HETEROCYCLES. Vol. 9, No. 3, 1978

REACTION OF 4-AZIDO-5-(1-CYANOETHYLIDINE)-1,3-DIMETHYL-2-PYRROLINONE WITH AMINES. A CONVENIENT SYNTHESIS OF 3-AMINOMETHYL-4-AMINO-5-(1-CYANOETHYLIDINE)-1-METHYL-2-PYRROLINONES

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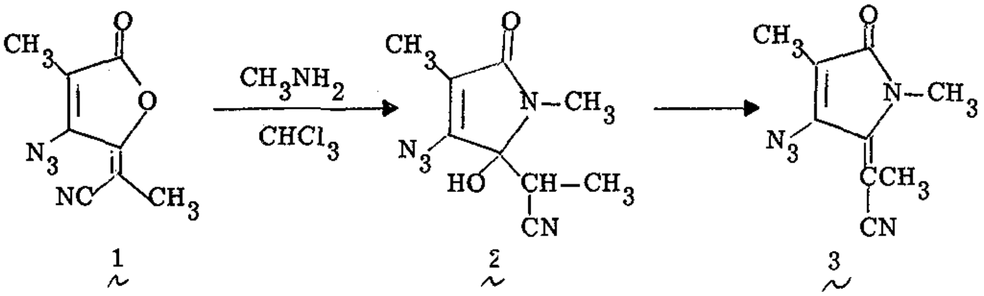
The reaction of 4-azido-5-(1-cyanoethylidine)-1,3-dimethyl-2-pyrrolinone with amines (piperidine, morpholine, pyrrolidine, and aniline) is described. This reaction results in the incorporation of an aminomethyl group at position -3 with concomitant reduction of the azide group to a primary amine, i.e., the formation of 3-aminomethyl-4-amino-5-(1-cyanoethylidine)-2-pyrrolinones, 6a-d.

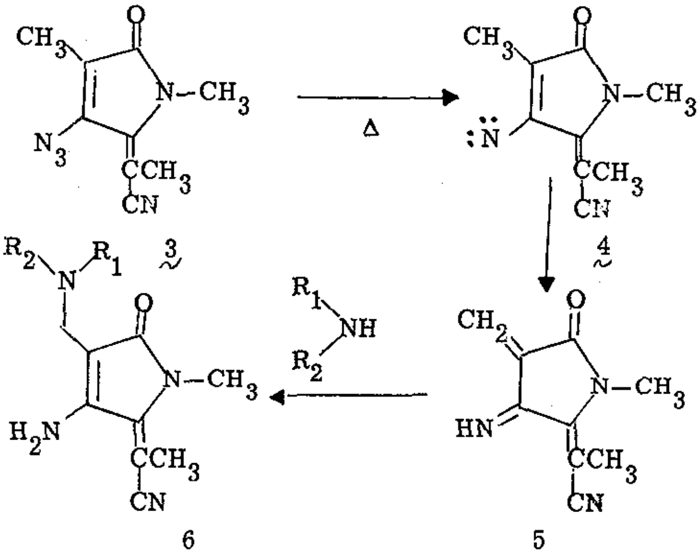
In conjunction with a general synthetic objective of developing new routes to highly substituted 2-pyrrolinones, we report here a unique reaction of 4-azido-5-(1-cyanoethylidine)-1,3-dimethyl-2-pyrrolinone (3) with amines. This reaction results in the incorporation of an aminomethyl group at position -3 with concomitant reduction of the azide moiety to a primary amine, i.e., the formation of 3-aminomethyl-4-amino-5-(1-cyanoethylidine)-1-methyl-2-

pyrrolinone (6a-d). This work was stimulated by the recent report of Yoshina and Kuo[1] who reported an analogous reaction of 7-azido-6-methyl-5,8-quinolindione with secondary amines.

The azidopyrrolinone, 3, was readily prepared from β-azido-γ-cyanoethylidine-α-methyl-$\Delta^{\alpha,\beta}$-butenolide[2] (1) upon treatment with methyl amine to give 4-azido-5-(1-cyanoethyl)-5-hydroxy-1,3-dimethyl-2-pyrrolinone (2): 79%; mp, 128-130 °C (decomp); ir (nujol, cm^{-1}) 3100, 2240, 2105, 1690; pmr ($CDCl_3$, δ) 0.97 d(3) J = 7 Hz, 1.77 s(3), 2.67 s(3), 3.55 q (1) J = 7 Hz, 7.38 s(1)(acidic). Anal. Calcd. for $C_9H_{11}N_5O_2$: C, 48.87; H, 5.01; N, 31.66. Found: C, 48.91; H, 5.56; N, 30.97. Mass: M.W. = 221; observed $M^+ - 28(N_2)$ = 193. Subsequent dehydration of 2 gave the desired azidopyrrolinone, 3, in 53% yield; mp, 100 - 102 °C (decomp); ir (nujol, cm^{-1}) 2200, 2090, 1700, 1605; pmr ($CDCl_3$, δ) 2.12 s(3), 2.33 s(3), 3.42 s(3); Anal. Calcd for $C_9H_9N_5O$: C, 53.20; H, 4.46; N, 34.46; Found: C, 52.44; H, 4.45; N, 34.70. In view of the fact that azidobutenolides such as 1 are readily available from the acid catalyzed rearrangement of 2,5-diazido-1,4-benzoquinones[2,3] and that they can be easily converted to azidopyrrolinones, as outlined here, one can envisage a variety of starting materials of structural type 3.



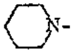
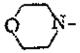
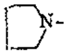
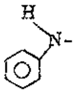
Conversion of **3** to the corresponding 3-aminomethyl derivatives, **6a-d**, was accomplished by slowly adding the azide **3** to a hot chlorobenzene solution (~ 120 °C) containing excess of the amine. The resulting Mannich base-type products, **6a-d**, were then isolated in ~50% yield by recrystallization and/or chromatography on silica gel, and their structures were determined by the spectral properties as provided in Table I. Although the mechanism of this reaction has not been determined, a nitrene intermediate, **4**, is proposed since 4-amino-5-(1-cyanoethylidine)-1,3-dimethyl-2-pyrrolinone was usually detected as a minor product of the reaction.



	Yield	R_1	R_2
6a	49%		
6b	50%		
6c	15%		
6d	59%	H	

TABLE I

Physical and Spectral Properties

	 R_1, R_2	Yield	m.p.	I.R. (nujol, cm^{-1})	pmr (δ ppm)	C^{13} mr (δ ppm)	Analysis	Color
6a		49%	214°- 215.5°C	3375, 3305 (shoulder) 2190, 1715 1665, 1605	in $CDCl_3$ 1.50 (6H, broad, piperidine) 1.67 (3H, S, CH_3) 2.50 (4H, broad, piperidine) 3.30 (2H, S, CH_2) 3.38 (3H, S, NCH_3) 6.33 (2H, broad, NH_2)	in $CDCl_3$ 6.61, 24.39, 26.07 28.07, 53.32, 59.09 83.59, 100.05, 120.91, 150.73, 151.99, 172.31	Calcd: C, 64.59; H, 7.74; N, 21.52 Found: C, 64.69; H, 7.82; N, 21.39	bright yellow
6b		50%	198° - 199 °C	3380, 3330 2190, 1705 1665, 1595	in $CDCl_3$ 1.75 (3H, S, CH_3) 2.47-2.73 (4H, m, morphine) 3.41 (2H, S, CH_2) 3.42 (3H, S, NCH_3) 3.57-3.83 (4H, m, morphine) 6.02 (2H, broad, NH_2)	in $CDCl_3$ 6.21, 27.58, 52.02 58.28, 66.49, 81.87 100.38, 120.18, 149.70, 151.81, 171.61	Calcd: C, 59.53; H, 6.92; N, 21.36 Found: C, 59.66, H, 7.06; N, 21.30	bright yellow
6c		15%	201°- 202°C	3340 (shoulder), 3280 2195, 1690, 1655 1640, 1630, 1590	in $CDCl_3$ 1.40-2.13 (4H, m, pyrrolidine) 1.70 (3H, S, CH_3) 2.20-3.00 (4H, m, pyrrolidine) 3.38 (3H, S, NCH_3) 3.47 (2H, S, CH_2) 6.32 (2H, broad, NH_2)	in $CDCl_3$ 6.29, 23.56, 27.71 52.64, 55.72, 83.97 99.94, 120.45, 150.35, 151.37, 171.99	Calcd: C, 63.39; H, 7.37; N, 22.75 Found: C, 63.47; H, 7.43; N, 22.95	bright yellow
6d		59%	196.5° 198 °C	3330, 3120, 2195 1700, 1660, 1600	in acetone - d_6 1. 68 (3H, S, CH_3) 3.30 (3H, S, NCH_3) 4.17 (2H, Std, CH_2) 5.52 (1H, broad, NH) 6.03 (2H, broad, NH_2) 6.63 - 7.47 (5H, m, aromatic)	in DMSO - d_6 6.46, 27.65, 43.16 86.98, 98.74, 113.18 117.69, 119.28, 129.05, 147.50, 149.09, 150.28, 171.11	Calcd: C, 67.15; H, 6.01; N, 20.88 Found: C, 67.20; H, 6.08; N, 20.82	bright yellow

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3. H. W. Moore, H. R. Shelden, D. W. Deters, and R. J. Wikholm, J. Am. Chem. Soc., **92**, 1675 (1970).
4. The authors wish to thank the National Science Foundation (CHE-06932) for financial support of this work.

Received, 27th December, 1977