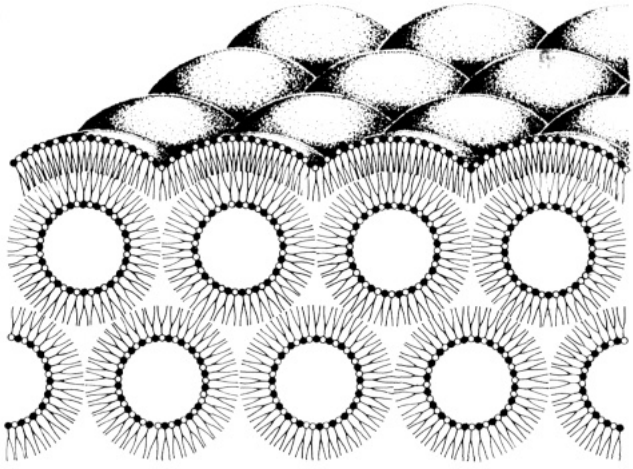

Figure 2. Schematic representation of the lipid aggregates formed with $N^+C_5Ala2C_{14}$ (O–C) and $(SO_3^-)C_5Ala2C_{14}$ (●–C) mixed at the equimolar ratio in water.

aggregates, in which an effective hydrogen-bonding interaction among head groups is presumably the predominant factor controlling the stabilization of such aggregates.

In conclusion, an attractive interaction among polar head groups of lipid molecules in aggregates is the primarily important factor for the formation of globular aggregates, and the subsequent hydrophobic interaction among these aggregates results in the closely packed arrangement. In addition, the hydrogen-belt domain in such aggregates may also be responsible for the morphological stabilization.

Registry No. $N^+C_5Ala2C_{14}$, 83825-02-9; $(SO_3^-)C_5Ala2C_{14}$, 95362-72-4.

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Regioselective Nucleophilic C-Alkylation of the Pyrrole Ring in an (η-Pyrrolyl)iodohydridorhenium Complex

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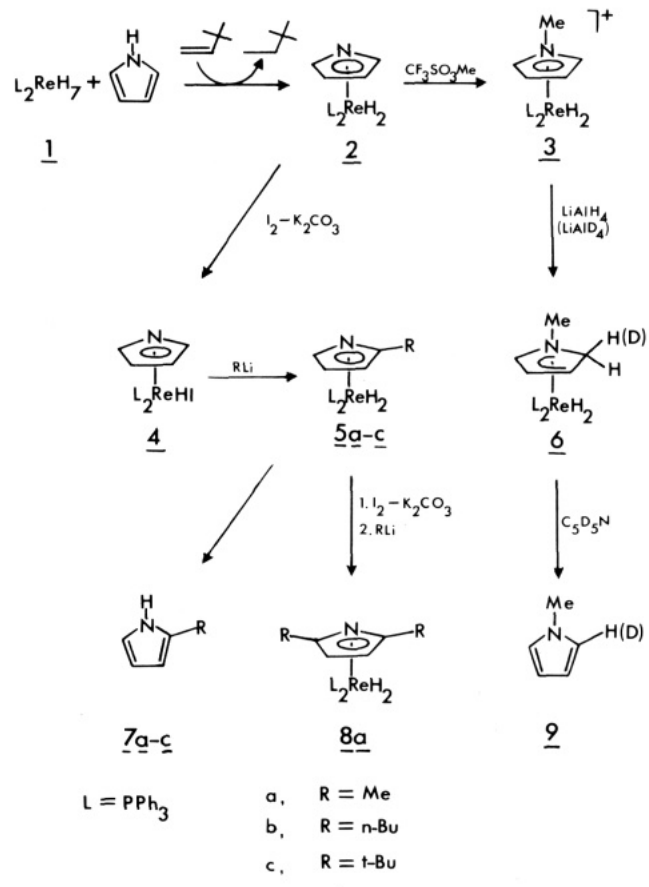
The electrophilic C-alkylation of pyrrole (as its magnesium salt) shows only modest selectivity for 2-substitution,[1,2] and C-alkylated pyrroles are generally prepared by less direct routes, including cyclization of acyclic precursors.[1] Here we report the preparation of an η-pyrrolyl iodo hydrido complex of rhenium **4** which undergoes *nucleophilic* C-alkylation in high yield (>90%) at the C-2 position of the pyrrolyl ligand. Whereas the activation toward nucleophiles of weakly nucleophilic organic molecules such as arenes by coordination to transition-metal centers offers one of the most useful synthetic strategies involving organotransition-metal complexes,[3] this kind of "Umpolung" does not seem to have been achieved previously in the case of the more nucleophilic aromatic nitrogen heterocycles.[4]

Scheme I



Our results are summarized in Scheme I (L = PPh_3). The η-pyrrolyl dihydrido complex **2**[5] was obtained in 61% yield by refluxing bis(triphenylphosphine)rhenium heptahydride (**1**)[6] with pyrrole (10 equiv) and 3,3-dimethylbutene (10 equiv) in THF (5 min).[7] Like pyrrole itself, this neutral complex reacts with

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(5) All the organometallic complexes described are yellow (or orange, **4**) air-stable crystalline solids; they gave satisfactory elemental analyses (C, H, N, P) (except for the deuterio analogues, which were not analyzed). Selected NMR data: **2** ^1H (80 MHz, CD_2Cl_2) δ 5.43 (s, H2, H5), 4.53 (s, H3, H4), −10.07 (t, J = 41 Hz, ReH_2); $^{31}P\{Ar\ H\}$ (162 MHz, CD_2Cl_2) δ 33.61 (downfield from external H_3PO_4) (t, J = 41 Hz). **3** ^1H (80 MHz, acetone-d_6) δ 6.51 (s, H2, H5), 5.45 (s, H3, H4), 2.71 (s, Me), −8.00 (t, J = 41 Hz, ReH_2). **4** ^1H (80 MHz, CD_2Cl_2) δ 5.64 (s, H2, H5), 4.49 (s, H3, H4), −10.23 (t, J = 48 Hz, ReH). **5a** ^1H (200 MHz, C_6D_6) δ 5.47 (s, H5), 4.49 (d, J = 2 Hz) and 4.21 (d, J = 2 Hz) (H3, H4), 2.23 (s, Me), −9.52 (t, J = 40 Hz, ReH_2). **5b** ^1H (200 MHz, C_6D_6) δ 5.51 (s, H5), 4.58 (d, J = 2 Hz) and 4.22 (d, J = 2 Hz) (H3, H4), 2.52, 1.51, 1.23 (m, $(CH_2)_3$), 0.79 (t, J = 8 Hz, CH_3), −9.49 (t, J = 40 Hz, ReH_2). **5c** ^1H (80 MHz, C_6D_6) δ 5.38 (s, H5) 4.67 (d, J = 2 Hz) and 3.80 (d, J = 2 Hz) (H3, H4), 1.13 (s, *t*-Bu), −9.28 (*t*, J = 40 Hz, ReH_2). **6**-H ^1H (200 MHz, acetone-d_6) δ 5.22 (dt, J = 3.6, 5.4 Hz, H5-exo), 5.04 (s, H2), 3.66 (d, J = 3.6 Hz, H5-endo), 3.30 (d, J = 3.6 Hz) and 1.50 (d, J = 3.6 Hz) (H3, H4), 1.33 (s, Me), −2.0 (br) and −10.8 (br) (ReH_2). **8a** ^1H (200 MHz, C_6D_6) δ 4.28 (s, H3, H4), 2.23 (s, Me), −9.43 (t, J = 40 Hz, ReH_2).

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electrophiles, and it was converted (CF_3SO_3Me in CH_2Cl_2, 20 °C; 88% yield) into the η-1-methylpyrrole dihydrido cation **3**, in the hope that the positive charge would promote nucleophilic attack, as occurs with cationic arene complexes.[3]

This first approach to the nucleophilic alkylation of pyrrole proved disappointing. Although the dihydrido cation **3** reacted smoothly (THF, 0 °C) with $LiAlH_4$ and $LiAlD_4$ to give (93% yield) the neutral dihydrido complexes **6**-H and **6**-D[8] [which were converted into 1-methylpyrrole (**9**-H) and 1-methyl-[2-^{2}H]pyrrole (**9**-D)[9] by heating in C_5D_5N (90 °C, 10 min)], only intractable mixtures were obtained with lithium alkyls or dimethyl sodiomalonate.

We have discovered, however, that lithium alkyls readily alkylate the neutral η-pyrrolyl iodo hydrido complex **4**, obtained in 80% yield by treatment of **2** with I_2 (1 equiv) and K_2CO_3 (excess) (CH_2Cl_2, 20 °C). Thus, **5a** was formed immediately and essentially quantitatively (92% isolated yield) when a solution of MeLi (1.2 equiv) was added to **4** (in THF, 0 °C); similarly, *n*-BuLi gave **5b** (90%), and *t*-BuLi (at −80 °C) gave **5c** (97%). The η-2-alkylpyrrolyl complexes **5a–c** could be converted into the free 2-alkylpyrroles **7a–c**[10] (**5a** and **5b** by heating at 90 °C in Me_2SO-d_6 containing HBF_4, and **5c** by vacuum pyrolysis at 150–180 °C).

The procedure could be repeated; the η-2-methylpyrrolyl complex **5a**, when treated successively with I_2–K_2CO_3 and MeLi, without isolating the intermediate iodo hydrido complex, gave the η-2,5-dimethylpyrrolyl complex **8a** (94% isolated yield). A special effort was made in this case to determine the regioselectivity of the reaction; no trace of the 2,3- or 2,4-dimethylpyrrolyl isomers could be detected in the crude, unrecrystallized η-2,5-dimethylpyrrolyl complex **8a** by 200-MHz ^{1}H NMR, indicating that the reaction is >98% regioselective.

$LiAlH_4$ and $LiAlD_4$ also reacted with the iodo hydrido complex **4**, but much more slowly (THF, 20 °C, 2 h), to give **5** (R = H) (≡**2**) and its 2-deuterio analogue **5** (R = D) (79% yield).[11]

This remarkably facile alkylation (**4** → **5**), in which nucleophilic attack on a coordinated aromatic moiety is accompanied by migration of hydrogen from carbon to metal and elimination of a good leaving group (halide) from the metal, appears to have some precedent in cyclopentadienyl transition-metal systems.[12] The presence of a leaving group is essential; the dihydrido complex **2** is not alkylated by lithium alkyls under the same conditions. We imagine that the reaction is either an entirely concerted nucleophilic process or, more probably, that it is initiated by a single electron transfer, followed by loss of iodide from the 19e radical anion of **4**.

Note Added in Proof. Since this communication was submitted, we have found that *aromatic* lithium reagents also react with the iodo hydrido complexes under the same conditions (0 °C), and with the same high regioselectivity and yield, as the aliphatic lithium reagents described above. Thus, **5** (R = Ph) and **5** (R = 5-methyl-2-furyl) were obtained from **4** in >85% yield. **8** (R = Ph) was obtained from **5** (R = Ph) in 87% yield without isolating the iodo hydrido intermediate and afforded pure 2,5-diphenylpyrrole (92%, no isomers detectable by NMR) upon treatment with Me_2SO–HBF_4.

(8) (a) The ^{1}H NMR and IR spectra of **6**-H and **6**-D indicate that hydride attacks the 1-methylpyrrole ring in **3** from the uncomplexed, exo side. The splitting pattern of the NMR signal of the introduced hydrogen (δ 5.22, absent in the spectrum of **6**-D) can be explained by long-range coupling with the two ^{31}P nuclei, characteristic for H-exo.[8b] Furthermore the medium-intensity band at 2820 cm^{-1} (ν(C–H) exo) in the IR spectrum of **6**-H is absent in the spectrum of **6**-D, in which ν(C–D) exo is observed at 2030 cm^{-1}. (b) Davies, S. G.; Moon, S. D.; Simpson, S. J.; Thomas, S. E. *J. Chem. Soc., Dalton Trans.* **1983**, 1805–1806.

(9) **9**-H was identified, without isolation, by comparison of its ^{1}H NMR spectrum with that of a commercial sample; integration of its ^{1}H NMR signals showed that **9**-D was deuteriated exclusively on C-2.

(10) **7a** and **7b** were identified, without isolation, by their ^{1}H NMR spectra.[2a] **7c** was isolated in 84% yield: ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.04 (br, NH) 6.69 (m, H5), 6.12 (m) and 5.94 (m) (H3, H4), 1.25 (s, *t*-Bu).

(11) Integration of its ^{1}H NMR signals showed that **5** (R = D) was deuteriated exclusively on C-2.

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Design of Stereoselective Etchants for Organic Crystals. Application for the Sorting of Enantiomorphs and Direct Assignment of Absolute Configuration of Chiral Molecules

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Despite the widespread use of etching in the material sciences,[1-3] the selection of appropriate etchants is generally done with a combination of "inspiration and intuition".[1]

Recently we reported changes in crystal habit induced during crystallization by the presence of minute amounts of additives with structures similar to that of the substrate.[4] A correlation was established between the molecular structure of the additive, the crystal structure of the substrate, and the affected growth directions. We found that the additive may bind stereoselectively to the affected crystal face, as if it were a substrate molecule, on the condition that its modified moiety emerges from the crystal surface. During the crystal's growth this adsorption hinders growth by disturbing deposition of oncoming layers on that face. During dissolution such additive molecules should adsorb in an analogous stereoselective manner only at those faces whose molecules are so oriented as to receive this additive. We report that a growth inhibitor of a particular face can act as an etchant of that same face during partial dissolution. The two examples covered here deal with etching by chiral additives of a mixture of enantiomorphous crystals of (*R*,*S*)-asparagine which, as a conglomerate, resolves spontaneously on crystallization and with the etching by chiral additives of the enantiotopic faces of the centrosymmetric crystal of glycine.

Growth experiments have shown that only *R* amino acid additives may bind to the surfaces of (*R*)-asparagine crystals, while the *S* additives may bind only to the (*S*)-asparagine crystals.[4a] The additive aspartic acid may bind only to those crystal faces of asparagine which allow its modified moiety, the hydroxyl oxygen, to emerge from the crystal surface, i.e., the {010} face (Figure 1a). A loss of energy due to replacement of the N—H···O- (carboxylate) hydrogen bond between asparagine molecules by an O···O repulsion between the hydroxyl oxygen of the β-carboxy group of aspartic acid and the carboxylate oxygen of asparagine inhibits the aspartic acid's adsorption when it approaches an {010} face in the reverse manner.[5] The conditions necessary for binding are met in two out of the four symmetry-related sites at the {010} faces of this orthorhombic $P2_12_12_1$ crystal.[6] When crystalline (*R*,*S*)-asparagine–H_2O is partially dissolved in a solution containing 20% (*R*)-aspartic acid, etch pits are formed only on the {010} faces[7] of the *R* crystals (Figure 1b); the *S* crystals remain

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(7) The crystals of asparagine were partially dissolved in a solution containing 50 mg of (*R*,*S*)-asparagine and 10 mg of (*R*)-aspartic acid per 1 mL of H_2O at 25 °C for 5 min. The etching was seen on the {010} faces under both optical and scanning electron microscopes.

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