(d, 1 H, $J$ = 9 Hz); exact mass calcd for $C_{34}H_{54}O_7Si_2$ 630.3408, found 630.3405.

**4-[3,4-Dihydro-5,7-dimethoxy-6-(3-methyl-2-butenyl)-2*H*-1-benzopyran-3-yl]-1,3-benzenediol (3a).** To 210 mg (0.33 mmol) of **3b** in 10 mL of methanol and 10 mL of THF was added a solution of 0.3 mL of concentrated sulfuric acid in 10 mL of methanol. The mixture was stirred at 20 °C for 2 h and then neutralized with a cold solution of sodium bicarbonate. The mixture was extracted with ethyl acetate, and the combined extracts were dried ($MgSO_4$), filtered, and evaporated in vacuo. The product was purified by preparative TLC (2:1 hexane–EtOAc) to afford 112 mg (90%) of **3a** as an oil: IR (film) 3305, 2910, 1614, 1200, 1119 cm$^{-1}$; $^1$H NMR $\delta$ 1.68 (s, 3 H), 1.78 (s, 3 H), 2.87 (dd, 1 H, $J$ = 11, 16 Hz), 3.03 (ddd, 1 H, $J$ = 2, 6, 16 Hz), 3.31 (d, 2 H, $J$ = 6 Hz), 3.45 (m, 1 H), 3.74 (s, 3 H), 3.78 (s, 3 H), 4.06 (t, 1 H, $J$ = 11 Hz), 4.32 (complex d, 1 H), 5.08 (br s, 1 H), 5.21 (t, 1 H, $J$ = 6 Hz), 5.30 (s, 1 H), 6.28 (s, 1 H), 6.30 (d, 1 H, $J$ = 3 Hz), 6.39 (dd, 1 H, $J$ = 3, 8 Hz), 6.98 (d, 1 H, $J$ = 8 Hz); $R_f$(**3a**) 0.27 (silica gel, 2:1 hexane–EtOAc); exact mass calcd for $C_{22}C_{28}O_5$ 370.1780, found 370.1779.

**2-[3,4-Dihydro-5,7-dimethoxy-6-(3-methyl-2-butenyl)-2*H*-1-benzopyran-3-yl]-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenol (14).** To 100 mg (0.27 mmol) of **3a** in 3 mL of dry dichloromethane at 20 °C were added 78 mg (0.52 mmol) of *tert*-butyldimethylsilyl chloride and 50 $\mu$L of triethylamine. After 20 h, the mixture was flash chromatographed (10 g of silica gel, 2 × 3 cm column, 10% EtOAc–hexane, 5-mL fractions) to afford 60 mg (57% based on recovered **3a**) of **14**, 20 mg of **3a**, and 65 mg of bissilylated product **16**. The desired monosilylated product **14** is a solid: mp 128–133 °C dec (sealed tube); IR ($CCl_4$) 3316, 2919, 1617, 1591, 1509, 1294, 1254, 1201, 1127, 1099, 1055, 994, 846 cm$^{-1}$; $^1$H NMR $\delta$ 0.10 (s, 6 H), 0.99 (s, 9 H), 1.70 (s, 3 H), 1.80 (s, 3 H), 2.84 (dd, 1 H, $J$ = 10, 16 Hz), 3.04 (dd, 1 H, $J$ = 6, 16 Hz), 3.30 (d, 2 H, $J$ = 7 Hz), 3.45 (br m, 1 H), 3.74 (s, 3 H), 3.80 (s, 3 H), 4.06 (t, 1 H, $J$ = 12 Hz), 4.34 (br d, 1 H, $J$ = 10 Hz), 4.96 (s, 1 H), 5.22 (t, 1 H, $J$ = 7 Hz), 6.28 (s, 1 H), 6.32 (d, 1 H, $J$ = 3 Hz), 6.44 (dd, 1 H, $J$ = 3, 8 Hz), 6.99 (d, 1 H, $J$ = 8 Hz); $R_f$(**14**) 0.27, $R_f$(**16**) 0.58 (silica gel, 10% EtOAc–hexane). Anal. Calcd for (**14**) $C_{28}H_{40}O_5Si$: C, 69.38; H, 8.32. Found: C, 69.25; H, 8.24.

**6-[3,4-Dihydro-5,7-dimethoxy-6-(3-methyl-2-butenyl)-2*H*-1-benzopyran-3-yl]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-(3-methyl-2-butenyl)phenol (15).** To 45 mg (0.095 mmol) of **14** in 2 mL of freshly distilled toluene at −78 °C was added 48 $\mu$L (0.12 mmol) of a 2.5 M solution of *n*-butyllithium in hexane. After the mixture was stirred at −78 °C for 15 min, 30 $\mu$L (0.25 mmol) of 2,2-dimethylallyl bromide was added, and the red mixture was allowed to warm to 20 °C. The mixture, protected from light by aluminum foil, was stirred at 20 °C for 18 h. During this time the color was discharged. The solvent was removed in vacuo at 20 °C, and the residue was introduced onto two preparative (1000-$\mu$m) silica gel plates. The plates were eluted with 15% EtOAc–hexane, and the band with an $R_f$ of 0.62 was extracted to afford 22 mg (48% based on 6 mg of recovered **14**) of product as an oil: IR (film) 3406, 2910, 1609, 1583, 1485, 1252, 1200, 1129, 1102, 1050, 910, 842, 783 cm$^{-1}$; $^1$H NMR $\delta$ 0.20 (s, 6 H), 1.0 (s, 9 H), 1.67 (s, 3 H), 1.77 (s, 3 H), 1.78 (s, 3 H), 1.84 (s, 3 H), 2.80 (dd, 1 H, $J$ = 10, 16 Hz), 3.00 (dd, 1 H, $J$ = 5, 16 Hz), 3.29 (d, 2 H, $J$ = 6 Hz), 3.2–3.5 (br m, 1 H), 3.45 (d, 2 H, $J$ = 6 Hz), 3.72 (s, 3 H), 3.77 (s, 3 H), 4.01 (t, 1 H, $J$ = 10 Hz), 4.32 (d, 1 H, $J$ = 8 Hz), 5.21 (m, 2 H), 5.60 (s, 1 H), 6.26 (s, 1 H), 6.42 (d, 1 H, $J$ = 8 Hz), 6.86 (d, 1 H, $J$ = 8 Hz); $R_f$(**15**) 0.45 (silica gel, 10% EtOAc–hexane); exact mass calcd for $C_{33}H_{48}O_5Si$ 552.3271, found 552.3265.

**(±)-5-*O*-Methyllicoricidin (1).** To 9 mg (0.016 mmol) of **15** in 2 mL of dry THF was added 600 $\mu$L of a solution of pyridine–hydrogen fluoride complex in THF.[11] The mixture was stirred under nitrogen at 20 °C for 28 h. The reaction was then quenched with 5 mL of water and extracted with ethyl acetate. The organic extracts were combined, dried ($MgSO_4$), and evaporated in vacuo to afford 9 mg of unpurified product. Preparative TLC (2:1 hexane–EtOAc) afforded 6 mg (85%) of **1**, which was in all respects identical with a sample of the natural product provided by Dr. Lam:[1] IR ($CCl_4$) 3430, 2930, 1612, 1588, 1452, 1201, 1129, 1100, 1063, 1030, 899 cm$^{-1}$; $^1$H NMR $\delta$ 1.68 (s, 3 H), 1.78 (s, 3 H), 1.80 (s, 3 H), 1.86 (s, 3 H), 2.80 (dd, 1 H, $J$ = 10.5, 16.5 Hz), 3.03 (ddd, 1 H, $J$ = 2, 3.5, 16.5 Hz), 3.30 (d, 2 H, $J$ = 7.5 Hz), 3.40 (m, 1 H), 3.46 (d, 2 H, $J$ = 6.5 Hz), 3.72 (s, 3 H), 3.79 (s, 3 H), 4.03 (t, 1 H, $J$ = 10.5 Hz), 4.32 (ddd, 1 H, $J$ = 2, 3.5, 10.5 Hz), 4.86 (s, 1 H), 5.24 (m, 2 H), 5.51 (s, 1 H), 6.26 (s, 1 H), 6.39 (d, 1 H, $J$ = 8 Hz), 6.86 (d, 1 H, $J$ = 8 Hz); $R_f$(1) 0.56 (silica gel, 2:1 hexane–EtOAc); exact mass calcd for $C_{27}H_{34}O_5$ 438.2406, found 438.2403.

**Acknowledgment.** We thank Mrs. Mary Ann Haas for the preparation of the manuscript and Mrs. Deborah Zink for the mass spectral analyses.

(11) Prepared by diluting 1 mL of commercially available (Aldrich) HF–pyridine with 7 mL of THF and 2 mL of dry pyridine.

# Cyanide as an Efficient and Mild Catalyst in the Aminolysis of Esters†

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*Received November 17, 1986*

Cyanide anion was found to be a versatile catalyst in the aminolysis of nonactivated esters. A comparative study on various catalysts, including (dimethylamino)pyridine, 2-hydroxypyridine, imidazole, and sodium cyanide, in the ammonolysis of ethyl (*S*)-1-ethyl-2-pyrrolidinecarboxylate (**1**) in methanol showed sodium cyanide to be the superior catalyst. Furthermore, the reaction was completely stereoconservative; i.e., less than 1% racemization occurred. Cyanide ion also proved to be an efficient catalyst in the transesterification with the solvent. Comparative studies on **1**, ethyl benzoate (**4**), ethyl 3-phenylpropionate (**5**), and ethyl phenoxyacetate (**6**) in aminolysis with ammonia, methylamine, and dimethylamine in methanol showed cyanide to be a general catalyst. The reactivity order for various esters was found to be $MeNH_2 > NH_3 > Me_2NH$.

In connection with a recently developed synthesis of (*S*)-2-(aminomethyl)-1-ethylpyrrolidine from L-proline,[1] we required an efficient stereoconservative[2] conversion of the ethyl ester **1** to the primary amide **2** (eq 1). We report here the finding that cyanide is an efficient, yet mild, catalyst in the aminolysis of aliphatic and aromatic esters with amines in alcoholic solution.

The aminolysis of esters is generally a sluggish reaction unless esters having good leaving groups such as nitro-

† This work was presented at the Swedish Organic Chemistry Meeting, "Organikerdagarna", Stockholm, 1986 (p 71), the French–Swedish Meeting in Selective Organic Synthesis, Lyon, 1986, and the Swedish–Israeli Symposium in New Trends in Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel, 1987.

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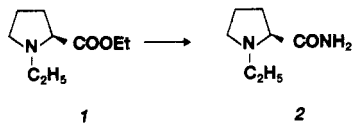
(2) Högberg, T.; Ulff, B. *J. Org. Chem.* **1984**, *49*, 4209–4214.

0022-3263/87/1952-2033$01.50/0 



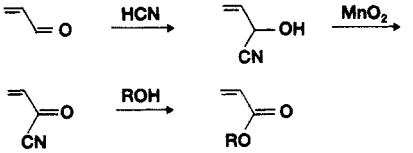

(1)

1 2

phenyl, thiophenyl, vinyl, hydroxylamines, and *N*-hydroxyimides are used.[3] Numerous acidic and basic catalysts have been investigated in order to enable the use of simple alkyl esters.[3] Especially, strongly basic catalysts (sodium amide,[4] sodium hydride,[5] sodium methoxide,[6] Grignard reagents,[7] butyllithium[8]) have been used to promote aminolysis of esters lacking sensitive functionality.

Of greater potential as chemoselective catalysts are 2-hydroxypyridine[9] and sodium 2- or 4-pyridinolate.[10] Carboxylic esters have also been transformed into carboxamides by a one-pot procedure involving saponification prior to coupling in the presence of bis(*o*-nitrophenyl) phenylphosphonate and tetrabutylammonium salts.[11] Other procedures rely upon the high nucleophilicity of aluminum amides. Thus, lithium aluminum hydride–amine complexes[12] and, in particular, dimethylaluminum amides[13] have proved to be useful reagents.

The ammonolysis shown in eq 1 of the ester with ammonia in a methanolic solution is extremely slow at room temperature. When the reaction is carried out at higher temperatures, e.g., in a pressure cylinder, the racemization tends to be a limitation. Likewise, the use of strongly basic catalysts is not compatible with such an epimerizable ester as 1. The requirement of cheap and easily manageable reagents made the use of aluminum amides less attractive. In the search for alternative methods, we noted that acyl cyanides are indicated as intermediates in the cyanide-catalyzed manganese dioxide oxidation of conjugated aldehydes to the corresponding esters (eq 2).[14]




(2)

Acyl cyanides act as mild acylating agents for various heteronucleophiles and carbon nucleophiles.[15] Furthermore, the hydrolysis of ethyl thioacetate is catalyzed by cyanide ion and by hydrogen cyanide.[16] The unique properties of the cyanide ion as a nucleophilic catalyst have also been utilized in other well-known reactions, i.e., the benzoin condensation[17] and the acylation of conjugated double bonds with aldehydes.[18] The facile reaction be-

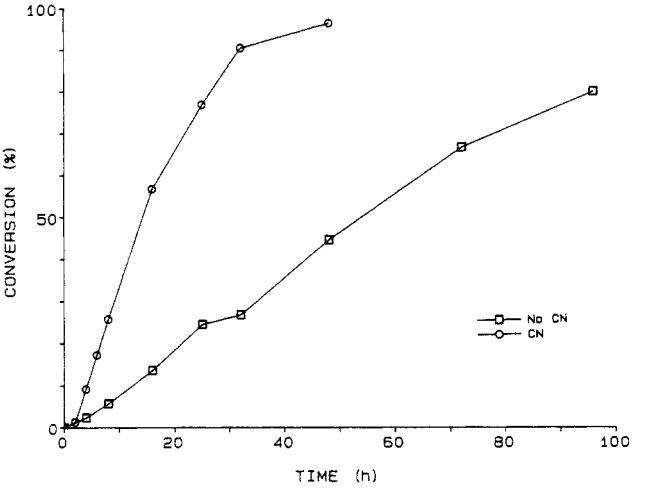



**Figure 1.** Ammonolysis of ethyl (*S*)-1-ethyl-2-pyrrolidinecarboxylate (1; 0.35 M) at 50 °C in 10–11 M methanolic ammonia solution with (○) or without (□) 10 mol % sodium cyanide in capped glass tubes.

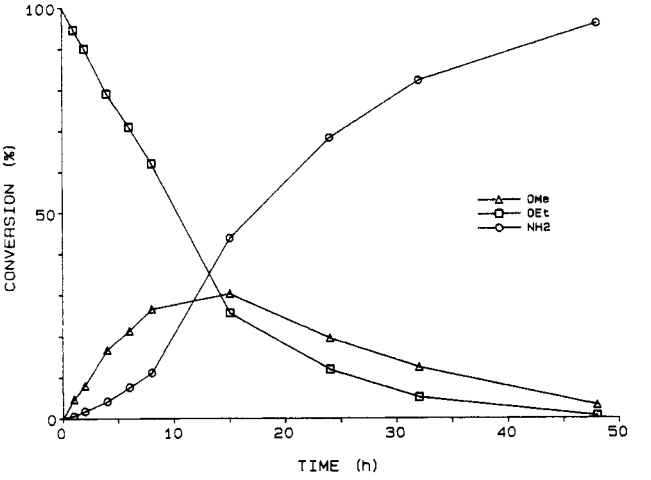



**Figure 2.** Ammonolysis of ethyl (*S*)-1-ethyl-2-pyrrolidinecarboxylate (1; 0.35 M) at 50 °C in 10.7 M ammonia in methanol in the presence of 10 mol % sodium cyanide in capped glass tubes. Key: ethyl ester 1 (□); methyl ester 3 (△); amide 2 (○).

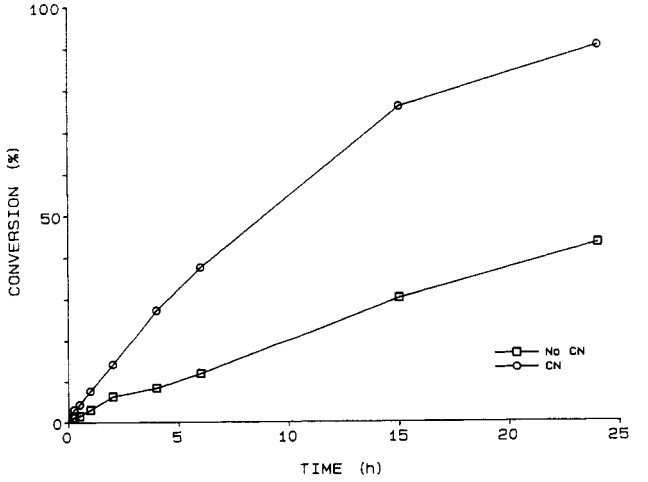



**Figure 3.** Transesterification of ethyl (*S*)-1-ethyl-2-pyrrolidinecarboxylate (1; 0.35 M) in methanol at 50 °C with (○) or without (□) 10 mol % sodium cyanide.

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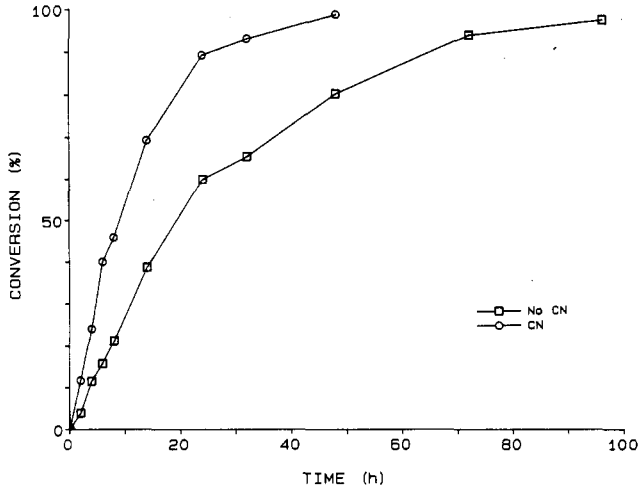
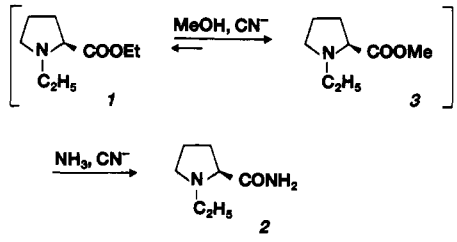



**Figure 4.** Ammonolysis of methyl (*S*)-1-ethyl-2-pyrrolidinecarboxylate (**3**; 0.35 M) at 50 °C in 11–12 M ammonia in methanol with (○) or without (□) 10 mol % sodium cyanide in capped glass tubes.

tween the unstable phthaloylglycyl cyanide and glycine ethyl ester indicated the inherent favorable properties of acyl cyanides in peptide synthesis.[19] Accordingly, we reasoned that cyanide might serve as a strong nucleophile with low basicity to provide the reactive acyl cyanide intermediate in the aminolysis of esters as well (eq 3).

$$\text{R–C(=O)–OR} \rightleftharpoons \text{R–C(=O)–CN} \longrightarrow \text{R–C(=O)–NH}_2 \qquad (3)$$

As can be seen in Figure 1, a considerable acceleration in the ammonolysis of the ethyl ester **1** was caused by the addition of 10 mol % sodium cyanide. A reaction temperature of ca. 50 °C was found to be sufficiently low to suppress the racemization. Transesterification with the solvent methanol took place to a surprisingly large extent during the reaction as shown by GC–MS studies (Figure 2). (Cf. the recently reported selective N-benzoylation of amino alcohols with benzoyl cyanide.[20]) Obviously, the ammonolysis of the ethyl ester **1** proceeds with concomitant formation of the methyl ester **3** followed by attack of ammonia. Both steps are likely to be catalyzed by cyanide. Transesterification of the ethyl ester **1** in methanol (Figure 3) and ammonolysis of the methyl ester **3** in methanolic ammonia (Figure 4) showed that to be the case (eq 4).




(4)

In order to compare the effectiveness of cyanide with other catalysts, we made a series of experiments with ca. 9 M ammonia in methanol at 50 °C (Table I). At this temperature, the racemization is less than the detection limit of 1%. As can be seen, most catalysts, including the promising bifunctional 2-hydroxypyridine[9] and the widely used acylation catalysts imidazole and (dimethylamino)-pyridine (DMAP),[21] gave no acceleration. Acid catalysis

**Table I. Influence of Catalysts on the Ammonolysis of Ethyl (*S*)-1-Ethyl-2-pyrrolidinecarboxylate (1) at 50 °C in ca. 9 M Ammonia in Methanol**

| | conversion,[b] % | | | conversion,[b] % | |
|---|---|---|---|---|---|
| catalyst[a] | 16 h | 38 h | catalyst[a] | 16 h | 38 h |
| no | 12 | 39 | $NH_4Cl$ | 10 | 32 |
| imidazole | 15 | 38 | $Me_2NOH$·HCl | 9 | 22 |
| (dimethylamino)pyridine | 15 | 40 | KI | 21 | 65 |
| 2-hydroxypyridine | 11 | 34 | NaCN | 53 | 97 |

[a] The reactions were carried out in capped glass tubes in the presence of 10 mol % catalyst. [b] The degree of conversion was measured by capillary GLC. The glass tubes were cooled in dry ice/acetone before withdrawing the analytical sample.

in the form of ammonium chloride or *N,N*-dimethylhydroxylammonium chloride even caused a slightly diminished conversion.[22] This observation is consistent with previous findings where ammonium chloride retards the reaction of methyl phenylacetate with ammonia in methanol.[6a] Notably, ammonium salts and amine salts accelerate the reaction between esters and liquid ammonia.[23] However, cyanide and, to a lesser extent, iodide[24] are excellent nucleophilic catalysts in this aminolytic reaction. Also, the reactions of methylamine and dimethylamine with the proline ester **1** in methanol are catalyzed by cyanide (Table II). However, the latter reaction is still too slow to be of preparative value. It should also be noted that methylamine reacts considerably faster than ammonia.

Extended studies revealed that the above observations are valid for the other nonactivated esters ethyl benzoate (**4**) and ethyl 3-phenylpropionate (**5**), as shown in Table II. Also, in these cases a superior reactivity of methylamine was found. The esters investigated showed a marked difference in reactivity with methylamine and dimethylamine, i.e., **5** > **4** > **1**. In order to reveal the influence of an $\alpha$-heterosubstituent, we studied the oxa analogue of **5**, i.e., ethyl phenoxyacetate (**6**). As can be seen in Table II, the ester **6** reacts extremely fast even at room temperature with ammonia in methanol. This fast aminolysis obviously makes the comparison of the influence of cyanide less reliable, but for practical purposes no catalyst is needed anyway. The capability of electronegative $\alpha$-substituents for enhancing the rate of aminolysis has been reported previously.[25]

It can be concluded that cyanide is an effective catalyst in the aminolysis of nonactivated aliphatic and aromatic esters with ammonia and primary and secondary amines. The reactivity order for various esters was found to be

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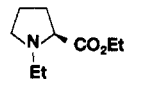
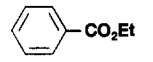
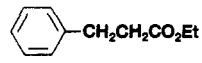
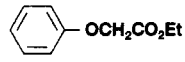
**Table II. Aminolysis of Ethyl Esters with 9–10 M Ammonia, Methylamine, or Dimethylamine in Methanol at 50 °C**

| no. | ester[a] | amine | time,[b] h | conversion,[c] % no | conversion,[c] % NaCN[d] | isol yield,[e] % | characterization of amide[f] |
|---|---|---|---|---|---|---|---|
| 1 |  | $NH_3$ | 38 | 39 | 97 | 72[g,h] | MS (EI) 142 (M)[g] |
| | | $MeNH_2$ | 8.5 | 46 | 88 | 84[j] | MS (CI) 157 (M + 1)[i] |
| | | $Me_2NH$ | 96 | 0 | 8 | | MS (EI) 170 (M)[k] |
| 4 |  | $NH_3$ | 50 | 57 | 79 | 64[h] | mp 126–128 °C (lit.[26] 128 °C) |
| | | $MeNH_2$ | 4 | 24 | 88 | 75[j] | mp 78.5–79 °C (lit.[27] 81.5–82 °C) |
| | | $Me_2NH$ | 117 | 8 | 39 | | mp 38–39 °C (lit.[28] 43 °C) |
| 5 |  | $NH_3$ | 32 | 69 | 91 | 87[h] | mp 99–99.5 °C (lit.[29] 100–101 °C) |
| | | $MeNH_2$ | 1.5 | 49 | 98 | 86[j] | mp 56–57 °C (lit.[30] 59–60 °C) |
| | | $Me_2NH$ | 78 | 52 | 80 | 75[j] | oil,[31] MS (EI) 177 (M) |
| 6 |  | $NH_3$ | 0.25[l] | 62 | 78 | 47[h] | mp 101–102 °C (lit.[32] 101 °C) |

[a] The ester concentration was 0.35 M in all experiments. The reactions were carried out in capped glass tubes. [b] Trial experiments to determine the appropriate reaction times were done prior to the comparative experiments. [c] The degree of conversion was measured by capillary GLC in parallel experiments with and without (no) NaCN. [d] The concentration of NaCN was 10 mol %. [e] Refer to combined cyanide-catalyzed experiments. Purification was by bulb-to-bulb distillation or recrystallization; see the Experimental Section. [f] All compounds had satisfactory $^1H$ NMR and mass spectra. [g] See the Experimental Section for complete procedure. [h] Recrystallization. [i] Data: bp 170 °C (11 mmHg); $[\alpha]_D^{20}$ −140° (c 0.8, $CHCl_3$). Anal. Calcd for $C_8H_{16}N_2O$: C, 61.51; H, 10.32; N, 17.93. Found: C, 61.38; H, 10.26; N, 17.78. [j] Distillation. [k] Not isolated from the reaction mixture. [l] Reaction carried out at room temperature.

$MeNH_2 > NH_3 > Me_2NH$. Cyanide catalysis is especially suited for sensitive substrates like the *N*-ethylproline ester **1**, and it offers a methodology to be tested in the acylation of other nucleophiles under mild conditions.

## Experimental Section

The experiments were conducted in small glass vials with gas-tight caps. The dead volume was minimized by the insertion of a glass rod. The glass vials were immersed in an oil bath at 50 °C. No vial was opened more than twice in connection with an experiment. The vials were cooled in dry ice/acetone before opening in order to minimize loss of ammonia or amine. All comparative experiments in Figures 1–4 and Table II were run simultaneously. GLCs were run on an SE-30 capillary column, and the amounts determined by a Hewlett-Packard 3390 A integrator, assuming identical response factors. $^1H$ NMR spectra were recorded on a Varian EM 360 A or a JEOL FX 200 spectrometer. Mass spectra were obtained on an LKB 9000 (EI/70 eV) or an LKB 2091 (EI/70 eV or CI/$CH_4$) instrument. Optical rotations were measured on an Optical Activity AA-100 polarimeter. Melting points of isolated amides were obtained on a Mettler FP 61 apparatus in open capillary tubes and are uncorrected. Elemental analyses were performed by Analytische Laboratorium, Elbach, West Germany, and are within ±0.4% of the theoretical values.

Esters **1** and **3** were synthesized by N-alkylation of the corresponding proline ester, and **4**–**6** were commercially available or made by conventional Fischer esterification.

Comparative studies on catalysts (Table I) were done with ethyl ester **1** (50 mg, 0.29 mmol) and catalyst (0.03 mmol) in 1.5 mL of ca. 9 M $NH_3$ in MeOH.

Aminolysis of esters **1**, **4**, **5**, and **6** (Table II) was done with 0.8 mmol of ester and 0.08 mmol of NaCN in 2.3 mL of 9–10 M $NH_3$, $MeNH_2$, or $Me_2NH$ in MeOH.

Amides were isolated from combined cyanide-catalyzed experiments. The reaction mixture was treated with brine and extracted with $CH_2Cl_2$, EtOAc, or $Et_2O$. The organic extracts were combined, dried ($MgSO_4$), and evaporated to yield a residue, which was purified by bulb-to-bulb distillation or by recrystallization.

**(−)-(*S*)-1-Ethyl-2-pyrrolidinecarboxamide (2).** A mixture of ethyl (*S*)-1-ethyl-2-pyrrolidinecarboxylate (**1**; 6.00 g, 35 mmol) and NaCN (70 mg, 3.5 mmol) in 100 mL of 9 M ammonia in methanol was heated to 45 °C in a sealed glass flask for 40 h. The solvent was evaporated, and the residue was dissolved in 250 mL of $CH_2Cl_2$ and washed with 100 mL of $H_2O$. The aqueous layer was extracted with 200 mL of $CH_2Cl_2$. The organic phases were combined, dried ($MgSO_4$), and evaporated to give 4.78 g (96%) of amide with 98% purity. Recrystallization from hexane/*i*-$Pr_2O$ (5:1) gave 3.58 g (72%) of the pure title amide: mp 110–111 °C; MS (EI, 70 eV) *m/z* (rel intens) 142 (M, 0.2%), 98 (100%), 70 (21%); $[\alpha]_D^{20}$ −123° (c 0.8, $CHCl_3$). The enantiomeric purity was determined by chromatography on a chiral GLC column (Chirasil-Val, 25 m) and found to be >99% *S* isomer. Anal. Calcd for $C_7H_{14}N_2O$: C, 59.13; H, 9.92; N, 19.70. Found: C, 58.95; H, 9.87; N, 19.58.

# Chiral Building Blocks for Fused Cyclopentanoids: Enantioselective Synthesis of 5-Methylbicyclo[3.3.0]oct-1-ene-3,6-dione and Derivatives

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*Received November 24, 1986*

An efficient enantioselective synthesis of (*R*)- or (*S*)-5-methylbicyclo[3.3.0]oct-1-ene-3,6-dione, a potentially useful chiral building block for natural product synthesis, is described that demonstrates the utility of asymmetric monoreduction of a suitable prochiral dione substrate by bakers' yeast.

Microorganisms might be considered as microscopic reaction vessels containing numerous enzymes complete with cofactors that can potentially react with unnatural substrates and thus provide asymmetric transformations

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