

Supporting Information for

Nucleophilic Metal Complexes as Acylation Catalysts: Solvent-Dependent "Switch" Mechanisms Leading to a Catalyzed Staudinger Reaction

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General. Unless otherwise stated, all reactions were carried out under strictly anhydrous, air-free conditions. All reagents used are commercially available from Aldrich and Strem Chemicals. All solvents were dried and distilled by standard procedures. The ^1H and ^{13}C NMR spectra were acquired on a Varian Unity Plus 400 MHz instrument in CDCl_3 . The ^1H (400 MHz) and ^{13}C chemical shifts (101 MHz) are given in parts per million (δ) with respect to internal TMS standard or residual solvent peaks. HPLC analysis of the chiral alcohol and rate determination experiments were performed with a Waters Millipore Model 510 head unit, a Chiracel OD column, a Waters Millipore Lambda-Max Model 481LC spectrophotometer and a Hewlett Packard integrator. Solution phase IR data were recorded on a Bruker IFS-55 FTIR spectrometer. $\text{NaCo}(\text{CO})_4$ (**1a**) and $[\text{Cp}_2\text{Co}^+\text{Co}(\text{CO})_4^-]$ (**1d**) were prepared according to literature methods.^{1, 2}

General acylation procedure. The anhydride (1 mmol) was added to a solution of the corresponding alcohol (1 mmol) and 10 mol % of metal catalyst in 3 mL of solvent. 2,6-di-tert-butyl-pyridine (1 mmol) was added in the case of polar solvents. Control experiments were conducted in the presence of 10 mol % 15-crown-5 (Entry 4, Table 2). After GC HPLC and/or ^1H NMR analysis of the reaction mixture indicated completion, the solution was washed with water, and the organic layer was separated, dried over Na_2SO_4 and filtered through a plug of Celite[®]. The solvent was evaporated to yield acylated product, which could be further purified by column chromatography (EtOAc/hexanes) on silica gel if necessary.

General procedure for the Staudinger reaction. Cobaltocenium cobaltate **1d** (18 mg, 0.05 mmol) and diphenylketene **8** (194 mg, 1 mmol) were dissolved in BTF (2 mL) and stirred at room temperature. The α -imino ester **7** (256 mg, 1 mmol) was then added to the solution.

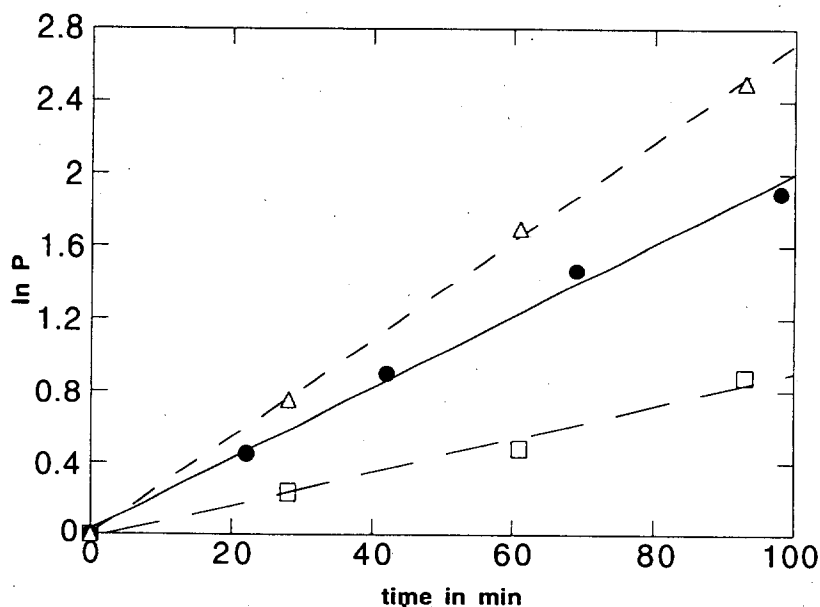
After completion of the reaction as indicated by TLC or HPLC, water was added, the organic layer was separated, dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was subjected to column chromatography (5-20% EtOAc/hexanes) on a small silica gel plug (2.5 x 3 cm) and provided 381 mg **10** (85% yield). Alternatively, the solid residue could be purified by recrystallization from Et_2O .

Ethyl-N-(toluenesulfonyl)-2-oxo-3,3-diphenylazetidide-4-carboxylate (10). The β -lactam product was obtained as a white crystalline solid: mp 189 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.01 (d, 2H), 7.50 (d, 2H), 7.35 (m, 5H), 7.20 (m, 3H), 7.05 (m, 2H), 5.35 (s, 1H), 3.80 (m, 2H), 2.45 (s, 3H), 0.85 (t, 3H) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 166.4, 164.9, 145.5, 136.5, 135.5, 135.2, 129.8, 129.0, 128.3, 128.4, 128.0, 127.7, 127.5, 70.9, 64.9, 61.8, 30.9, 21.8, 13.5 ppm; IR (CH_2Cl_2): 1797 s, 1755 s, 1603 s cm^{-1} ; Anal. Calcd for $\text{C}_{25}\text{H}_{23}\text{NO}_5\text{S}$: C, 66.80; H, 5.16; N, 3.12. Found C, 66.93; H, 5.29; N, 3.21.

General procedures for kinetics experiments of alcohol acylation: Experiments were performed at room temperature in 2 mL of solvent where acetic anhydride (9 mmol) was present in ten-fold excess relative to the concentration of benzyl alcohol (0.9 mmol), which was, in turn, large relative to the concentration of cobalt-based catalyst **1a** (0.18 mmol). The background (uncatalyzed) rate was negligible under these conditions. Aliquots (10 μL) were taken at specified time intervals and quenched with ethanol (0.1 mL). The product was quantified by HPLC analysis with 2-chlorotoluene as the internal standard. Under these conditions the reaction was found to follow strictly pseudo-first-order conditions at low substrate conversions (<20 %, rate = $k'[\mathbf{4b}]$ where k' implicitly includes the concentrations of catalyst and anhydride).

Figure 3 (see below) illustrates in representative runs the effect of solvent on the rate of acylation of benzyl alcohol by acetic anhydride at low substrate conversions. The slope of each line represents the phenomenological rate constant k' ($k'_{\text{Tol}} = 0.027 \times 10^{-6} \text{ min}^{-1}\text{M}^2$; $k'_{\text{CH}_3\text{CN}} = 0.02 \times 10^{-6} \text{ min}^{-1}\text{M}^2$; $k'_{\text{THF}} = 0.01 \times 10^{-6} \text{ min}^{-1}\text{M}^2$). As substrate conversion increased (to greater than 25%), downward curvature became noticeable. The relative rate constants were thus determined ($k_{\text{THF}} = 1$; $k_{\text{CH}_3\text{CN}} = 2$; $k_{\text{toluene}} = 2.7$). HPLC retention times (10% i-PrOH/hexanes, 0.8 mL/min): 2-chlorotoluene = 8.6 min, benzyl acetate = 10.4 min, benzyl alcohol = 15.5 min.

Figure 3: Dependence of the rate of reaction on solvent in the acylation of benzyl alcohol using $\text{NaCo}(\text{CO})_4$ as catalyst [Δ Toluene, \square THF, \bullet CH_3CN].



General procedures for kinetics experiments of the catalyzed Staudinger reaction:

For the catalyzed Staudinger reaction, standard solutions of α -imino ester **7**, diphenylketene **8** and catalyst **1d** [$\text{Cp}_2\text{Co}^+\text{Co}(\text{CO})_4^-$] were prepared (e.g. 1 mM scale) in BTF. This experiment was conducted in several different runs employing a varying (e.g. 1:1, 2:1 and 1:2) molar ratio of imine to ketene. The catalyst concentration was kept constant (e.g. 0.2 mM). Aliquots (20 μL) were taken at specified time intervals and quenched with ethanol (0.5 mL). The product was quantified by HPLC analysis with 2-chlorotoluene as the internal standard. Varying the concentration of imine produced no apparent change in rate of reaction from 1-10 mM, whereas varying the concentration of ketene revealed a first-order rate dependence. HPLC retention times (10% EtOH/hexanes, 0.8 mL/min): 2-chlorotoluene = 5.4 min, ethyl diphenylacetate = 7.6 min, β -lactam **10** = 12.4, 13.0 min., α -imino ester **7** = 15.9 min.

- (1) J. J. Brunet, C. Sidot, P. Caubere, *J. Organomet. Chem.* **1980**, *204*, 229.
- (2) T. M. Bockmann, J. K. Kochi, *J. Am. Chem. Soc.* **1989**, *111*, 4669.