# The Effect of Temperature on Yields and Product Ratios during the Synthesis of Cryptands containing the Ferrocene Unit

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The condensation of 1,1′-bis(chlorocarbonyl)ferrocene with diaza-18-crown-6 gives 1,1′-(1,4,10,13-tetraoxa-7,16-diazacyclo-octadecane-7,16-diyldicarbonyl)ferrocene (**3**) and its dimer 1,1″; 1′,1‴-bis(1,4,10,13-tetraoxa-7,16-diaza-cyclo-octadecane-7,16-diyldicarbonyl)bisferrocene (**4**); the overall yields of (**3**) and (**4**) and the product ratios are dependent upon the reaction temperature.

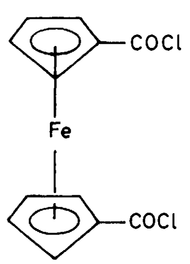
Numerous macrocyclic compounds containing oxygen, sulphur, and nitrogen as the electron donor heteroatoms have been synthesised.[1,2] These compounds are capable of complexing a wide variety of metallic and organic cations often with a high degree of specificity[1–3] and this property has been used in phase transfer catalysis,[4] selective ion transport,[5,6] resolution of chiral molecules,[7] and to some extent electron transport studies.[2d]

The syntheses and n.m.r. spectra of macrocyclic compounds containing the ferrocene unit as an integral part of the macrocyclic skeleton have been reported recently.[8,9] It was shown that the condensation of 1,1′-bis(chlorocarbonyl)-ferrocene (**1**) with diaza-18-crown-6 (**2**) under conditions of high dilution gave the monomeric cryptand (**3**) as the major product together with its dimeric analogue (**4**). This communication reports that the yields of monomer and dimer, and the

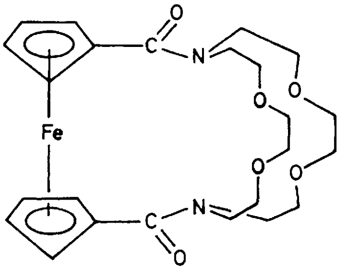
**Table 1.** Percentage yields of (**3**) and (**4**) as a function of temperature with toluene as solvent.[a]

| *T*/°C | % Yield of (**3**)[b] | % Yield of (**4**)[b] |
|---|---|---|
| 100 | 63 | 2 |
| 20 | 65 | 5 |
| −20 | 62 | 9 |
| −40 | 17 | 15 |
| −70 | 6 | 20 |

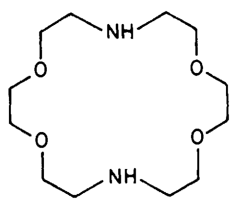
[a] The normal conditions involved dropwise addition of the reactants (60 ml; $6.3 \times 10^{-3}$ M of each in toluene) over 3 h into vigorously stirred toluene (100 ml) to give a final nominal concentration of $1.7 \times 10^{-3}$ M in monomer. [b] Yields are based on h.p.l.c. using a reverse phase column (Perkin Elmer C8, $10\mu$) and acetonitrile–water (39:61) as eluant; the remainder of each reaction mixture was polymeric.



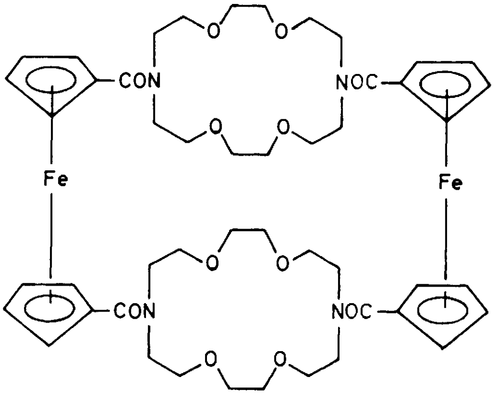
**(1)**



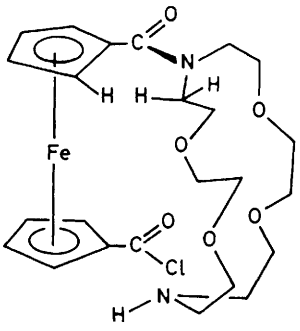
**(3)**



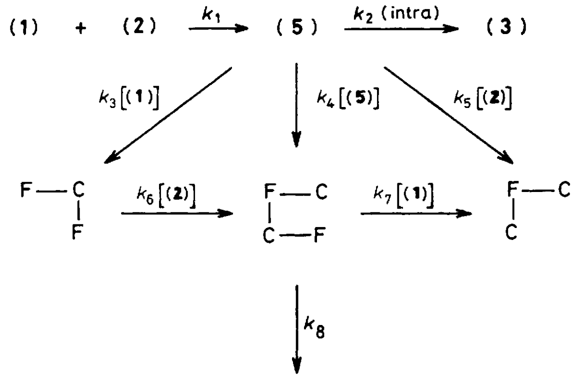
**(2)**



**(4)**



**(5)**



**Scheme 1.** F = ferrocenyl unit; C = crown unit. (Each step involves the elimination of hydrogen chloride.)

*High temp.*: $k_2 > k_3[(\mathbf{1})]$ or $k_4[(\mathbf{5})]$ or $k_5[(2)]$; hence (**3**) is formed.

*Low temp.*: $k_2 < k_3[(\mathbf{1})]$ or $k_4[(\mathbf{5})]$ or $k_5[(2)]$; hence (**4**) is formed.

product ratio, are dependent on the temperature at which the condensation reaction is carried out.

The yields of monomer and dimer at various temperatures calculated from h.p.l.c. data are reported in Table 1. The experimental findings show clearly that using high temperature conditions, good yields of monomer are obtained with low yields of dimer. At low temperatures relatively large amounts of dimer are obtained although the overall total yield of monomer plus dimer drops from 70 to 30% and high molecular weight oligomeric products comprise the material balance. A reaction kept at −70 °C for 8 h and −40 °C for a further 8 h failed to improve the overall yield of monomer plus dimer showing that the product ratios are due to the reaction conditions and not to incomplete reaction. Subsequent experiments at low temperature using more concentrated solutions (up to a nominal maximum of $1 \times 10^{-2}$ M in reactants) and in another case a 2 : 1 excess of (**2**) failed to improve the yield of dimer. Furthermore, varying the rates of addition of the two reactants (0.5 *vs.* 6.0 h) at standard concentrations and 20 °C had no effect on the resultant monomer : dimer ratio. Mandolini has pointed out[9] that the so-called E.M. value ($k_{\text{intra}}/k_{\text{inter}}$) is a vital factor in determining the ratio of products in cyclisation reactions. Since in our case, cyclisation involves a minimum of 15 atoms (taking a conservative estimate of the ferrocene unit as being equivalent to 3 atoms) the E.M. value should lie between 0.01 and 0.05 M. The visual evidence of colour change and precipitation of triethylamine hydrochloride suggests that the initial condensation of (**1**) and (**2**) to (**5**) occurs rapidly at −70 °C but even if the subsequent cyclisation is slow, the concentration of (**5**) never exceeds $1 \times 10^{-2}$ M and under our normal conditions cannot exceed $1.7 \times 10^{-3}$ M. Thus all experiments but one were conducted well below the estimated E.M. value and the results suggest strongly that temperature rather than concentration is the critical factor controlling the condensation process. This may be due either to different temperature coefficients for monomer ($k_2$) *vs.* dimer ($k_3$, $k_4$, or $k_5$) formation (see Scheme 1), or to the influence of temperature-dependent bond rotations on the course of the condensation reactions.

Earlier, variable temperature n.m.r. studies of **(4)**[10] revealed two distinct dynamic processes within the molecule involving rotation about the ferrocene–carbonyl bond ($\Delta G^‡$ 50 kJ mol$^{-1}$, $T_c$ −10 °C) and rotation about the N–CO bond ($\Delta G^‡$ 67 kJ mol$^{-1}$, $T_c$ +60 °C). At low temperatures bond rotation (ferrocene–CO and CO–N) in **(5)** would be slowed and model studies suggest that if the CO–N bond is rigid, attack of the second amino function in **(5)** on the carbonyl halide would meet with considerable steric hindrance originating from the enforced proximity of several hydrogen atoms, whereas free rotation of the amide link would alleviate such interactions. If it is assumed that $\Delta S^‡$ = *ca.* 0 for bond rotations, an estimate of the rate coefficients for both rotational processes may be made and at 223 K, where the onset of preferential dimer formation occurs, $k$ (ferrocene–CO, rotation) = 6.0 s$^{-1}$, giving $t_{\frac{1}{2}}$ = 0.12 s, whereas $k$(CO–N rotation) = $9.3 \times 10^{-4}$ s$^{-1}$, corresponding to $t_{\frac{1}{2}}$ = 750 s. Thus hindered rotation about the CO–N bond may well be the factor responsible for the decrease in monomer yield. Experiments are in progress to establish whether similar systems exhibit product ratios dependent upon temperature and hence to elucidate the exact origin of the effect and the results will be reported in the full paper.

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