Synthesis of 2-Aminomethyl-1,10-phenanthroline. A new Chelating Agent and Versatile Synthon for other Chelating Compounds

J. F. J. Engbersen*, A. Koudijs, M. H. A. Joosten and H. C. van der Plas*

Laboratory of Organic Chemistry, Agricultural University, De Dreijen 5,
6703 BC Wageningen, The Netherlands

Received November 7, 1985

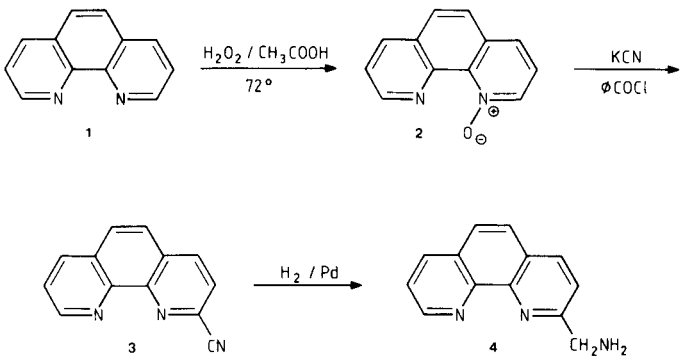
The synthesis of 2-aminomethyl-1,10-phenanthroline (**4**) from 1,10-phenanthroline (**1**) is described. The reduction of 2-cyano-1,10-phenanthroline (**3**) to **4** in the presence of 10% palladium on carbon in acetic acid under mild reaction conditions also proved to be a very efficient method for conversion of cyanopyridines to methylaminopyridines.

J. Heterocyclic Chem., **23**, 989 (1986).

Compounds with a 1,10-phenanthroline ring attract special attention due to their good metal ion complexing properties [1]. Several 1,10-phenanthrolines are used as analytical reagent [2] and a variety of 1,10-phenanthroline metal complexes have found application in organic synthesis. The complexing capability of the 1,10-phenanthroline ring is also encountered in biological model studies in which compounds are designed containing the 1,10-phenanthroline ring in the vicinity of a biomimetic reaction centre, allowing to mimic the role of metalloenzymes [3]. Synthesis of this type of model compounds requires the presence of a functional group on the phenanthroline nucleus being able to couple the biomimetic reaction centre.

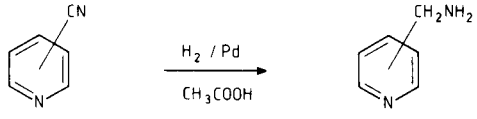
We wish to report in this communication the synthesis of 2-aminomethyl-1,10-phenanthroline (**4**). The presence of an aminomethyl group at the 2-position of the ring considerably increases the capability for metal ion complexation. Moreover, this functionality enables the construction of model compounds in which metal ion complexation is possible. For example, in connection with our interest in the role of metal ion catalysis in NAD(H) model reactions we have introduced at position 2 of **4** a nicotinamide moiety providing us with an NAD(H) model compound capable of intramolecular metal ion catalysis [4]. Compound **4** is prepared from 1,10-phenanthroline (**1**) according to the following route.

Scheme 1



The literature procedure [5] for the synthesis of 1,10-phenanthroline 1-oxide (**2**) from **1** has been slightly modified which results in an improved yield and purity of **2**; consequently also 2-cyano-1,10-phenanthroline (**3**), is obtained in better yield (92%) and higher purity (mp 239-241°). For the reduction of **3** to **4** none of the published methods which have been more or less successfully applied for reduction of a cyano group attached to a pyridine nucleus gave satisfactory results. This is attributed to the ease of reduction of the phenanthroline ring. Thus, reduction of **3** with sodium borohydride [6], lithium aluminium hydride [7], and catalytic hydrogenations in the presence of chromium (II) acetate [8], platinum oxide and Raney nickel [9] gave mixtures of products with a reduced ring system. However, hydrogenation of **3** in acetic acid in the presence of 10% palladium on carbon under very mild reaction conditions (room temperature, 18 psi) was found to be highly successful; **4** was obtained in yields of 90% or higher. No secondary amines were formed. This procedure proved to have a broader scope since 2-, 3-, and 4-cyanopyridine could also successfully be converted into the aminomethyl analogues in yields higher than 90%.

Scheme 2



The method is more advantageous than the other methods for the conversion of cyanopyridines into aminomethylpyridines since mild reaction conditions are required and high yields are obtained.

EXPERIMENTAL

1,10-Phenanthroline 1-Oxide (**2**).

To a solution of 9.4 g (0.05 mole) of 1,10-phenanthroline monohydrate in 60 ml of acetic acid was added 6.0 ml of 30% hydrogen peroxide. The temperature was carefully maintained at 72° for 3 hours after which an additional 6.0 ml of 30% hydrogen peroxide was added. Heating was continued for 3 hours. After cooling 4 ml of 30% hydrogen peroxide was

added and the solution was kept overnight at room temperature. The solution was concentrated *in vacuo* to approximately 25 ml, then 75 ml of water was added and evaporation *in vacuo* was continued to a volume of approximately 25 ml. To the remaining dark-brown oil *ca.* 250 g of solid sodium carbonate was added and the mass was extracted with 7 x 25 ml portions of hot chloroform. The chloroform solution was stirred for 1 hour with decolorizing charcoal and magnesium sulfate. After filtration and evaporation 8.6 g (92%) of **2** was obtained as a white greenish solid, mp 182-185° (lit [5] 180-181°).

2-Aminomethyl-1,10-phenanthroline (**4**).

A solution of 1 g (5 mmole) of **3** (obtained in 92% yield from **2** according to the literature procedure [5]) in 60 ml of acetic acid was hydrogenated at 18 psi at room temperature in the presence of 200 mg of 10% palladium on carbon. After 30 minutes the reaction mixture was filtered over celite and the residue was washed with 3 x 5 ml of hot acetic acid. The solution was evaporated *in vacuo* and the residue was recrystallized from chloroform/ether, yield 1.18 g of the acetate salt of **4**, mp 170-172°; ^{1}H nmr (DMSO-d_6): δ 2.50 (s, 3H, acetate), 4.55 (s, 2H, CH_2), 7.81 (m, 2H, H-3 and H-8), 8.07 (s, 2H, H-5 and H-6), 8.60 (d, 2H, H-4 and H-7), 9.09 (dd, 1H, H-9).

Anal. Calcd. for $C_{13}H_{11}N_3.C_2H_4O_2.H_2O$: C, 62.70; H, 5.96. Found: C, 62.85; H, 5.88.

2-, 3-, and 4-Aminomethylpyridine.

The same procedure as described for the reduction of **3** was applied for the reduction of 2-cyanopyridine, 3-cyanopyridine and 4-cyanopyridine yielding the acetate salts of 2-aminomethylpyridine (**5**, 90%, mp 127°), 3-aminomethylpyridine (**6**, 93%, mp 113°), and 4-aminomethylpyridine (**7**, 94%, mp 95°), respectively.

Anal. Calcd. for $C_6H_8N_2.C_2H_4O_2$: C, 57.13; H, 7.19. Found: **5**, C, 56.87, H, 6.89. **6**, C, 57.23, H, 7.01. **7**, C, 56.84, H, 7.31.

REFERENCES AND NOTES

[1] L. A. Summers, *Adv. Heterocyclic Chem.*, **22**, 1 (1978).

[2] E. D. McKenzie, *Coord. Chem. Rev.*, **6**, 189 (1971), R. D. Gillard, *Coord. Chem. Rev.*, **16**, 67 (1975).

[3] R. Breslow, R. Fairweather and J. Keana, *J. Am. Chem. Soc.*, **89**, 2135 (1967); D. S. Sigman, G. M. Wahl and D. J. Creighton, *Biochemistry*, 2236 (1972); D. J. Creighton, J. Hajdu and D. S. Sigman, *J. Am. Chem. Soc.*, **98**, 4619 (1976), T. H. Fife, T. J. Przystas and V. L. Squillacote, *J. Am. Chem. Soc.*, **101**, 3017 (1979).

[4] J. F. J. Engbersen, A. Koudijs and H. C. van der Plas, to be published.

[5] E. J. Corey, A. L. Borror and T. Foglia, *J. Org. Chem.*, **30**, 288 (1965).

[6] S. E. Ellzey, Jr., J. S. Wittmann III, and W. J. Connick, Jr., *J. Org. Chem.*, **30**, 3945 (1965); S. Yamada and Y. Kikugawa, *Chem. Ind.*, 1325 (1967).

[7] J. H. Boyer, R. Borgers and I. T. Wolford, *J. Am. Chem. Soc.*, **79**, 678 (1957).

[8] R. Graf, *J. Prakt. Chem.*, [2], **140**, 39 (1934); *ibid.*, **146**, 88 (1936).

[9] F. E. Gould, G. S. Johnson and A. F. Ferris, *J. Org. Chem.*, **25**, 1658 (1960); S. Biniecki and Z. Kabzinska, *Acta Pol. Pharm.*, **26**, 277 (1969).