One-Step Synthesis of the Degradation-Resistant Ligands $H_2NCR_2CR_2NH_2$ (R = Me, Et)

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The useful title ligands 2,3-dimethylbutane-2,3-diamine (**2**) and 3,4-diethylhexane-3,4-diamine (**3**) were synthesized in one step from Me_2CHNH_2 and Et_2CHNH_2 by dehydrodimerization in a modified Mercat reaction.

Ethylenediamine (en, **1**) is one of the most useful ligands in coordination chemistry, and it has been extensively employed both by itself[1] and as part of many macrocyclic systems.[2] It is known that **1** and ligand systems derived from it can relatively easily degrade, especially under oxidative conditions. Careful study[3] has identified the backbone C–H bonds as the site of initial attack.

Replacing sensitive C–H bonds by the less reactive C–Me group is a standard strategy in such situations. The reason that it is very rarely employed in the case of **1** is that $H_2NCMe_2CMe_2NH_2$ (**2**), which we will call tetrameda, has been synthesized by a tedious multistep route which involves bromination as well as the intermediacy of potentially explosive dinitro compounds. A new multistep route was reported some years ago but does not yet appear to have been used in inorganic synthesis.[4]

On the rare occasions when **2** has been studied as a ligand,[5] it has been found to show good stability under oxidizing conditions and good crystallinity of its derivatives, also a very desirable feature in a ligand. In addition to its use in coordination chemistry, it is also useful in the synthesis of pterin analogues for bioinorganic studies. In this case, the methyl groups prevent undesirable tautomerization.[6]

Results

2 and **3** have now been synthesized by a modified Mercat[7] route in 20–40% yield on a 0.5-g scale (eq 1). The identity of the product has been confirmed by MS, NMR, and microanalytical data on the oxalate salts. **2** and **3** themselves are hygroscopic and give poor analytical data.

$$2R_2CHNH_2 \rightarrow H_2NCR_2CR_2NH_2 + H_2 \qquad (1)$$

Discussion

Our work on the Mercat process[8] has shown that a variety of organic compounds can be conveniently dimerized photochemically on a multigram scale by mercury photosensitization. The mechanistic pathway is outlined in eqs 2–6. The experimental justification for this picture is discussed in the literature.[9] In principle, **2** and **3** should be accessible in one step from the readily available from *i*-$PrNH_2$ and 3-pentylamine by this route.

In practice, we find that procedure fails using the conditions previously described (Hg vapor, 254-nm light, vapor phase). It seemed likely that the mercury excited state, Hg*, was binding

$$Hg + h\nu \rightarrow Hg^* \qquad (2)$$

$$Hg^* + RCH_2CH_3 \rightarrow Hg + RCH^{\bullet}CH_3 + H^{\bullet} \qquad (3)$$

$$H^{\bullet} + RCH_2CH_3 \rightarrow RCH^{\bullet}CH_3 + H_2 \qquad (4)$$

$$2RCH^{\bullet}CH_3 \rightarrow RCH(CH_3)CH(CH_3)R \qquad (5)$$

$$2RCH^{\bullet}CH_3 \rightarrow RCH{=}CH_2 + RCH_2CH_3 \qquad (6)$$

to the amine nitrogen and not to the C–H bond of *i*-$PrNH_2$. We know that this is a problem for other amine substrates but that it can often be circumvented by moving to H atoms as abstractors.[7] Experimentally, this is achieved by adding H_2 to the system. Under these conditions reaction 7 produces H atoms which abstract H directly from the weakest C–H bond, without leading to undesirable exciplex formation.

$$Hg^* + H_2 \rightarrow 2H + Hg \qquad (7)$$

Surprisingly, the reaction with primary amines still failed to give useful yields of product. To explain this, we developed a working hypothesis, by which disproportionation of the intermediate radicals (eq 8) leads to the corresponding imines.[10] These

$$i\text{-}PrNH_2 + Me_2C{=}NH \rightarrow (Me)_2C{=}N\text{-}i\text{-}Pr + NH_3 \qquad (8)$$

are attacked by amine to give the N-substituted imines **4** and **5**. If the attacking amine is the product diamine, this leads to parasitic removal of the desired product; if the attacking amine is the starting material, this leads to formation of an undesired product. In either case, the yield is decreased and the isolation procedure made more complicated.

Recently, we have developed a strategy to improve this situation. It consists of running the reaction in ammonia rather than hydrogen. Under these conditions, H atoms are still formed via eq 9, but now the formation the N-substituted imine is greatly reduced because NH_3, present in excess, shifts the equilibrium

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in eq 8 toward the left and so back to the starting educts, *i*-$PrNH_2$ and $Me_2C{=}NH$. The isopropylideneamine, we thought, could be attacked by another isopropyl radical in order to form the desired product via eq 11 or the imine could undergo H atom attack to give the $Me_2C^{\bullet}\text{-}NH_2$ radical, which would give the same diamine product on dimerization.

$$Hg^* + NH_3 \rightarrow {}^{\bullet}NH_2 + H^{\bullet} \quad (9)$$

$$2{}^{\bullet}NH_2 \rightarrow N_2 + 2H_2 \quad (10)$$

$$Me_2C^{\bullet}\text{-}NH_2 + Me_2C{=}NH \rightarrow Me_2C(NH_2)Me_2CNH^{\bullet} \quad (11)$$

$$Me_2C(NH_2)Me_2CNH^{\bullet} + NH_3 \rightarrow (Me_2CNH_2)_2 + {}^{\bullet}NH_2 \quad (12)$$

Using this strategy, we have now been able to synthesize **2** and **3** in one step from the corresponding monoamines in 20–40% yield and on a 0.1–0.5-g scale (see Experimental Section).

These useful diamines are therefore now available for application in coordination chemistry.

Experimental Section

NMR spectra were determined on a Bruker 250-MHz instrument, and GCMS analysis was carried out on a HP 5890 gas chromatograph (29 m × 0.25 mm i.d. capillary column coated with a 0.25-μm film of SE 30) connected with a HP 5971A MS detector. Substrates were used as received from Aldrich Co.

Caution! Mercury vapor is toxic, and appropriate precautions must be taken.

General Method. Substrates (always in excess, starting weight shown for each case) were placed in a quartz tube (0.67 L, 1.5 L) equipped with a reflux condenser, and a drop of mercury was added. Ammonia was passed into the system through a long needle which dipped into the substrate. After 20 min, the system was filled with ammonia and the lamps were turned on (Rayonet 128-W photoreactor from Southern New England Ultraviolet Corp. with 16 low-pressure Hg bulbs, circular array). The ammonia flow rate was maintained at the value mentioned under the individual compounds below for the whole reaction time. The reaction temperatures were not controlled but remained in the range 20–50 °C. For dimerization of *i*-propylamine a cooled condenser (dry ice/bromobenzene; −30 °C) is recommended.

The crude reaction mixture of products collects by condensation inside the quartz vessel. Further separation of starting material, imine, and diamine was carried out by rotary evaporation and distillation or by column chromatography (alumina adsorption, 80–200 mesh, Fisher Scientific Co.). Ethyl acetate was used to elute the imine, after which chloroform/methanol eluted the diamine. The diamines were recrystallized from ether.

Details for Individual Compounds. Diamines. Data are reported as follows: amount of amine used, flow rate of ammonia, temperature of reaction vessel, reaction time, yield (based on amine converted), production rate of diamine; ^{13}C-NMR (CD_3OD) in ppm; MS in *m*/*e* (%). Unreacted amine was recovered.

2,3-Dimethylbutane-2,3-diamine (2): 45 g (0.76 mol) of isopropylamine, 20 mL of NH_3/min, 32 °C, 24 h, 504 mg (1.1 mmol, 39%), 21 mg/h (0.18 mmol/h), conversion 504 mg; ^{13}C-NMR 26.01 (q, CH_3), 56.06 (s, C–NH_2); MS 101 (0.5; $M^+ - CH_3$), 84 (8), 58 (100), 43 (6), 42 (25), 41 (14), 39 (6). Anal. Found for the oxalate: C, 46.92; H, 8.52; N, 13.51. Calcd for $C_8H_{18}O_4N_2$: C, 46.62; H, 8.73; N, 13.58.

3,4-Diethylhexane-3,4-diamine (3): 22.5 g (0.26 mol) of 3-pentylamine, 20 mL of NH_3/min, 45 °C, 26.5 h, 0.450 g (2.6 mmol; 20%), 17 mg/h (0.10 mmol/h), conversion 451 mg; ^{13}C-NMR 9.89 (q, CH_3), 28.41 (t, CH_2), 61.81 (s, C–NH_2); MS 143 (1; $M^+ - C_2H_5$), 126 (9), 99 (4), 86 (100), 69 (4), 56 (8), 44 (8). Anal. Found for the of oxalate: C, 55.15; H, 10.02; N, 10.60. Calcd for $C_{12}H_{26}O_4N_2$: C, 54.98; H, 9.91; N, 10.68.

Imines. *N*-Isopropylisopropylideneamine (4): ^{13}C-NMR (acetone-d_6) 25.54 (q*, CH_3), 26.70 (q*, CH_3), 34.48 (q, CH_3), 59.73 (d, N–CH), 163.6 (s, C=N); MS 99 (8), 84 (100), 68 (7), 43 (12), 42 (75), 41 (25), 39 (24). [Note that here and below an asterisk denotes overlapping resonances.]

***N*-(3-Pentyl)-3-pentylideneamine (5)**: ^{13}C-NMR (acetone-d_6) 11.13 (q*, CH_3), 11.23 (q*, CH_3), 11.83 (q*, CH_3), 24.54 (t, CH_2), 29.80 (t, CH_2), 32.40 (t, CH_2), 62.09 (d, N–CH), 171.8 (s, C=N); MS 155 (16), 127 (16), 126 (100), 82 (19), 71 (10), 56 (75), 55 (12), 43 (14), 41 (20), 39 (7).

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Registry No. **2**, 20485-44-3; **2** oxalate, 142188-56-5; **3**, 137946-65-7; **3** oxalate, 142188-57-6; **4**, 3332-08-9; **5**, 142188-55-4; *i*-$PrNH_2$, 75-31-0; $(CH_3CH_2)_2CHNH_2$, 616-24-0; Hg, 7439-97-6.