Reissert Compound Studies. XXII. A Novel Cyclization[1]

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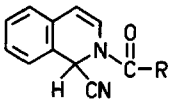
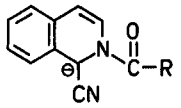
Among the most useful synthetic reactions of Reissert compounds[3] [1-acyl-2-cyano-1,2-dihydroquinolines (N-acyl-1,2-dihydroquinaldonitriles) and 2-acyl-1-cyano-1,2-dihydroisoquinolines (**1**; N-acyl-1,2-dihydroisoquinaldonitriles)] are those carried out in the presence of a strong base. For example, anion **2** has been reported to undergo rearrangement to ketones of the type **3** and alkylation to compounds of the type **4**[3]. Thus, if one dissolves **1** in dimethylformamide and adds sodium hydride **3** is obtained, but if one also adds an alkyl halide **4** is obtained[4].



1



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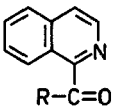

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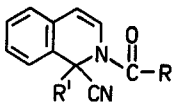
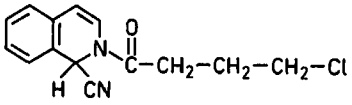
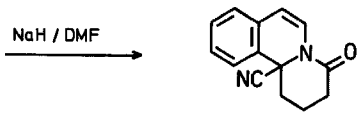


4

In order to study the competition between alkylation and rearrangement, and also in hopes of obtaining a novel cyclic system we have reacted isoquinoline and potassium cyanide with 4-chlorobutanoyl chloride to give the Reissert compound **1** (R = $CH_2CH_2CH_2Cl$). Treatment of **1** (R = $CH_2CH_2CH_2Cl$) with sodium hydride in dimethylformamide led to alkylation and the isolation of the lactam **5**:



1 (R = CH_2-CH_2-CH_2-Cl)



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The effect of chain length in **1**, the reactions of **5** and other aspects of this reaction are being studied.

2-(4-Chlorobutanoyl)-1,2-dihydroisoquinaldonitrile (1, R = $CH_2CH_2CH_2Cl$): To a mixture of isoquinoline (10.33 g, 0.08 mol) in methylene chloride (100 ml) and potassium cyanide (15.62 g, 0.24 mol) in water (40 ml) was added dropwise with stirring 4-chlorobutanoyl chloride (32.4 g, 0.16 mol). The mixture was stirred at room temperature for 7 hr and the phases separated. The aqueous phase was washed with methylene chloride and the combined methylene chloride solutions were washed with 5% hydrochloric acid, 5% aqueous sodium hydroxide,

and water and dried over magnesium sulfate. The solvent was evaporated and the residue recrystallized from ethanol; yield: 8.2 g (38%); m.p. 89–91°.

$C_{14}H_{13}ClN_2O$	calc.	C 64.49	H 5.02	N 10.74
	found	64.34	4.95	10.63

I.R. (KBr): $\nu_{max} = 1670^{-1}$.

4-Oxo-11b-cyano-1,2,3,4-tetrahydro-11b*H*-benzo[a]quinolizine (5): To a solution of **1** (R = $CH_2CH_2CH_2Cl$; 2.6 g, 0.01 mol) in dimethylformamide (40 ml) was added with stirring a suspension of 50% sodium hydride (0.5 g, 0.01 mol) in mineral oil. The mixture was stirred for 1.5 hr, filtered, and the filtrate poured onto ice. The solid product was isolated by filtration and recrystallized from ethanol; yield: 0.7 g (32%); m.p. 126–128°.

I.R. (KBr): $\nu_{max} = 1670\ cm^{-1}$.

N.M.R. ($CDCl_3$): 6.23 δ (d, 1), 2.17–3.10 δ (m, 6), 7.29 δ (m, 5).

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[1] Part XXI, see R. Piccirilli, F.D. Popp, Canad. J. Chem. **47**, 3261 (1969).

[2] National Science Foundation Undergraduate Research Participant.

[3] F.D. Popp, Adv. Heterocyclic Chem. **9**, 1 (1968), for leading references.

[4] F.D. Popp, J.M. Wefer, J. Heterocyclic Chem. **4**, 183 (1967).