Reissert Compound Studies. XXIII. Reaction of the Anion with Some Difunctional Compounds (1)

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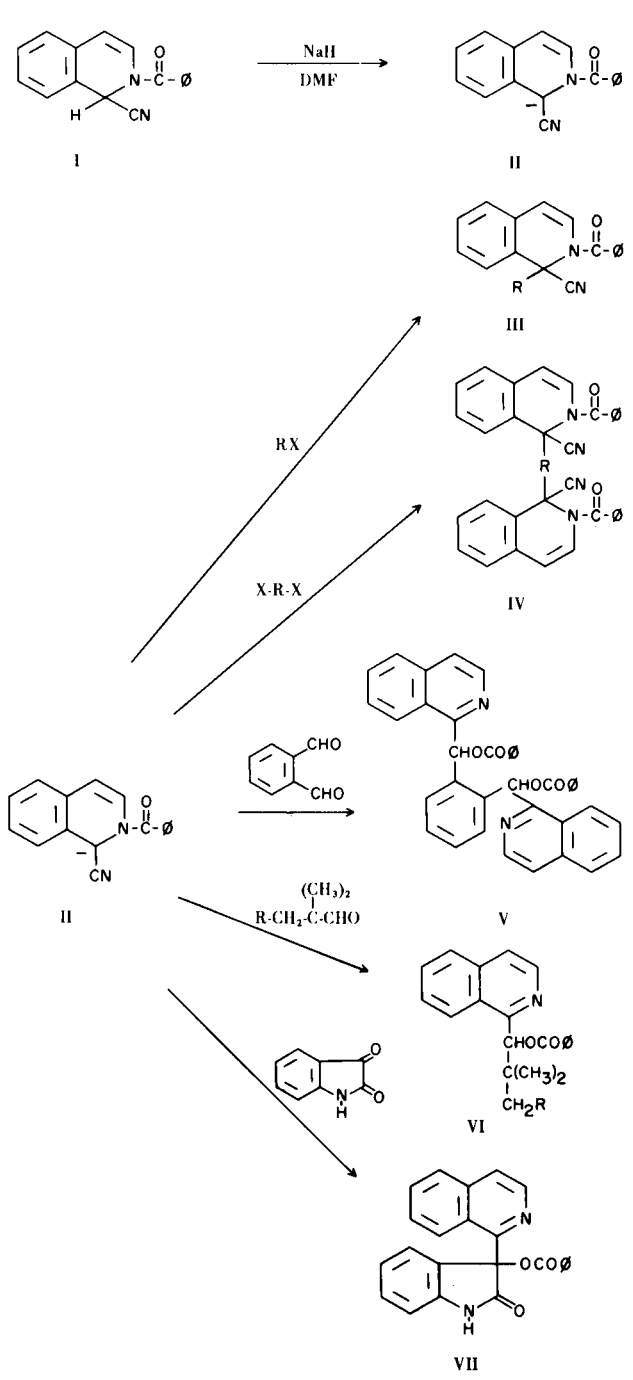
Some of the more interesting and important reactions of Reissert compounds (3) (I) are those undergone by the anion II. As further evidence of the utility of the sodium hydride-dimethylformamide-room temperature method of generation of the anion II (4) we wish to report on the reaction of this anion with a variety of difunctional compounds.

Thus the use of alkyl halides containing amide, imide, and ethylenic substituents gave III while the use of a number of dihalides gave IV. These compounds are indicated in Table I. Reaction of the anion II with *o*-phthalaldehyde gave V while use of 3-(dimethylamino)-2,2-dimethylpropionaldehyde and its methiodide gave VI (R = $(CH_3)_2N$ and $(CH_3)_3N^+I^-$ respectively). VI (R = $(CH_3)_2N$) was converted to VI (R = $(CH_3)_3N^+I^-$) by reaction with methyl iodide. Compound VI (R = $(CH_3)_3N^+I^-$) was the only product isolated from the reaction of II with the quaternary ammonium compound. Several other quaternary ammonium groups also were not displaced by II under the conditions used. Thus the methiodide of *N,N*-dimethylbenzylamine and of *N,N*-dimethylformamide dimethyl acetal gave as the only isolatable products those resulting from rearrangement and elimination of II. The reaction of II with isatin gave VII.

In the course of this work several new Reissert compounds were prepared from isoquinoline and substituted acyl chlorides. These compounds are shown in Table II.



EXPERIMENTAL

All melting points are corrected. Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan.

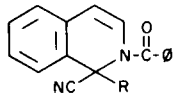
Alkylation Reactions (4).

N-benzoyl-1,2-dihydroisoquinaldonitrile (I) and an equimolar quantity of the alkyl halide (ratio of 2:1 in the case of dihalides) were dissolved in dimethylformamide and an equimolar quantity of 50% sodium hydride in oil was added with stirring. The stirring was continued for 1 to 2 hours and the reaction mixture was poured onto ice. The products (III and IV) thus obtained are included in Table I.

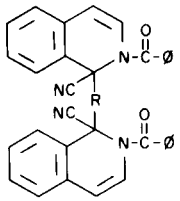
Condensation with *o*-Phthalaldehyde.

In a similar manner 0.02 mole of I and 0.01 mole of *o*-phthalaldehyde in DMF with 0.02 mole of 50% sodium hydride in oil gave a 45% yield of V, m.p. 198-200° from DMF-water; ir (potassium bromide): 1730, 1685 cm^{-1}.

TABLE I



III

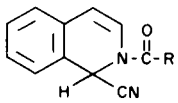


IV

Halide used	Product	Yield	M.P. (a)	*Anal.* Calcd. / Found C	H	N	ir(KBr)	cm^{-1}
N-(2-Bromoethyl)-phthalimide	$C_{27}H_{19}N_3O_3$ (III)	35	204-205	74.81 74.53	4.42 4.44	9.69 10.02	1780 1680	1720 1655
N,*N*-Diethyl-1-chloroacetamide	$C_{23}H_{23}N_3O_2$ (III)	95	137-138 (b)	73.97 73.93	6.21 6.23		1695	1640
Cinnamyl bromide	$C_{26}H_{20}N_2O$ (III)	25	78-80 (c)	82.95 82.78	5.35 5.43		1685	1645
2,3-Bis(bromomethyl)-quinoxaline	$C_{44}H_{30}N_6O_2$ (IV)	63	160-162	78.32 77.99	4.48 4.60	12.46 12.75	1685	1645
1,3-Dibromopropane	$C_{37}H_{28}N_4O_2$ (IV)	95	130-132	79.26 79.06	5.03 5.06		1680	1650
1,4-Dichloro-2-butene	$C_{38}H_{30}N_4O_2$ (IV)	95	217-218 (d)	79.41 79.28	5.26 5.08		1690	1650
α,α′-Dibromo-*o*-xylene	$C_{42}H_{30}N_4O_2$ (IV)	70	216-217 (e)	81.01 80.67	4.86 5.13		1675	1640

(a) Recrystallized from ethanol unless otherwise noted. (b) Recrystallized from ethanol-water. (c) Recrystallized from hexane. (d) Recrystallized from DMF-water. (e) Recrystallized from benzene-hexane.

TABLE II



R	Formula	Yield	M.p. (a)	*Anal.* Calcd. / Found C	H	N	ir(KBr)	cm^{-1}
$ClCH_2CH_2$-	$C_{13}H_{11}ClN_2O$	12	130-131	63.29 63.53	4.49 4.48	11.36 11.48	1680	1635
$ClCH_2CH_2CH_2$-	$C_{14}H_{13}ClN_2O$	39	89-91	64.49 64.34	5.02 4.95	10.75 10.63	1670	1635
$ClCH_2CH_2CH_2CH_2$-	$C_{15}H_{15}ClN_2O$	53	104-106	65.57 65.65	5.50 5.45	10.20 10.30	1670	1630
	$C_{15}H_{10}N_2OS$	99	150-151	67.65 67.48	3.78 3.79	10.52 10.48	1645	1625
$C_6F_5CH_2$	$C_{18}H_9F_5N_2O$	20	166-168	59.35 59.42	2.49 2.66	7.69 7.60	1690	1650

(a) Recrystallized from ethanol.

Anal. Calcd. for $C_{40}H_{28}N_2O_4$: C, 79.98; H, 4.69; N, 4.66. Found: C, 79.93; H, 4.92; N, 4.59.

Esters VI.

In a similar manner 0.005 mole of I and 0.005 mole of 3-(dimethylamino)-2,2-dimethylpropionaldehyde in DMF with 0.005 of 50% sodium hydride in oil gave 28% of VI (R = $(CH_3)_2N$), m.p. 157-158° from ethanol; ir (potassium bromide): 1720, 1625 cm^{-1}.

Anal. Calcd. for $C_{23}H_{26}N_2O_2$: C, 76.21; H, 7.23; N, 7.73. Found: C, 76.32; H, 7.39; N, 7.89.

Use of the methiodide of this aldehyde in this procedure gave a 33% yield of VI (R = $(CH_3)_3N^+I^-$), m.p. 189-190° from ethanol; ir (potassium bromide): 1710, 1640 cm^{-1}.

Anal. Calcd. for $C_{24}H_{29}IN_2O_2$: C, 57.15; H, 5.80; N, 5.56. Found: C, 57.13; H, 5.75; N, 5.57.

Treatment of the first product with methyl iodide gave a compound identical in all respects with the second product.

Reaction of II with Isatin.

In a similar manner 0.01 mole of I and 0.01 mole of isatin in 40 ml. of DMF with 0.01 mole of 50% sodium hydride in oil gave a 61% yield of VII, m.p. 245° from DMF-water; ir (potassium bromide): 3770, 1710 (broad) cm^{-1}.

Anal. Calcd. for $C_{24}H_{16}N_2O_3$: C, 75.78; H, 4.24; N, 7.36. Found: C, 75.61; H, 4.38; N, 7.42.

Preparation of Reissert Compounds.

Reaction of isoquinoline, potassium cyanide, and the appropriate acyl chloride in methylene chloride-water (5) gave the Reissert compounds listed in Table II.

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