Isomerization of 1a with NaSPh. Method B was used with NaSPh (132 mg, 1.0 mmol) and **1a** (264 mg, 1.0 mmol) in 3.0 mL of CH_3CN for 2 h. The products were identified as 2,3-dimethyl-1,4-naphthoquinone (58 mg, 31%), **2a** (161 mg, 61%), and **1a** (34 mg, 13%).

Isomerization of 1b with NaSEt. Method B was used with NaSEt (67 mg, 0.8 mmol) and **1b** (261 mg, 0.8 mmol) in 3.0 mL of CH_3CN for 45 min. The products were identified as 2,3-dimethyl-1,4-naphthoquinone (6 mg, 4%), **2b** (245 mg, 94%), and **1b** (18 mg, 7%).

Isomerization of 1a with Sodium Methoxide. Sodium methoxide (11 mg, 0.2 mmol) was added to a solution of **1a** (106 mg, 0.4 mmol) in acetonitrile (1.0 mL) in an ice bath under Ar for 1.5 h. The reaction solution was worked up as described in method B. The products were identified as **2a** (92 mg, 87%) and **1a** (16 mg, 15%). When ethanol was used as the solvent at room temperature only **2a** and **1a** were obtained.

Acknowledgment. I am grateful to Frederick G. Bordwell and Mark W. Holladay for helpful discussions.

Registry No. **1a**, 78870-54-9; **1b**, 78870-55-0; **2a**, 78870-56-1; **2b**, 78870-57-2; 2,3-dimethyl-1,4-naphthoquinone 2,3-epoxide, 53948-58-6; 2,3-dimethyl-1,4-naphthoquinone, 2197-57-1.

A Facile Synthesis of *N*-Acyl-2-pyrrolines

George A. Kraus* and Kent Neuenschwander

Department of Chemistry, Iowa State University, Ames, Iowa 50011

Received June 11, 1981

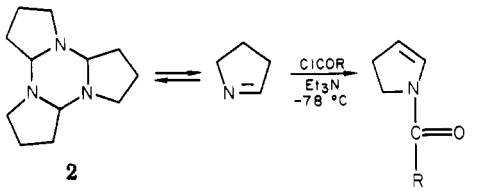
In conjunction with our studies of the amidoalkylation reaction,[1] multigram quantities of *N*-acyl-2-pyrrolines (**1**) were needed. Interestingly, only a few methods for the synthesis of this class of compounds had been reported. Stille and co-workers prepared **1** by a novel transition metal mediated isomerization of *N*-acyl-3-pyrrolines[2] and also cyclized (acylamino)butyraldehydes to produce **1**.[3] Although these methods are excellent for small-scale preparation, large-scale reactions would entail considerable expense. Acylation of 1-pyrroline with an acid chloride or alkyl chloro carbonate would be an attractive route to **1**. This reaction is well-known for acyclic imines.[4] Cushman has recently reported an elegant synthetic use of this reaction.[5] However, 1-pyrroline is unstable and has been little studied.[6] The trimer of 1-pyrroline, **2**, is readily available by oxidation of pyrrolidine with sodium peroxodisulfate and 0.5% silver nitrate[7] and has been used as a synthetic equivalent of 1-pyrroline.[8]

After several unsuccessful attempts to obtain **1** by the reaction of alkyl chloroformates with **2**, we decided to explore the possibility that **2** could dissociate into 1-pyrroline upon heating. Flow pyrolysis at 320 °C followed by reaction with methyl chloroformate afforded modest yields of **1** (R = OCH_3) but was accompanied by much decomposition. Interestingly, Nomura had noted that **2** "decomposed" at 50 °C.[7] This observation prompted us to distill a 0.1 M tetrahydrofuran (THF) solution of freshly prepared **2** into a flask *precooled to −78 °C*. The addition of triethylamine and methyl chloroformate afforded a 77% yield of **1** (R = OCH_3), based on the trimer consumed. Presumably the trimer dissociates in the refluxing tetrahydrofuran solution and 1-pyrroline codistills with the tetrahydrofuran. Trimerization must be slow at −78 °C. The products can be purified by distillation or column chromatography on silica gel. The results of our acylation experiments are given in Table I.

Table I. Preparation of 1

acylating agent	% yield[a] of product	1, R
CH_3OCOCl	78	OCH_3
$EtOCOCl$	79	OEt
CH_3COCl	71	CH_3
$PhCH_2OCOCl$	74	$PhCH_2O$
$ClCH_2COCl$	57	$ClCH_2$
Cl_3CCH_2OCOCl	39	Cl_3CCH_2O

[a] Yield is based on consumed trimer and weight of purified product. Typically 55-60% of the trimer is consumer on a 50-mmol scale.



2 **1**

This method permits the preparation of multigram quantities of **1**. The availability of solutions of 1-pyrroline should assist further investigations into the chemistry of 1-pyrrolines.

Experimental Section

Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. THF was distilled from $LiAlH_4$ prior to usage. Infrared spectra were determined on a Acculab 6 spectrometer. NMR spectra were determined by using either a Hitachi Perkin-Elmer R-20B 60-MHz or a Varian HA-100 100-MHz instrument. ^{13}C NMR spectra were determined on a JEOL FX-90Q Fourier transform spectrometer. Both proton and carbon chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. High-resolution mass spectra were recorded on an AEI MS-902 high-resolution mass spectrometer.

General Procedure. The trimer (10.35 g, 50 mmol, 0.1 M in THF) was distilled through a short-path distillation appartus into a flask cooled to −78 °C. Triethylamine (10.1 g, 100 mmol) was added. The acylating agent (100 mmol) was then added dropwise and the suspension was allowed to warm to ambient temperature overnight. The product that was obtained after filtration and removal of the solvent in vacuo was purified by distillation or column chromatography.

***N*-(Methoxycarbonyl)-2-pyrroline**: bp 77–80 °C (12 mmHg); NMR ($CDCl_3$) δ 2.66 (br t, J = 9 Hz, 2 H), 3.72 (s, 3 H), 3.74 (t, J = 9 Hz, 2 H), 5.14 (m, J = 2, 4 Hz, 1 H), 6.55 (br m, 1 H); ^{13}C NMR ($CDCl_3$) δ 28.1, 44.5, 51.6, 107.6, 128.6, 152.2; IR (film) 1700, 1620 cm^{-1}. High-resolution mass spectrum requires m/e 127.06333, found 127.06346.

***N*-(Ethoxycarbonyl)-2-pyrroline**: NMR ($CDCl_3$) δ 1.28 (t, J = 7 Hz, 3 H), 2.62 (br t, J = 9 Hz, 2 H), 3.77 (br t, J = 9 Hz, 2 H), 4.17 (q, J = 7 Hz, 2 H), 5.00 (m, 1 H), 6.52 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 28.6, 44.8, 66.9, 107.8, 129.2; IR (film) 1700, 1620 cm^{-1}.

***N*-Acetyl-2-pyrroline.** The boiling point is 70 °C at 1 mmHg (Kugelrohr). The spectrum is complicated since **3** exists as a

(1) Kraus, G. A.; Neuenschwander, K. *Tetrahedron Lett.* **1980**, *21*, 3841.
(2) Stille, J. K.; Becker, Y. *J. Org. Chem.* **1980**, *45*, 2139.
(3) Becker, Y.; Eisenstadt, A.; Stille, J. K. *J. Org. Chem.* **1980**, *45*, 2145. A similar transformation has also been reported by Sato: Sata, S. *Nippon Kagaku Zasshi* **1969**, *90*, 404.
(4) Yang, N. C.; Lenz, G. R. *Tetrahedron Lett.* **1967**, 4897. Breederveld, H. *Recl. Trav. Chim. Pays-Bas* **1960**, *79*, 1197.
(5) Cushman, M.; Choong, T.-C.; Valko, J. T.; Kolek, M. P. *J. Org. Chem.* **1980**, *45*, 5067.
(6) Goldschmidt, B. M. *J. Org. Chem.* **1962**, *27*, 4057. Bonnett, R.; Clark, V. M.; Giddy, A.; Todd, A. *J. Chem. Soc.* **1959**, 2087.
(7) Nomura, Y.; Ogawa, K.; Takeuchi, Y.; Tomoda, S. *Chem. Lett.* **1977**, 693.
(8) Petrillo, E. W.; Spitzmiller, E. R. *Tetrahedron Lett.*, **1979**, 4929.

0022-3263/81/1946-4791$01.25/0

rotameric pair:[2] NMR ($CDCl_3$) δ 2.07 and 2.17 (s, 1 H), 2.72 (m, 2 H), 3.87 (t, J = 9 Hz, 2 H), 5.26 (m, 1 H), 6.93 and 6.50 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.1, 21.5, 27.8, 29.6, 44.2, 45.7, 110.1, 111.1, 128.4, 128.9, 165.6; IR (film) 1640, 1610 cm^{-1}. The high-resolution mass spectrum requires m/e 111.06842, found 111.06798.

***N*-[(Benzyloxy)carbonyl]-2-pyrroline**: NMR ($CDCl_3$) δ 2.67 (br t, J = 9 Hz, 2 H), 3.80 (t, J = 9 Hz, 2 H), 5.10 (m, 1 H), 5.19 (s, 2 H), 6.60 (m, 1 H), 7.36 (s, 5 H); ^{13}C NMR ($CDCl_3$) δ 28.6, 45.1, 66.9, 108.6, 128.0, 128.4, 129.1, 136.6; IR (film) 1705, 1620 cm^{-1}.

***N*-(Chloroacetyl)-2-pyrroline.** The spectrum is complicated since **5** exists as a rotameric pair: NMR ($CDCl_3$) δ 2.72 (m, 2 H), 4.04 and 4.10 (s, 2 H), 4.88 (m, 2 H), 5.33 (m, 1 H), 6.65 and 6.85 (m, 1 H); IR (film) 1655, 1615 cm^{-1}.

***N*-[(2,2,2-Trichloroethoxy)carbonyl]-2-pyrroline**: NMR ($CDCl_3$) δ 2.56 (br t, J = 8.5 Hz, 2 H), 3.70 (br t, J = 8.5 Hz, 2 H), 4.60 (s, 2 H), 5.02 (m, 1 H), 6.44 (m, 1 H); IR (film) 1715, 1620 cm^{-1}.

Acknowledgment. We thank Professor T. J. Barton for valuable suggestions. We thank the Alfred P. Sloan Foundation for support of this work.

Registry No. 1 (R = OCH_3), 76460-88-3; 1 (R = OEt), 68471-56-7; 1 (R = CH_3), 23105-58-0; 1 (R = $PhCH_2O$), 68471-57-8; 1 (R = $ClCH_2$), 78964-97-3; 1 (R = Cl_3CH_2O), 78964-98-4; **2**, 5981-17-9.

Synthesis and Atropisomer Separation of Porphyrins Containing Functionalization at the 5,15-Meso Positions: Application to the Synthesis of Binuclear Ligand Systems

Maxwell J. Gunter* and Lewis N. Mander

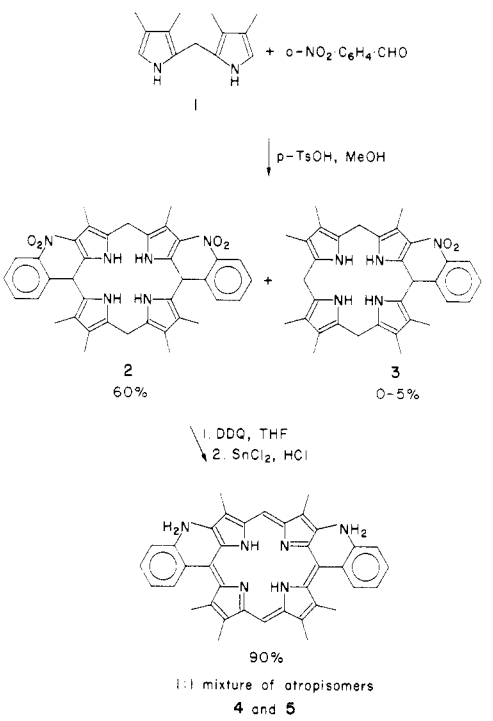
Research School of Chemistry, Australian National University, Canberra, A.C.T. 2600, Australia

Received May 21, 1981

The synthetic model approach has been particularly successful in probing the relationship between structure and function of the active sites of heme-containing proteins.[1] An array of "capped", "strapped", "picket-fence", and other variously described sterically constrained porphyrins has been synthesized, together with porphyrins containing a variety of potentially ligating "tails". Most of the syntheses described are lengthy, low yielding, or allow little convenient variation. More importantly, there are no syntheses described which unambiguously allow facial discrimination, either with regard to attaching a (functionalized) "strap", or to constraining two attached ligand "tails" (either identical or dissimilar) to opposite faces of the porphyrin. We now describe an efficient synthesis of such a system. The utility of this approach is demonstrated by the synthesis of a porphyrin-containing ligand system appropriate for cytochrome *c* oxidase models: an [NS_2] ligand "strap" as a potential binding site for Cu(II) ions is linked across one face of a porphyrin capable of binding Fe. Full experimental details of the ligand synthesis are now presented, and the properties of the Fe/Cu complexes are described elsewhere.[2]

meso-(Ortho-substituted)aryl porphyrins offer an advantage in the synthesis of suitable model systems in that restricted rotation around the meso C–aryl C bond allows the possibility of separation of atropisomers.[3] Additional alkyl substituents on the pyrroles should further enhance stability toward isomerization.[4] Thus, a synthesis of an appropriately disubstituted porphyrin incorporating these concepts was planned and executed as outlined in Scheme I.

Scheme I



The (tetramethyldipyrryl)methane **1** was obtained by standard procedures: ethyl 3,4,5-trimethylpyrrole-2-carboxylate (conveniently prepared in large quantities by either of two[5,6] modifications to the original[7] procedure) was converted via the 2-acetoxymethyl derivative to diethyl 3,3′,4,4′-tetramethyl-2,2′-dipyrrylmethane-5,5′-dicarboxylate;[8] hydrolysis and decarboxylation[9] gave **1**. Condensation of **1** with *o*-nitrobenzaldehyde produced a good yield of the porphyrinogen **2**, together with a variable (0–5%) yield of the monoaryl porphyrinogen **3**, which presumably arises through the well-documented[10] acid-catalyzed rearrangement of the di- or tetrapyrrole intermediates. Variations in reaction time, temperature, catalyst, or solvent generally resulted in either increased yields of **3** at the expense of **2** or, alternatively, mixtures of the corresponding porphyrins were isolated in considerably

(1) For a review, see: J. P. Collman, *Acc. Chem. Res.* **10**, 265 (1977); J. W. Buchler, *Angew. Chem., Int. Ed. Engl.*, **17**, 407 (1978).
(2) M. J. Gunter, L. N. Mander, K. S. Murray, and P. E. Clark, manuscript submitted to *J. Am. Chem. Soc.*
(3) This is the basis of Collman's "picket-fence" [J. P. Collman, R. R. Gagne, C. A. Reed, T. R. Halbert, G. Lang, and W. T. Robinson, *J. Am. Chem. Soc.*, **97**, 427 (1975)], and subsequent "tailed picket-fence" porphyrin synthesis [J. P. Collman, J. I. Brauman, K. M. Doxsee, T. R. Halbert, E. Bunnenberg, R. E. Linder, G. N. LaMar, J. Del Gaudio, G. Lang, and K. Spartalian, *ibid.*, **102**, 4182 (1980)].
(4) The synthesis of other sterically crowded *meso*-aryloctaalkyl porphyrins has been described. B. Evans and K. M. Smith, *Tetrahedron Lett.*, 443 (1977); H. Ogoshi, H,. Sugimoto, T. Nishiguchi, T. Watanabe, Y. Matsuda, and Z. Yoshida, *Chem. Lett.* 29 (1978).
(5) J. B. Paine III in "The Porphyrins", D. Dolphin, Ed., Academic Press, New York, 1979, Vol. 1, Chapter 4, p 107.
(6) C.-B. Wang and C. K. Chang, *Synthesis*, 548 (1979).
(7) E. Bullock, A. W. Johnson, E. Markham, and K. B. Shaw, *J. Chem. Soc.*, 1430 (1958).
(8) A. W. Johnson, I. T. Kay, E. Markham, R. Price, and K. B. Shaw, *J. Chem. Soc.*, 3416 (1959).
(9) P. S. Clezy and A. W. Nichol, *Aust. J. Chem.*, **11**, 1835 (1965). A series of Carius tubes was found more convenient than a stainless steel pressure vessel for the decarboxylation reaction.
(10) J. B. Paine III in "The Porphyrins", D. Dolphin, Ed., Academic Press, New York, 1979, Vol. 1, p 163 et seq.

0022-3263/81/1946-4792$01.25/0