96. Synthesis of 2,2-Dimethyl-1,2-Dihydro-3*H*-pyrrol-3-one

Preliminary Communication

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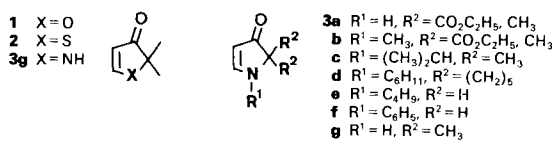
The title compound **3g** is obtained *via* two different routes, either in a multistep synthesis starting from 2-amino-2-methylpropionic acid (methylalanine) or by light-induced, oxidative dealkylation of the corresponding *N*-isopropyl derivative **3c**.

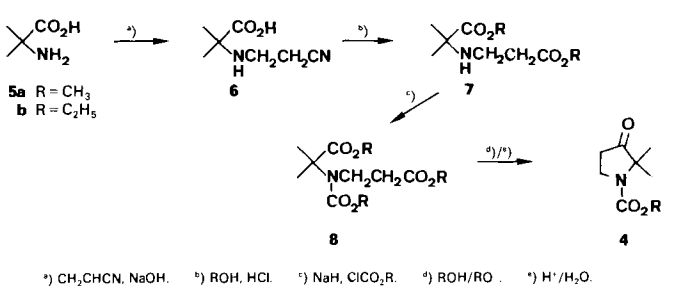
In the course of our investigations on the photochemical behaviour of 5-membered, heterocyclic ketones, we had synthesized the ketonic tautomers of 3-hydroxyfuran and 3-hydroxythiophene, **1** and **2**, respectively [1] [2]. Up to now, compounds **3** containing an



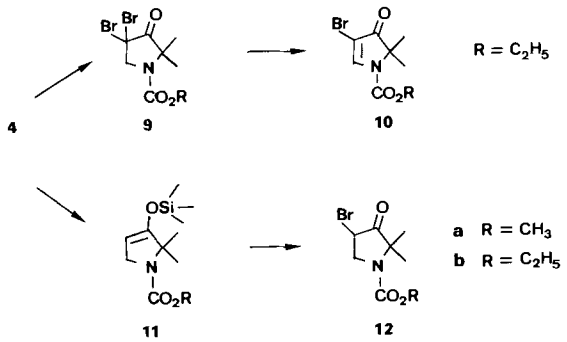
analogously blocked pyrrolinone substructure were either stabilized by an ester group on the sp^3-hybridized C-atom, *e.g.* **3a** [3] and **3b** [4], or they had an alkyl group on the N-atom, *e.g.* **3c** [2] and **3d** [5]. Very recently, the C-unsubstituted compounds **3e** and **3f** have been synthesized and found to be reasonably stable at −20° [6]. We now report the synthesis of the hitherto unknown 4,5-unsubstituted pyrrole **3g** *(Scheme 1)*.

First, we developed a new synthetic approach to the 3-oxopyrrolidine-1-carboxylates 4 [7–9] as potential precursors of **3g**, starting with cheaply available methylalanine (**5**) *via* **6**, **7**, and **8**, in 35% overall yield *(Scheme 1)*.

Scheme 1



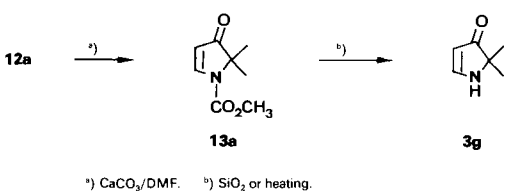
Scheme 2



Bromination of **4** (as described for **4b**) affords the geminal dibromopyrrolidinone **9** exclusively, the intermediate monobromo ketone apparently reacting much faster than **4** itself. Dehydrobromination of **9** gives bromo-enone **10** (80% overall yield). Conversion of **4** to the silyl ether **11** and subsequent bromination affords the desired monobromo-pyrrolidinones **12** in 75–80% yield *(Scheme 2)*.

In contrast to the easy and efficient dehydrobromination sequence **9**→**10**, treatment of **12a** or **12b** with either $LiCl/Li_2CO_3$ or $CaCO_3$ in DMF proceeds less cleanly affording mixtures of **13** and other unidentified products. While the attempted chromatographic purification of **13b** failed due to partial decomposition (the compound was characterized by GC/MS), either chromatography (SiO_2, CH_2Cl_2/MeOH 95:5) or preparative GC of **13a** affords the decarbomethoxylated title compound **3g** in 26% yield *(Scheme 3)*.

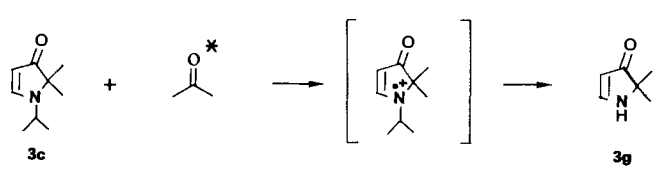
Scheme 3



a) $CaCO_3$/DMF. b) SiO_2 or heating.

A second independent route to **3g** consists in the light-induced oxidative dealkylation [10] of **3c**. Thus, prolonged irradiation (λ = 300 nm) of an acetone solution of **3c** affords **3g** in 45% isolated yield. Although this latter method *(Scheme 4)* seems shorter and more efficient, upscaling becomes difficult due, in part, to the preparation of **3c** (by vacuum flash pyrolysis) and mainly due to the very slow rate of the photoconversion.

Scheme 4



Experimental Part

2-[N-(2'-Cyanoethyl)amino]-2-methylpropionic Acid (**6**). Stirring of equimolar amounts of methylalanine (**5**), acrylonitrile, and NaOH in H_2O for 12 h at r.t. [11] affords **6** in 90% yield, m.p. 213°. MS: 141 ($M^{+\cdot} - 15$), 43 (100).

Methyl 2,2-Dimethyl-3-oxopyrrolidine-1-carboxylate (**4a**). Treatment of **6** with methanolic HCl for 12 h [11] affords **7a** in 65% yield, b.p. 59°–63°/0.01 Torr. MS: 203 ($M^{+\cdot}$), 70 (100). Reaction of **7a** with methyl chloroformate and $NaHCO_3$ in benzene [11] affords **8a** in 85% yield, b.p. 119°–121°/0.01 Torr. MS: 261 ($M^{+\cdot}$), 202 (100). Treatment of **8a** with NaOMe in benzene and subsequent saponification, and decarboxylation of the β-ketoester with oxalic acid [12] affords **4a** in 70% yield, b.p. 85°–90°/0.01 Torr. ^{1}H-NMR ($CDCl_3$): 3.72 (*s*, 3 H); 3.66 (*m*, 2 H); 2.57 (*m*, 2 H); 1.39 (*s*, 6 H). MS: 171 ($M^{+\cdot}$), 66 (100).

Ethyl 2,2-Dimethyl-3-oxopyrrolidine-1-carboxylate (**4b**). Similar procedure as for **4a**, using EtOH, ethyl chloroformate, and NaOEt leads to a 37% yield from **6**, b.p. 200°–202°/14 Torr. MS: 185 ($M^{+\cdot}$), 42 (100%).

Ethyl 4,4-Dibromo-2,2-dimethyl-3-oxopyrrolidine-1-carboxylate (**9**). Treatment of **4b** with Br_2 in CCl_4, evaporation of the solvent, and chromatography (SiO_2, CH_2Cl_2) affords **9** in 91% yield, m.p. 93°. ^{1}H-NMR ($CDCl_3$): 4.41 (*s*, 2 H); 4.25 (*q*, 2 H); 1.68 (*s*, 6 H); 1.35 (*t*, 3 H). MS: 343 ($M^{+\cdot}$), 42 (100).

Ethyl 4-Bromo-2,2-dimethyl-3-oxo-2,3-dihydro-1H-pyrrol-1-carboxylate (**10**). A mixture of 500 mg LiCl, 1.34 g Li_2CO_3, and 3 g **9** were stirred at 95° in 100 ml DMF for 10 h. After cooling to r.t., 20 ml aq. AcOH were added and the mixture extracted with CH_2Cl_2. The org. phase was washed with H_2O and dried ($MgSO_4$). After evaporation of the solvent, chromatography (SiO_2, CH_2Cl_2) afforded 2.6 g (87%) **10**, m.p. 93°. UV (MeCN): 303 (4.05). ^{1}H-NMR ($CDCl_3$): 8.45 (*s*, 1 H); 4.35 (*q*, 2 H); 1.52 (*s*, 6 H); 1.38 (*t*, 3 H). MS: 262 ($M^{+\cdot}$), 29 (100).

Methyl 4-Bromo-2,2-dimethyl-3-oxopyrrolidine-1-carboxylate (**12a**). Treatment of **4a** with LDA and Me_3SiCl in THF at −78° [13] and subsequent bromination of the ether **11a** with Br_2 in CCl_4 affords **12a** (crude product) in 80% yield. ^{1}H-NMR ($CDCl_3$): 4.48 (*dd*, C*H*Br). MS: 250 ($M^{+\cdot}$), 56 (100).

2,2-Dimethyl-1,2-dihydro-3H-pyrrol-3-one (**3g**). a) *From* **12a.** A mixture of 700 mg **12a** and 2.8 g of $CaCO_3$ in 10 ml DMF was kept at 95° under N_2 for 3 h. After filtration and evaporation of the solvent at r.t./1 Torr, chromatography (SiO_2, CH_2Cl_2/MeOH 95:5) afforded 80 mg (25%) of **3g**, m.p. 125°–127°. UV (MeCN): 301 (3.90). ^{1}H-NMR ($CDCl_3$): 7.95 (*t*, *J* = 3.4); 5.49 (NH); 5.16 (*dd*, *J* = 3.4, 1.2); 1.30 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$): 206.7 (*s*); 162.5 (*d*); 96.7 (*d*); 63.7 (*s*); 23.5 (*q*). MS: 111 ($M^{+\cdot}$), 42 (100).

b) *From* **3c.** A degassed soln. of 30 mg ($2 \cdot 10^{-4}$ mol) of **3c** [2] in 5 ml of acetone was irradiated in a *Rayonet RPR-100* photoreactor (300-nm lamps) for 120 h. Evaporation of the solvent and chromatography (SiO_2, CH_2Cl_2/MeOH 95:5) affords 10 mg (45%) of **3g.**

REFERENCES

[1] P. Margaretha, *Tetrahedron Lett.* **1971,** 4871.

[2] E. Anklam, R. Ghaffari-Tabrizi, H. Hombrecher, S. Lau, P. Margaretha, *Helv. Chim. Acta* **1984,** *67,* 1402.

[3] M. Beyer, R. Ghaffari-Tabrizi, M. Jung, P. Margaretha, *Helv. Chim. Acta* **1984,** *67,* 1535.

[4] R. Ghaffari-Tabrizi, P. Margaretha, H. W. Schmalle, *Helv. Chim. Acta* **1984,** *67,* 1957.

[5] H. J. Gordon, J. C. Martin, H. McNab, *J. Chem. Soc., Chem. Commun.* **1983,** 957.

[6] H. McNab, L. C. Monahan, *J. Chem. Soc., Chem. Commun.* **1985,** 213.

[7] R. Kuhn, G. Osswald, *Chem. Ber.* **1956,** *89,* 1423.

[8] G. E. Langford, H. Auksi, J. A. Gosbee, F. N. McLachlan, P. Yates, *Tetrahedron* **1981,** *37,* 1091.

[9] A. G. Schultz, T. H. Fedynyshyn, *Tetrahedron* **1982,** *38,* 1761.

[10] P. Mariano, J. L. Stavinoha, in 'Synthetic Organic Photochemistry', Ed. W. M. Horspool, Plenum Press, New York, 1984, p. 181.

[11] L. L. McKinney, E. H. Uhing, E. A. Setzkorn, J. C. Cowan, *J. Am. Chem. Soc.* **1952,** *74,* 5183.

[12] M. Viscontini, H. Bühler, *Helv. Chim. Acta* **1967,** *52,* 1289.

[13] L. F. Tietze, T. Eicher, in 'Reaktionen und Synthesen im Organisch-Chemischen Praktikum', G. Thieme Verlag, Stuttgart, 1981, p. 384.