Nitroalkanes in C–C Bond Forming Reactions: A Crystal Structure of a Complex of a Guanidine Catalyst and a Nitroalkane Substrate†

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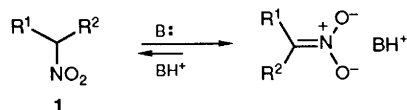
1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD), a good catalyst for nitroalkanes in C–C bond forming reactions, forms a 1 : 1 complex **3** with α-nitrotoluene as a substrate, as shown by a crystal structure determination.

Nitroalkanes have been used surprisingly little in catalytic enantioselective C–C bond forming reactions,[1] despite the possibility of short routes to optically active amines,[2] β-amino alcohols[3] (e.g. ephedrine) and α-amino acids.[4] Our first attempts using cinchona alkaloids[1a] as chiral basic catalysts in Michael and Henry reactions resulted in slow conversions and low enantioselectivities.‡ The unknown mode of complexation between the cinchona alkaloids and the nitroalkanes hampered further development of these catalysts to give higher enantioselectivities.

In our view, to be able to develop a chiral catalyst, the catalyst should bind to the nitroalkane substrate **1** in a predictable, tight and well defined manner. In a base catalysed C–C bond forming reaction the achiral nitroalkane **1** is converted into the prochiral nitronate anion **2** (Scheme 1). The intermediate nitronate anion **2** serves as an ideal handle for the catalyst. Fixation of this nitronate anion by the catalyst is essential. At this stage in the reaction the stereochemistry at C-α in the product is determined. The catalyst should possess, after protonation, a structural element complementary to the structure of this nitronate anion **2**. Here we report a crystal structure of a complex **3** of an achiral catalyst model, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) and α-nitrotoluene (Fig. 1).

The bicyclic guanidine TBD is an excellent catalyst for Michael and Henry reactions of nitroalkanes in toluene.[5] Exemplary is the Michael addition of nitroethane to methyl vinyl ketone (both 0.1 mmol dm^{-3}) using 10% TBD as the catalyst. This afforded 5-nitrohexan-2-one (75%) within 5 min. Quinine as the catalyst gave 75% of 5-nitrohexan-2-one only after 122 h (enantiomeric excess, e.e., 13%).

Single crystals§ of the complex **3** were obtained from a solvent mixture of toluene and pentane. The complex **3** shows a double hydrogen bridge bonding mode between the substrate and the catalyst. The hydrogen bonding atoms H(5) and

H(7) were refined individually. The H···O distances of 1.97(3) and 1.99(3) Å respectively indicate real hydrogen bonds.[6] The angles O(11)–H(5)–N(5) of 176.0(3)° and O(12)–H(7)–N(9) of 174.0(3)° show that the hydrogen bonds are approximately linear. The dihedral angle between the guanidine plane N(5)–C(6)–N(7) and the nitronate plane O(11)–N(13)–O(12) is 39.6%. The 'head-to-head' orientation in **3** satisfies the demand for a tight and predictable complexation between the catalyst and the nitroalkane.

NMR studies (^{1}H, ^{13}C and 2DNOE) also suggested a 'head-to-head' orientation of the two ionic components in solution. 300 MHz ^{1}H NMR spectra of a 1 : 1 mixture of TBD and α-nitrotoluene in C₆D₆ showed deprotonation of α-nitrotoluene. The signal of the two C-α methylene protons (δ 5.43, s) disappeared, and was replaced by a one-proton singlet in
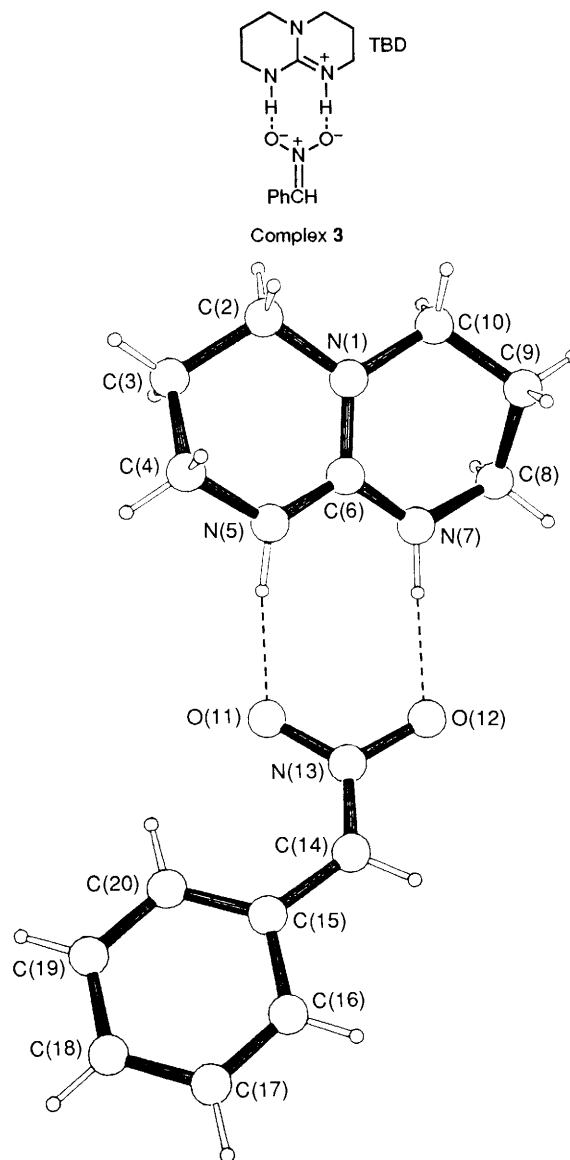

Complex 3

† The Society regrets the delay in the publication of this communication, which prevented its publication simultaneously with that from P. H. Boyle, M. A. Convery, A. P. Davis, G. D. Hosken and B. A. Murray, J. Chem. Soc., Chem. Commun., 1992, 239, and accepts responsibility for the delay.

‡ Both Michael and Henry reactions have been carried out using cinchona alkaloids as the catalysts. In all cases the e.e.s did not exceed 25% (unpublished results).

§ Crystal data for **3** at 130 K, C₇H₁₄N₃·C₇H₆NO₂, M_r = 276.34, monoclinic, space group $P2_1/a$, a = 10.338(2), b = 10.627(2), c = 13.232(3) Å, β = 93.95(2)° and V = 1456.2 Å,³ Z = 4, D_c = 1.266 g cm^{-3}, λ = 0.71073 Å, μ(Mo-Kα) = 0.82 cm^{-1}. Final R = 0.041 and R_w = 0.048 for 2470 reflections. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

Scheme 1 The first step in a base catalysed addition reaction of nitroalkanes

Fig. 1 The crystal structure of the salt **3** of TBD and α-nitrotoluene

the aromatic region (δ 7.56, s). A 1:2 mixture of TBD and α-nitrotoluene in C_6D_6 showed two distinct pairs of signals for the deprotonated and complexed nitronate anion and the free α-nitrotoluene. ^{13}C NMR spectra showed distinct signals for all six aromatic carbon atoms in a 1:1 mixture, indicating a relatively slow rotation of the phenyl group, due to conjugation with the C=N double bond. 2DNOE experiments in C_6D_6 revealed no interaction between any of the hydrogens of the two ionic components ruling out a stacked or sandwich structure of the complex in solution.

The crystal structure **3** is, to the best of our knowledge, the first example of a complex of a basic catalyst and a nitroalkane substrate. It combines the two aspects of recognition and catalysis. The type of complexation is analogous to the complexation of carboxylate,[7] phosphate[7a,8] and nitrate[9] anions by the guanidinium moiety. The reported complexation of a nitrate anion by Schmidtchen[10] showed a similar binding mode.

Enantioselective catalysis, for introducing chirality at C-α of the nitroalkane, requires differentiation between the *Re*-site and the *Si*-site of the prochiral nitronate anion. This goal might be achieved by the use of a chiral analogue of TBD.[10] Experiments with a chiral bicyclic guanidine, kindly placed at our disposal by Prof. J. de Mendoza, are currently under investigation and will be published in due course.

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