1:1. Destillation i.V. (0.08 Torr, 125–130°) gave ligand **17** (37%). – IR. ($CHCl_3$): 1625. – $^1$H-NMR. ($CDCl_3$): 0.86, 0.88 (2*t*, 6 H, 2 $CH_3CH_2$); 1.25 (br., 20 H, 2$(CH_2)_5CH_3$); 2.2 (*m*, 4 H, 2 ring-$CH_2$); 2.86, 2.90 and 2.92 (3*s*, 6 H, 2 N–$CH_3$); 3.3 (*m*, 4 H, N–$CH_2$ and 2 CH); 3.75 (*t*, 2 H, N–$CH_2$). – $^{13}$C-NMR. ($CDCl_3$): 14.0 (*t*, 2 $CH_3CH_2$); 22.1 and 22.4 (2*t*, ring-C); 22.6 (*t*, 2 $CH_2CH_3$); 27.2, 28.5, 28.8 and 29.1 (4*t*, $CH_2$); 31.8 (*t*, 2 $CH_2CH_2CH_3$); 33.4 and 34.6 (2 *qa*, 2 N–$CH_3$); 38.0, 38.5, 38.6 and 39.1 (4*d*, 2 CH); 47.9 and 49.6 (2*t*, 2 N–$CH_2$); 173.0, 173.1, 173.2 and 173.3 (4*s*, 2 CO). – MS.: 366 (19, $M^+$), 238 (23), 210 (26), 184 (17), 156 (17), 128 (100), 57 (46), 44 (27), 43 (26).

$C_{22}H_{42}N_2O_2$ (366.59) Calc. C 72.08 H 11.55 N 7.64% Found C 71.99 H 11.64 N 7.56%

*Preparation of* N,N,N′,N′-*tetraisobutylglutaramide* (**19**). The crude product (65%) was purified by flash chromatography (35 kPa) on silica gel with ethyl acetate/hexane 4:6. Destillation i.V. (0,04 Torr, 120–125°) gave ligand **19** (40%). – IR. ($CHCl_3$): 1630. – $^1$H-NMR. ($CDCl_3$): 0.84 and 0.88 (2*d*, 24 H, 8 $CH_3$); 1.95 (*m*, 6 H, 4 CH and $CH_2CH_2CH_2$); 2.39 (*t*, 4 H, 2 $CH_2CO$); 3.07 and 3.16 (2*d*, 8 H, 4 N–$CH_2$). – $^{13}$C-NMR. ($CDCl_3$): 20.0 and 20.2 (2 *qa*, 8 $CH_3$); 21.3 (*t*, $CH_2CH_2CH_2$); 26.5 and 27.8

(2*d*, 4 CH); 32.4 (*t*, 2 $CH_2CO$); 52.9 and 55.3 (2*t*, 4 $CH_2N$); 172.7 (*s*, 2 CO). – MS.: 354 (5, $M^+$), 227 (17), 226 (100), 198 (8), 184 (6), 170 (28), 128 (22), 86 (13), 57 (23), 41 (13).

$C_{21}H_{42}N_2O_2$ (354.58) Calc. C 71.14 H 11.94 N 7.90% Found C 71.33 H 12.00 N 7.88%

*General procedure for the preparation of ligands* **11**, **12**, *and* **15**. The anhydride (1 mol-equiv.) was reacted with the amine (1 mol-equiv.) in toluene at RT. over night. After evaporation of the solvent the residue was dissolved in diethyl ether and the organic phase washed with water. Dicyclohexylcarbodiimide (1 mol-equiv., *Fluka, puriss.*) dissolved in ethyl acetate was added to a solution of the product (1 mol-equiv.) and *p*-nitrophenol (1 mol-equiv. *Fluka, puriss. p.a.*) in ethyl acetate. The reaction was completed by stirring over night at RT. The solution was filtered and the filtrate concentrated i.V. This monoester (1 mol-equiv.) was reacted under reflux with the amine (2 mol-equiv.) in $CHCl_3$ over night.

*Preparation of* cis-N,N′-*diheptyl*-N,N′-*dimethyl-1,2-cyclohexanedicarboxamide* (**11**). The crude product was purified by flash chromatography (40 kPa) on silica gel with ethyl acetate/hexane 1:1. Destillation i.V. (0.07 Torr, 138–141°) gave ligand **11** (57%). – IR. ($CHCl_3$): 1633. – $^1$H-NMR. ($CDCl_3$): 0.86 (*t*, 6 H, 2 C–$CH_3$); 1–1.7 (br., 28 H, 2($CH_2$)$_5CH_3$, 4 ring-$CH_2$); 1.8–2.5 (br., 2 H, 2 CH); 2.5–3.7 (br., 10 H, 2 N–$CH_3$, 2 N–$CH_2$). – $^{13}$C-NMR. ($CDCl_3$): 14.1 (*qa*, 2 $CH_3CH_2$); 22.6 (*t*, 2 $CH_2CH_3$); 23.4, 26.4, 26.9, 27.3, 28.9 and 29.1 (6*t*, $CH_2$); 31.9 (*t*, 2 $CH_2CH_2CH_3$); 33.7 and 35.6 (2 *qa*, 2 N–$CH_3$); 39.8 (*d*, 2 CH); 47.9 and 50.2 (2*t*, 2 $CH_2N$); 174.2 and 174.5 (2*s*, 2 CO). – MS.: 394 (1, $M^+$), 266 (100), 238 (10), 168 (12), 156 (9), 128 (8.5), 57 (17), 44 (6), 43 (6).

$C_{24}H_{46}N_2O_2$ (394.64) Calc. C 73.04 H 11.75 N 7.10% Found C 73.08 H 11.70 N 7.09%

*Preparation of* cis-N,N,N′,N′-*tetraisobutyl-1,2-cyclohexanedicarboxamide* (**12**). The crude product was purified by flash chromatography (40 kPa) with ethyl acetate/hexane 3:7. Destillation i.V. (0.02 Torr, 120–124°) gave ligand **12** (25%). – IR. ($CHCl_3$): 1635. – $^1$H-NMR. ($CDCl_3$): 0.87 (*d*, 24 H, 8 $CH_3$); 1–2.5 (br., 14 H, 4 ring-$CH_2$, 2 ring-CH, 4 CH); 2.5–3.4 (br., 8 H, 4 N–$CH_2$). – $^{13}$C-NMR. ($CDCl_3$): 20.4 (*qa*, 8 $CH_3$); 23.4 and 27.2 (2*t*, 4 ring-C); 26.7 and 28.4 (2*d*, 4 $CH(CH_3)_2$); 39.7 (*d*, 2 ring-CH); 54.0 and 56.3 (2*t*, 4 N–$CH_2$); 174.6 (*s*, 2 CO). – MS.: 394 (1, $M^+$), 338 (1), 282 (1), 266 (100), 238 (6), 210 (13), 166 (4), 154 (6), 128 (11), 81 (6), 57 (18), 41 (8).

$C_{24}H_{46}N_2O_2$ (394.64) Calc. C 73.04 H 11.75 N 7.10% Found C 73.40 H 11.47 N 7.06%

*Preparation of* N,N′-*diheptyl*-N,N′-*dimethylmaleinamide* (**15**). The crude product was purified by flash chromatography (40 kPa) with ethyl acetate/hexane 1:1. Destillation i.V. (0.07 Torr, 142–145°) gave ligand **15** (21%). – IR. ($CHCl_3$): 1620; 1660. – $^1$H-NMR. ($CDCl_3$): 0.87 (*t*, 6 H, 2 $CH_3$); 1.24 and 1.55 (br., 20 H, 2($CH_2$)$_5CH_3$); 2.95 and 3.08 (*s*, 6 H, 2 $CH_3$); 3.40 (*m*, 4 H, 2 $CH_2$); 7.36 (*s*, 2 H, CH=CH). – $^{13}$C-NMR. ($CDCl_3$): 14.1 (*qa*, 2 $CH_3$); 22.6 (*t*, 2 $CH_2CH_3$); 26.6, 26.9, 27.1, 29.1, 29.2 (5*t*, $CH_2$); 31.8 (*t*, 2 $CH_2CH_2CH_3$); 34.1 and 35.5 (2 *qa*, 2 N–$CH_3$); 48.3 and 50.2 (2*t*, 2 N–$CH_2$); 131.1, 131.2, 131.3, 131.4 (4*d*, 2 CH=); 164.9 and 165.1 (2*s*, 2 CO). – MS.: 338 (5, $M^+$), 253 (32), 211 (62), 210 (100), 182 (13), 112 (46), 57 (38), 44 (26), 43 (19).

$C_{20}H_{38}N_2O_2$ (338.53) Calc. C 70.96 H 11.31 N 8.27% Found C 70.86 H 11.09 N 8.16%

*Preparation of* (R,S)-N,N′-*diheptyl*-N,N′,*2,3-tetramethylsuccinamide* (**10**). 2,3-Dimethylsuccinic anhydride was obtained by treatment (5 h, 80°) of 2,3-dimethylsuccinic acid (*Fluka, purum;* 1 mol-equiv.) with thionyl chloride (*Fluka, puriss. p.a.;* 30 mol-equiv.) in benzene containing a catalytic amount of dimethylformamide. The anhydride (1 mol-equiv.) was reacted with *N*-heptyl-*N*-methylamine (*Fluka,* purum; 2 mol-equiv.) in benzene for 15 h at RT. to yield *N*-heptyl-*N*,2,3-trimethylsuccinicmonoamide. Ligand **10** was obtained by reacting this monoamide with *N*-heptyl-*N*-methylamine in the presence of isobutyl chloroformate and *N*-methylmorpholine according to [21] [22]. The crude product was purified by flash chromatography (35 kPa) on silica gel with chloroform/ether 1:4 (yield: 28%). – IR. ($CHCl_3$): 1615. – $^1$H-NMR. ($CDCl_3$): 0.87 (*t*, 6 H, 2 $CH_3CH_2$); 1.05 (*d*, 6 H, 2 $CH_3CH$); 1.2–1.8 (br., 20 H, 2($CH_2$)$_5CH_3$); 2.92 and 3.03 (2*s*, 6 H, 2 N–$CH_3$); 3.1 (br., 2 H, 2 CH); 3.3 (*m*, 4 H, 2 N–$CH_2$). – MS.: 368 (5, $M^+$), 240 (100), 224 (6), 212 (14), 156 (13), 128 (33), 57 (19), 43 (8).

$C_{22}H_{44}N_2O_2$ (368.60) Calc. C 71.68 H 12.03 N 7.61% Found C 71.45 H 11.99 N 7.50%

*Preparation of* N,N′-*diheptyl*-N,N′-*dimethylbicyclo[2.2.1]-5-hepten-2*endo,*3*endo-*dicarboxamide* (**14**). Hydrolysis of bicyclo[2.2.1]-5-hepten-2*endo*,3*endo*-dicarboxylic anhydride (*Fluka,* purum) in water

(2½ h, reflux) gave the corresponding dicarboxylic acid. Ligand **14** was prepared *via* the *p*-nitrophenyl ester as described above and purified by flash chromatography (35 kPa) on silica gel with ethyl acetate/hexane 9:1 (yield: 18%). – IR. ($CHCl_3$): 1650. – $^1$H-NMR. ($CDCl_3$): 0.87 (*m*, 6 H, 2 C–$CH_3$); 1.1–1.9 (br., 22 H, 2($CH_2$)$_5CH_3$ and 2 H–C(7)); 2.78 and 2.90 (2*s*, 6 H, 2 N–$CH_3$); 3.0–3.4 (br., 8 H, 2 N–$CH_2$, 4 CH); 6.23 (*s*, 2 H, 2 CH=). – MS.: 404 (14, $M^+$), 275 (100), 248 (14), 210 (73), 156 (15), 128 (22), 112 (21), 57 (42), 43 (22).

$C_{25}H_{44}N_2O_2$ (404.63) Calc. C 74.21 H 10.96 N 6.92% Found C 73.49 H 10.87 N 6.84%

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