**Registry No.**—Ia, 10476-70-7; Ib, 10476-71-8; Ic, 10476-72-9; Id, 10476-73-0; Ie, 10476-74-1; *cis* IIa, 10476-75-2; *trans* IIa, 10476-76-3; *cis* IIb, 10476-77-4; *trans* IIb, 10476-78-5; *cis* IIc, 10476-79-6; VI, 10476-80-9.

**Acknowledgment.**—The author is indebted to the National Science Foundation for partial support of this project from Grant GP 5945.

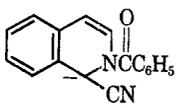
## Reissert Compound Studies. XVI. Reaction of 2-Benzoyl-1,2-dihydroisoquinaldonitrile with Lactones[1]

JOHN M. WEFER[2] AND FRANK D. POPP

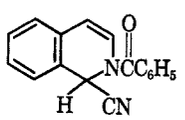
*Department of Chemistry, Clarkson College of Technology, Potsdam, New York*

*Received December 28, 1966*

We have recently reported[1,3] that the Reissert anion (I) can be conveniently generated at room temperature using sodium hydride in dimethylformamide. We now wish to report use of this system in two novel reactions of 2-benzoyl-1,2-dihydroisoquinaldonitrile (II) with β-propiolactone and β-butyrolactone.



I



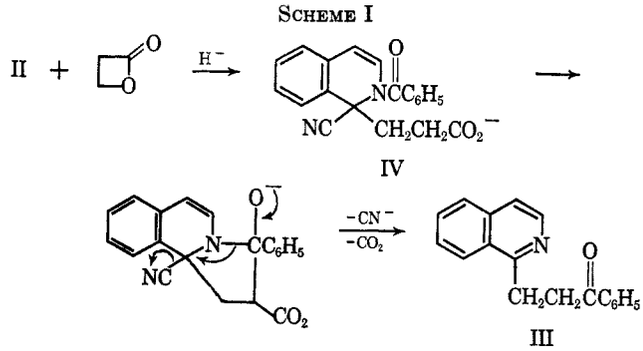
II

Reaction of II with β-propiolactone and sodium hydride in dimethylformamide led to the formation of β-(1-isoquinolyl)ethyl phenyl ketone (III). Formation of III can be rationalized according to Scheme I. Opening of the lactone by I followed by rearrangement of IV and decarboxylation gives rise to III.

The structure of III was confirmed by an alternative synthesis from the anion II and β-bromopropiophenone. This alkylation gave an intermediate corresponding in composition to the enol ester V or diketone VI; alkaline hydrolysis of this substance led to III.

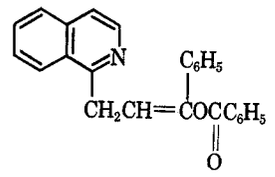
Reaction of II with β-butyrolactone did not produce a simple homolog of III but rather 1-(1-isoquinolinyl)-

SCHEME I

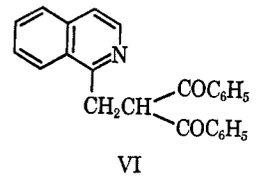


IV

III



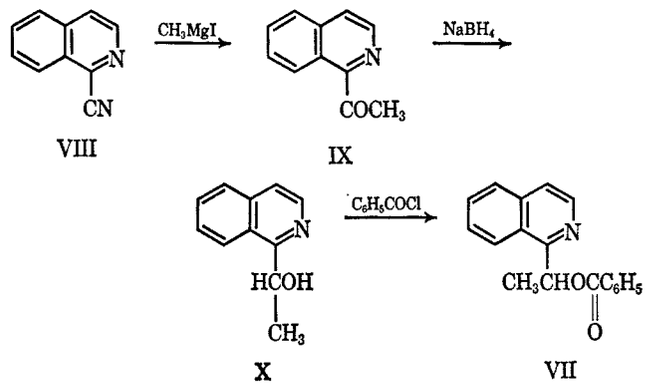
V



VI

ethyl benzoate (VII). The structure of VII was established by unequivocal synthesis according to Scheme II,

SCHEME II



VIII IX X VII

and by low temperature[4] condensation of II with acetaldehyde, which also gave VII.

Any mechanism (analogous to Scheme I) in which the anion I cleaves the lactone ring as a first step toward the formation of VII suffers from the disadvantage that the lactone must be opened in an unusual fashion (*i.e.*, cleavage of a carbon–carbon bond), and that a two-carbon fragment must be eliminated prior to or during the rearrangement step. Since VII was also formed by condensation of II with acetaldehyde and since acetaldehyde could be detected when β-butyrolactone was treated with sodium hydride in dimethylformamide (albeit in low yield), it may be that II actually reacts with acetaldehyde formed *in situ*. The greater steric hindrance to nucleophilic attack by I at the β-carbon of β-butyrolactone relative to β-propiolactone causes the reaction to follow a different pathway, initiated by nucleophilic attack by hydride at the lactone carbonyl, leading to the cleavage into what appear to be two molecules of acetaldehyde. The fact that VII is obtained in much higher yield than is acetaldehyde (in the absence of I) can be accounted for by the immediate reaction of I with acetaldehyde while in the absence of I the acetaldehyde can undergo other base-catalyzed reactions.

Treatment of II with either γ-butyro-, γ-valero-, or γ-decalactone and sodium hydride in dimethylformamide gave only 1-benzoylisoquinoline indicating that five-membered lactones are either too stable to react under these conditions or react too slowly to compete with the rearrangement to the ketone.[1,3]

For purposes of comparison the above reactions were attempted using phenyllithium in ether–dioxane at −20°.[4,5] In all cases tried (β-propio-, β-butyro-, and γ-valerolactone) starting Reissert compound (II) was recovered.

(1) Part XV: F. D. Popp and J. M. Wefer, *J. Heterocyclic Chem.*, in press.

(2) U. S. Public Health Service Predoctoral Fellow (1-F1-GM-25,896) from Institute of General Medical Sciences.

(3) F. D. Popp and J. M. Wefer, *Chem. Commun.*, 207 (1966).

(4) L. R. Walters, N. T. Iyer, and W. E. McEwen, *J. Am. Chem. Soc.*, **80**, 1177 (1958).

(5) V. Boekelheide and J. Weinstock, *ibid.*, **74**, 660 (1952).

### Experimental Section[6]

**Reaction of II with β-Propiolactone (Preparation of III).**—2-Benzoyl-1,2-dihydroisoquinaldonitrile (II) (0.01 mole) and β-propiolactone (0.02 mole) were dissolved in 40 ml of dimethylformamide and 30% sodium hydride in oil (0.01 mole) was added to the stirred solution. After 1.5 hr stirring the mixture was poured onto 500 g of ice and filtered after standing. A solid (mp 104–109°) was obtained and recrystallized from hexane to give a 19% yield of III, mp 111–112° ($\lambda_{KBr}^{max}$ 1730 and 1665 cm$^{-1}$).

*Anal.* Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.47; H, 6.03; N, 5.26.

A picrate (mp 202–204°) from ethanol, was prepared.

*Anal.* Calcd for $C_{24}H_{18}N_4O_8$: C, 58.78; H, 3.70; N, 11.43. Found: C, 58.83; H, 3.81; N, 11.32.

The 2,4-dinitrophenylhydrazone of III was prepared (mp 192–193°) from ethanol–dimethylformamide.

*Anal.* Calcd for $C_{24}H_{19}N_5O_4$: C, 65.30; H, 4.34; N, 15.87. Found: C, 65.42; H, 4.91; N, 15.98.

**Preparation of III.**—Reaction of 0.01 mole of II with 0.01 mole of β-bromopropiophenone and sodium hydride in dimethylformamide as above afforded a gum in 68% yield. Recrystallization from hexane–ethyl acetate gave a good recovery of solid (V or VI), mp 172–172.5° ($\lambda_{KBr}^{max}$ 1740, 1700, 1630, 835 cm$^{-1}$).

*Anal.* Calcd for $C_{25}H_{19}NO_2$: C, 82.17; H, 5.24; N, 3.83. Found: C, 81.80; H, 5.43; N, 3.59.

A picrate (mp 163–164°) from ethanol, was prepared.

*Anal.* Calcd for $C_{31}H_{22}N_4O_9$: C, 62.73; H, 3.57; N, 9.44. Found: C, 62.52; H, 3.58; N, 9.27.

The crude intermediate (V or VI) obtained above (2.0 g) was refluxed for 1.5 hr in 50 ml of 50% ethanol containing 8 g of potassium hydroxide. Dilution with water and filtration gave a white solid (mp 108–109°) in 88% yield. Recrystallization from hexane gave mp 111–112°. This material was identical to compound III as demonstrated by mixture melting point and infrared spectra.

**Reaction of II with β-Butyrolactone (Preparation of VII).**—The reaction was carried out as described above for β-propiolactone on a 0.01 molar scale. A white solid was isolated and recrystallized from hexane–ethyl acetate to give a 50% yield, mp 85–86° ($\lambda_{KBr}^{max}$ 1755 and 1665 cm$^{-1}$).

*Anal.* Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.48; N, 5.05. Found: C, 78.13; H, 5.48; N, 5.08.

A picrate (mp 204–205°) from ethanol, was prepared.

*Anal.* Calcd for $C_{24}H_{18}N_4O_9$: C, 56.92; H, 3.58; N, 11.06. Found: C, 56.88; H, 3.64; N, 11.20.

**1-(1-Isoquinolinyl)ethyl Benzoate (VII).**—To a stirred solution of 0.02 mole of 2-benzenesulfonyl-1,2-dihydroisoquinaldonitrile[7] in 80 ml of dimethylformamide was added 0.02 mole of 30% sodium hydride in oil. After 1 hr the mixture was poured onto 500 g of ice and isoquinaldonitrile (VIII) (80%) (mp 86–88°) was collected. Without further purification VIII was treated with methyl magnesium iodide as reported[8] to give 1-acetylisoquinoline (IX) as a yellow oil in 72% yield ($\lambda_{KBr}^{max}$ 1700 and 1625 cm$^{-1}$). Compound IX (0.0115 mole) was dissolved in 30 ml of methanol and 0.25 g of sodium borohydride was added with stirring. After 0.5 hr the mixture was poured onto ice and extracted with methylene chloride. 1-(1-Isoquinolinyl)ethanol (X) was isolated in 91% yield as an oil from the dried ($Na_2SO_4$) organic phase ($\lambda_{KBr}^{max}$ 3400 and 1630 cm$^{-1}$). The oil (X) (0.0097 mole) was refluxed with 1.8 g (0.0129 mole) of benzoyl chloride in 50 ml of pyridine for 1 hr. After being poured onto ice, 2.61 g (97%) of white solid was collected. Recrystallization from hexane–ethyl acetate gave mp 87–88°. This material was identical with VII prepared from β-butyrolactone as demonstrated by mixture melting point and infrared spectra.

**Condensation of II with Acetaldehyde.**—Acetaldehyde and II were reacted with phenyllithium in ether–dioxane at −20° as reported for other aldehydes.[4] A solid (mp 85–87°) from hexane–ethyl acetate, was isolated in 60% yield. This material was identical with VII as demonstrated by mixture melting point and infrared spectra.

**Treatment of β-Butyrolactone with Sodium Hydride.**—β-Butyrolactone (5 g) in 100 ml of dimethylformamide was treated with 5 g of 30% sodium hydride in oil while a stream of nitrogen was percolated through the mixture and into a reagent solution of 2,4-dinitrophenylhydrazine. In this manner low yields of acetaldehyde–2,4-dinitrophenylhydrazone (mp 144–146°) were obtained. The reaction was accompanied by the generation of considerable heat and polymer formation.

**Registry No.**—II, 844-25-7; III, 10293-89-7; picrate of III, 10293-90-0; 2,4-dinitrophenylhydrazone of III, 10293-91-1; V, 10293-92-2; picrate of V, 10293-93-3; VI, 10293-94-4; picrate of VI, 10293-95-5; VII, 10293-96-6; picrate of VII, 10293-97-7; VIII, 1198-30-7.

(6) All melting points are corrected. Analyses were by Spang Microanalytical Laboratory, Ann Arbor, Mich. We wish to thank the Tennessee Eastman Co. for a sample of β-butyrolactone.

(7) J. M. Wefer, A. Catala, and F. D. Popp, *J. Org. Chem.*, **30**, 3075 (1965).

(8) A. Kaufmann, P. Dandliker, and H. Burkhardt, *Ber.*, **46**, 2929 (9113).

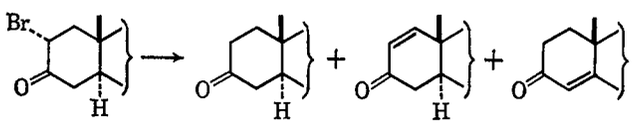
## α-Halo Ketones. IV.[1] Reductive Dehalogenation by Substituted Pyridines

E. W. WARNHOFF AND D. R. MARSHALL[2]

*Department of Chemistry, University of Western Ontario, London, Ontario, Canada*

*Received December 19, 1966*

In part II of this series[3] the reaction of a typical cyclic α-halo ketone, 2α-bromocholestan-3-one (partial structure **1**), with a variety of alkyl-substituted pyridines was examined. It was found that, in addition to dehydrobromination (with and without rearrangement) and displacement, reductive debromination to cholestan-3-one (partial structure **2**) occurred. Accurate analysis for the reduction product was complicated both by the fact that the starting bromo ketone




**1** **2** **3** **4**

was discovered to contain 12% of **2**, and by the analytical method. The difficulty in separating a small amount of **2** from a large amount of **3** made it most convenient to estimate cholestan-3-one as the remainder after $\Delta^1$- and $\Delta^4$-cholesten-3-one (partial structures **3** and **4**) had been determined from tlc spot intensities and ultraviolet measurements.

In a subsequent paper, Nace and Iacona[4] repeated the reaction of γ-collidine with pure **1** from which the contaminating cholestan-3-one had been removed by chromatography on silica gel. A shoulder corresponding to cholestan-3-one was observed in the glpc chromatogram and infrared spectrum of the reaction product, but it was claimed that the saturated ketone amounted to less than 2% of the total product. The authors concluded that "the reduction reaction is not significant in the reaction of bromo ketones with collidine."[4] Although the yields (20–46%) of cholestan-3-one reported in our earlier work[3] were admitted to be subject to cumulative error, it was certain that more than 2% of **2** was produced in the γ-collidine re-

(1) Part III: E. W. Warnhoff, *J. Org. Chem.*, **28**, 887 (1963).

(2) Province of Ontario Graduate Fellow, 1966–1967.

(3) E. W. Warnhoff, *J. Org. Chem.*, **27**, 4587 (1962).

(4) H. R. Nace and R. N. Iacona, *ibid.*, **29**, 3498 (1964).