J. Chem. Soc. (C), 1966

Reissert Compound Studies. Part XIII.¹ Model Reactions Based on 2-Benzoyl-1,2-dihydroisoquinaldonitrile

By H. W. Gibson and F. D. Popp

Aryl-1-isoquinolylmethyl benzoates prepared from 2-benzoyl-1,2-dihydroisoquinaldonitrile were hydrolysed to aryl-1-isoquinolylmethonols. These alcohols were oxidised to the corresponding ketones and reduced to the corresponding 1-benzylisoguinolines.

SINCE the discovery of the reaction of Reissert compounds with aldehydes by McEwen *et al.*,² this reaction has proved valuable in the synthesis of four alkaloids 3-6 and in synthetic approaches to several other alkaloids.^{7,8} As part of a programme of work designed to demonstrate the general utility of Reissert compounds in alkaloid synthesis, we have studied model reactions based on compounds derived from 2-benzoyl-1,2-dihydroisoquinaldonitrile (I). Earlier we reported the condensation of the lithium salt of (I) with a series of nineteen substituted



benzaldehydes (II) to give the esters (III).9 In the present Paper we report the remainder of our model

- ¹ Part XII, F. D. Popp, H. W. Gibson, and A. C. Noble, J. Org. Chem., 1966, **31**, 2296. ² L. Walters, N. Iyer, and W. E. McEwen, J. Amer. Chem.
- Soc., 1958, 80, 1177.
- ³ F. D. Popp and W. E. McEwen, J. Amer. Chem. Soc., 1957, **79**, 3773.
- ⁴ H. W. Gibson, F. D. Popp, and A. Catala, J. Heterocyclic Chem., 1964, 1, 251.
- ⁵ H. W. Gibson, F. D. Popp, and A. C. Noble, J. Heterocyclic Chem., 1966, 3, 99.

reactions, as well as some others with Reissert compounds.

Further condensation reactions with substituted benzaldehydes (II) and other aldehydes were carried out and the results are given in Table 1.

Sixteen aryl-1-isoquinolylmethyl benzoates (III) reported both previously,9 and in the present Paper, were hydrolysed, in good yield, to the aryl-1-isoquinolylmethanols (IV) by the method of McEwen et $al.^2$ (see Table 2). The attempted hydrolysis of *o*-nitrophenyl-1isoquinolylmethyl benzoate (III; $R^1 = NO_2$, $R^2 = R^3$ $= R^4 = H$), however, gave no product and this reaction is being studied further.

The 1-aroylisoquinolines (V) prepared from the alcohols (IV) by oxidation with sodium dichromate in acetic acid, in generally excellent yield are given in Table 3. Several of these ketones (V) were reduced with sodium borohydride in methanol to regenerate the alcohols (IV) (Table 2).

The Huang-Minlon modification of the Wolff-Kishner reaction was applied to 1-benzoylisoquinoline (V; $R^1 = R^2 = R^3 = R^4 = H$ and 1-(p-benzyloxybenzoyl)isoquinoline (V; $R^1 = R^2 = R^4 = H$, $R^3 = PhCH_2 O^{-1}$) to give the benzylisoquinolines (VI; $R^1 = R^2 = H$) and (VI; R = H, $R' = PhCH_2 \cdot O^{-}$) in yields of 97 and 82%, respectively. 1-(p-Bromobenzoyl)isoquinoline (V; $R^3 = Br$, $R^1 = R^2 = R^4 = H$) under the same conditions, however, underwent complete loss of bromine. It is known¹⁰ that aromatic halogen compounds in the presence of hydrazine and base undergo coupling reactions with loss of halogen, and together with the

⁶ F. D. Popp, H. W. Gibson, and A. C. Noble, J. Org. Chem., 1966, **31**, 2296. ⁷ H. W. Gibson, Ph.D. Dissertation, Clarkson College of

- Technology, 1965. ⁸ F. D. Popp and W. E. McEwen, J. Amer. Chem. Soc., 1958,
- 80, 1181.
- ⁹ F. D. Popp and H. W. Gibson, J. Heterocyclic Chem., 1964, **1**, 51.
- ¹⁰ M. Busch et al., Chem. Ber., 1929, 62, 2612; J. prakt. Chem., 1936, 146, 1; 1940, 155, 163.

evidence of the elemental analysis, it is thought that this product is a dimer of 1-benzylisoquinoline coupled at the 4'-positions.

This loss of bromine together with the apparent cleavage of the methoxy-groups during the Wolff-Kishner reaction of 1-(p-benzyloxybenzoyl)-6,7-dimethoxyisoquinoline⁵ prompted us to seek other routes to

It was possible to remove the benzyl masking group from the benzyloxy-compounds in (IV), (V), and, (VI) by heating under reflux with 15% hydrochloric acid to give the corresponding phenols in excellent yield (see Tables 2-4).

Debenzylation of *p*-benzyloxyphenyl-1-isoquinolylmethanol (IV; $R^1 = R^2 = R^4 = H$, $R^3 = PhCH_2 O^-$)

TABLE 1

Isoquinolylmethyl benzoates

CH(R).O.COPh

	Vield]	Found (%))	Required (%)		
R	(%)	М. р.	c	н	N	Ċ	н	N
4-Ph·CH ₂ ·O·C ₆ H ₄ ⁻	68	151—153° a, b						
$3-PhCH_2 O (p-MeOC_6H_3)$	39	110-112 °	77.9	5.3	2.95	78.3	5.3	2.95
$3-\operatorname{BrC}_{6}\operatorname{H}_{4}^{-}$	48	$165 - 166^{d}$	66·0	3.9	$3 \cdot 5$	66.0	$3 \cdot 9$	3.32
l-Naphthyl-	62	$177 - 178^{d}$	82.8	5.25	$3 \cdot 4$	$83 \cdot 2$	4.9	3.6
1-Furfuryl	57	145-146 ^b	$76 \cdot 1$	$5 \cdot 3$	3.95	76-6	4.5	4.25
PhCH ₂ -	68	132—133 ^b	81.5	$5 \cdot 3$	4.0	81.2	$5 \cdot 4$	4 ·0

^a Previously reported,⁹ yield 40%, m. p. 151—153°. ^b Recrystallised from ethanol. ^c Recrystallised from ethyl acetate-dioxan-hexane. ^d Recrystallised from ethanol-dioxan-water.

TABLE 2

Aryl-1-isoquinolylmethanols (IV)

				Viold		Found (%)			Required (%)		
R'	\mathbf{R}^{2}	R³	\mathbb{R}^4	(%)	М. р.	C	H	N	c	H	N
		HO-		100 ª 76 °	150-151° 5	76 .6	$5 \cdot 5$	$5 \cdot 2$	76.5	$5 \cdot 2$	$5 \cdot 6$
		PhCH, O-		96	$170 - 172^{d}$	80.9	5.7	$4 \cdot 0$	80.9	5.6	4.1
	MeO-	HO-		84 °	$162 - 165^{b}$	72.4	5.45	4.9	72.6	$5 \cdot 4$	5.0
	MeO-	PhCH, O-		100	92—94 °	77.6	5.6	3.7	77.6	5.7	$3 \cdot 8$
	Ph•CH,•O-	MeO-		90	104-106	77.5	5.6	3.7	77.6	5.7	3.8
	Br	PhCH ₃ ·O-		100	g						
	Br-	HO		67 °	178—180 ^b	58.2	3.7	4.1	58.2	3.7	$4 \cdot 2$
	MeO-	PhCH.•O-	\mathbf{Br}	100	g						
PhO·CH	MeO-	-		95	110-111	77.6	5.75	$3 \cdot 9$	77.6	5.7	$3 \cdot 8$
MeO-	MeO-			100	$128 - 130^{f}$	73.1	5.85	4.8	$73 \cdot 2$	5.8	4.7
	MeO-			90	$96 - 97^{f}$	76.85	5.8	4.8	77.0	5.7	5.3
	-0-0	-O-CHO-		94	82-84 f	72.95	4.7	4.9	73.1	4.7	5.0
	Cl	Čl–		100	116-119 h	63.1	3.8	4.45	$63 \cdot 2$	3.65	4.6
				95 j							
		Br-		100	111-1121	61.2	3.9	4.45	$61 \cdot 2$	3.85	4.5
	Br-			100	g						
	Br-	MeO-		100	e g						
				93 j	0						
Br–		MeO-	MeO-	100	103-107 *	58.0	4.5	3.7	57.8	$4 \cdot 3$	3.7
Ben	zo-			80	147-149	84.0	5.05	4.8	84.2	5.3	4.9
		MeO-		79i	97—99 i, f						
				98	106-109 k, t						
NO.				Õ							

 NO_2

^a By hydrolysis of p-benzoyloxyphenyl-1-isoquinolylmethyl benzoate. ^b Recrystallised from hexane-ethyl acetate. ^c By cleavage of benzyl ether. ^d Recrystallised from ethanol-dioxan. ^e Recrystallised from ethanol. ^f Recrystallised from ethanol-water. ^e Product was a gum, used in later reactions without purification. ^h Recrystallised from hexane. ⁱ Prepared from hydroxy-compound by treatment with dimethyl sulphate, reported ² m. p. 97—98°. ^j Yield by sodium borohydride reduction of corresponding ketone. ^k Reported, ² m. p. 108·5—109·5°. ⁱ Picrate, m. p. 157·8—160·2° from ethanol (Found: C, 56·6; H, 3·7; N, 12·3. C₂₂H₁₆N₄O₈ requires C, 56·9; H, 3·5; N, 12·1%).

the compounds (VI). The best route was found to be reduction of the alcohol (IV) with hydrogen bromide and zinc dust in acetic acid. The 1-benzylisoquinolines formed by the various methods are given in Table 4. It should be noted that with the p-benzyloxy-compound, concomitant debenzylation occurred resulting in the isolation of the corresponding phenol.

gave (IV; $R^1 = R^2 = R^4 = H$, $R^3 = OH$) which upon methylation with dimethyl sulphate gave the known² p-methoxy-compound (IV; $R^1 = R^2 = R^4 = H$, $R^3 = OMe_3$). Reduction of p-benzyloxyphenyl-1-iso-quinolylmethanol (IV; $R^1 = R^2 = R^4 = H$, $R^3 =$ PhCH2·O-) with hydrogen bromide and zinc dust gave the benzyl compound (VI; R = H, R' = OH) which

was also obtained by the Wolff-Kishner reduction of 1-(p-benzyloxybenzoyl)isoquinoline (V; $R^1 = R^2 = R^4 =$ H, $R^3 = PhCH_2 \cdot O^{-}$) followed by debenzylation. The melting point of the compound prepared by these two methods did not agree with the reported value for either the compound or its hydrate.¹¹ Treatment of (VI; R = H, R' = OH) with dimethyl sulphate gave 1-(p-methoxybenzyl)isoquinoline (VI; R = H, R' = OMe)

trum, and elemental analysis of the compounds prepared in this work, it is believed that the structural assignments reported here are the correct ones.

During the preparation of 1-benzoylisoquinolines by heating (I) with sodium hydride in xylene, under reflux,¹² the red colour typical of the Reissert anion was observed. The addition of 1 mol. of benzaldehyde to the reaction mixture, gave phenyl-1-isoquinolylmethyl benzoate in

TABLE 3	
1-Aroylisoquinolines	(V)

	R³		Vield		Found (%)			Required (%)		
\mathbb{R}^2		\mathbb{R}^4	(%)	М. р.	C	Ĥ	N	C	H	N
	PhCH.O-		87	$124 - 126^{\circ a}$	81.3	$4 \cdot 8$	$4 \cdot 1$	81.4	5.05	4.1
	HO-		73 0	204-205 °	77.2	$4 \cdot 5$	5.5	77.1	4.45	5.6
MeO-	PhCH, O-		97	$165 - 166^{d}$	77.8	$5 \cdot 2$	3.75	78.0	$5 \cdot 2$	$3 \cdot 8$
MeO-	HO-		97 5	187—189 <i>°</i>	73.0	4.6	$5 \cdot 1$	$73 \cdot 1$	4.7	$5 \cdot 0$
Ph·CH.·O-	MeO-		75	193194 d,f	60.1	$3 \cdot 8$	9.3	60.2	3.7	9.4
Br-	PhCH, O-		69	146—147 °	65.75	$3 \cdot 8$	3.3	66.0	3.9	3.35
MeO-	PhCH.O-	Br-	75	121 - 123 a	64.3	$4 \cdot 0$	$2 \cdot 9$	64.3	4.05	$3 \cdot 1$
MeO-	-		93	150—151 ^{d, f}	60·1	$3 \cdot 8$	9.2	60.2	3.7	9.4
MeO-			91	90-91 9	73.7	$5 \cdot 1$	4.7	73.7	$5 \cdot 2$	4.8
MeO-			64	159-161 ^{d, f}	55.9	$3 \cdot 5$	11.45	56.1	3.3	11.4
-0-0	CHO-		89	136-138 ¢	73.65	4.1	4.8	73.6	4.0	5.05
Cl-	Ĉl−		89	131—132 ª	63.4	2.95	4.6	63.6	3.0	4.6
	Br-		86	100-101 *	61.5	$3 \cdot 2$	4.5	61.6	$3 \cdot 2$	$4 \cdot 5$
Br-			74	115—116 ª	61.6	$3 \cdot 2$	4.4	61.6	$3 \cdot 2$	4.5
Br	MeO-		100	133-134 9	59.8	3.7	4 ·0	59.7	3.5	4·1
	MeO-	MeO-	100	115-116 °	$58 \cdot 1$	$3 \cdot 8$	$3 \cdot 7$	58.1	3.8	$3 \cdot 8$
	R ² MeO- Ph·CH ₂ ·O- Br- MeO- MeO- MeO- MeO- Cl- Br- Br-	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

^a Recrystallised from hexane. ^b By cleavage of the benzyl ether. ^c Recrystallised from ethanol-hexane. ^d Recrystallised from ethanol-water. Ketone was a gum or oil, m. p. and analysis for picrate. ^e Recrystallised from hexane-ethyl acetate.

TABLE 4

1-Benzylisoquinoline (VI)

		Vield]	Found (%)	Required (%)		
\mathbf{R}	R'	(%)	M. p.	c	H	N	c	H	N
	PhCH ₂ •O-	97 a 82 a	$178 - 180^{\circ b - a}$ $120 - 121^{\circ, e}$	84·8	5.9	4.25	84.9	$5 \cdot 9$	$4 \cdot 3$
	Br– HO–	100 ª 75 Ø	$166-167^{b, c, j}$ $177-179^{i, j}$	$\frac{58.9}{81.6}$	$3.7 \\ 5.7$	$12\cdot 3$ $5\cdot 9$	81.7	$5 \cdot 6$	6 ·0
_	MeO-	83 * 100 *	169-170 ^{b, c, l}	57.6	4.0	11.5	57.7	3.8	11.7
Br–	MeO-	80 ^h	$178 - 179^{b, c, m}$	49.4	$3 \cdot 5$	9.8	49·6	3.1	10.02

^a By Wolff-Kishner method. ^b Compound an oil or gum, m. p. and analysis for picrate. ^c Recrystallised from ethanol. ^d Reported m. p. 181–182°. ^e Picrate, m. p. 158–159° ^e (Found: C, 62·7; H, 4·05; N, 10·3. C₂₉H₂₂N₄O₈ requires C, 62·8; H, 4·0; N, 10·1%). ^f Found: Br, 0·0; it is believed that this is a dimer of 1-benzylisoquinoline coupled at the 4'-positions (dimer bispicrate requires (C₄₄H₃₀N₈O₁₄) (C, 59·1; H, 3·4; N, 12·5). ^g By cleavage of the benzyl ether. ^h By hydrogen bromide-zinc dust method. ⁱ Recrystallised from ethyl acetate. ^j Reported ¹¹ m. p. 235–237°. ^k By methylation of R' = OH. Reported ¹¹ m. p. 190°. ^m Found: Br, 14·3 requires Br, 14·3.

whose picrate had a melting point not in agreement with the reported value.¹¹ Since the intermediate alcohol



was successfully converted to the known p-methoxyphenyl-1-isoquinolylmethanol, and in view of the synthetic route, and the evidence of the infrared spec19% yield, demonstrating that the anion postulated in the alkylations of Reissert compounds was an intermediate in the rearrangement. It was found that this anion could also be formed in toluene, benzene, and tetrahydrofuran heated under reflux, but not in petroleum ether-dioxan. In benzene, addition of benzaldehyde gave a 79% yield of (IV; $R^1 = R^2 = R^3 = R^4$ = H) compared to 88% ² by the less convenient phenyllithium method. Other variables were investigated and the optimum conditions are given in the Experimental section.

In the course of this study some effort was directed

¹¹ M. Ikehara, Pharm. Bull. Japan, 1955, **3**, 294.

¹² V. Boekelheide and J. Weinstock, J. Amer. Chem. Soc., 1952, **74**, 660.

towards the preparation of various analogues of Reissert compounds. Although an attempt to prepare (VII; $R = NO_2$, $R' = PhCH_2 O^-$) by treatment of the benzyl bromide salt of isoquinoline with potassium cyanide in aqueous solution was unsuccessful, a compound whose elemental analysis corresponded to (VII; R = CN, R' = PhCH₂-) was formed in nearly quantitative yield. The corresponding ethyl iodide salt gave a red oil, presumably (VII; R = CN, R' = Et). Two analogues of these compounds, 2-(3,4- and 2,3-dimethoxybenzyl)-6,7-dimethoxy-1,2-dihydroisoquinaldonitriles, have been reported 13 although no attempt has been made to employ them as Reissert compounds. Treatment of the benzyl bromide salt of isoquinoline with potassium thiocyanate in aqueous solution gave a nearly quantitative yield of low-melting oily solid believed to have been (VII; R = CNS, $R' = PhCH_2^{-}$).

Treatment of either the cyano- or thiocyano-compounds of the benzyl series (VII; R = CN or CNS, $R' = Ph CH_2^-$) with ethanolic picric acid resulted in the formation of a compound whose elemental analysis was consistent with an empirical formula $C_{22}H_{16}N_4O_7$ in which the cyano- or thiocyano-groups had been eliminated. The evolution of hydrogen cyanide was noted with the cyano-compound. Similarly, the ethyl compound (VII; R = CN, R' = Et) when treated with ethanolic picric acid gave hydrogen cyanide and a product of empirical formula $C_{17}H_{14}N_4O_7$. These compounds are identical with 2-benzylisoquinolinium picrate and 2-ethylisoquinolinium picrate, respectively.

Compounds of the type (VII; $R = CN, R' = PhCH_2$ -) appear not to behave as typical Reissert compounds since treatment with phenyl-lithium or sodium hydride failed to give an anion as is typically obtained from Reissert compounds.



6,7-Dimethoxy-3,4-dihydroisoquinoline was treated with benzoyl chloride and potassium cyanide to give an 18% yield of a compound thought to be 2-benzoyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinaldonitrile (VIII).

EXPERIMENTAL

Aryl-1-isoquinolylmethyl Benzoates (III).—To a solution of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) (2.00 g., 0.0077 mole) in anhydrous ether (45 ml.) and dioxan (15 ml.) at -30° was added a solution of phenyl-lithium (0.0077 mole) in ether under a nitrogen atmosphere. To the resultant deep red mixture there was added a solution of the aldehyde (0.0077 mole) in ether and/or dioxan. The mixture was stirred under a nitrogen atmosphere at a temperature of less than -20° for 1 hr., and then allowed to warm slowly to room temperature. After a total of 5—12 hr. stirring, the mixture was washed with water, 0.5M-hydrochloric acid, and water. After removal of the solvents *in vacuo*, the product (Table 1) was obtained by trituration of the residue with an appropriate solvent.

Aryl-1-isoquinolylmethanols (IV).—A solution of the benzoate (III) (0.5 g.), potassium hydroxide (3.0 g.), water (25 ml.), and ethanol (50 ml.) was heated under reflux for 5—24 hr. Most of the ethanol was removed in vacuo and the mixture diluted with water. Filtration or ether extraction gave the alcohols (Table 2).

1-Aroylisoquinolines (V).—To a solution of the alcohol (IV) (0.002 mole) in glacial acetic acid (10 ml.) was added sodium dichromate (0.66 g., 0.0022 mole) in glacial acetic acid (5 ml.). The mixture was heated on a steam-bath for a few minutes, diluted with an equal volume of water, and basified with ammonium hydroxide. Filtration, or chloroform extraction, gave the ketones (Table 3).

Sodium Borohydride Reduction of 1-Aroylisoquinolines.— To a solution or suspension of (V) in methanol was added a slight excess of sodium borohydride. After stirring for 0.5 hr., the mixture was poured on to crushed ice and the product was isolated by filtration or extraction. The compounds prepared in this manner are given in Table 2.

Wolff-Kishner Reduction of 1-Aroylisoquinolines.—A solution of (V) (0.002 mole) and 95 + % hydrazine (4.55 ml.) in triethylene glycol (20 ml.) was heated under reflux for 2 hr. and the water and the excess of hydrazine then removed. The mixture was heated to 220° and potassium hydroxide (0.75 g.) was added a pellet at a time. After the reaction had subsided, heating under reflux was continued for 1 hr. and the mixture then cooled and poured on to ice. Filtration, or ether extraction, gave the products (Table 4).

Hydrobromic Acid-Zinc Dust Reduction of Aryl-1-isoquinolylmethanols.—Hydrogen bromide was bubbled through a solution of the alcohol (IV) in 10—20 times its own weight of glacial acetic acid for about 20 min. The mixture was set aside overnight and then treated with an eleven-fold excess of zinc dust with stirring during a period of 30 min. After heating on the steam-bath for 20—30 min., the mixture was filtered, diluted with water, basified with ammonium hydroxide, and either extracted with chloroform, or filtered to give the 1-benzylisoquinolines (Table 4).

Cleavage of Benzyl Ethers.—A solution of the benzyl ether (0.001 mole) and 15% hydrochloric acid (10 ml.) was heated under reflux for 30 min., diluted with water, and washed with chloroform. Ammonium hydroxide was then added until the turbidity of the mixture appeared to be greatest. The product (Tables 2—4) was then isolated by filtration or chloroform extraction.

Methylation of p-Hydroxyphenyl-1-isoquinolylmethanol and 1-(p-hydroxybenzyl)isoquinoline.—To a mixture of the phenol (0.00159 mole) and sodium hydroxide (0.004 mole) in water (8 ml.) was added dimethyl sulphate (0.2 ml.) and the mixture heated under reflux for 1 hr. After cooling, extraction with ether yielded the two compounds given in Tables 2 and 4.

Sodium Hydride Method for the Condensation of 2-Benzoyl-1,2-dihydroisoquinaldonitrile with Benzaldehyde.—To a solution of the Reissert compound (I) (1.3 g., 0.005 mole) in benzene (25 ml.) heated under reflux, was added sodium hydride (0.54 g., 0.01 mole) (50% in mineral oil). After 3 min., benzaldehyde (0.5 ml., 0.005 mole) was added. Heating under reflux was continued for 2 hr. and then the

¹³ R. D. Haworth and W. H. Perkin, jun., J. Chem. Soc., 1925, 1434; R. D. Haworth, W. H. Perkin, jun., and J. Rankin, *ibid.*, p. 1444.

J. Chem. Soc. (C), 1966

mixture was filtered, washed with water, 0.5M-hydrochloric acid, and water. Evaporation and trituration of the residue with cold ether gave phenyl-1-isoquinolylmethyl benzoate (1.28 g., 79%), m. p. 164—166° (lit.,² m. p. 166.6—167.6°.

2-Benzyl-1,2-dihydroisoquinaldonitrile (VII).—The quaternary salt resulting from isoquinoline (12·9 g., 0·100 mole) and benzyl bromide (17·1 g., 0·100 mole) on mixing, was washed with ether and dissolved in water (125 ml.). To the solution was added potassium cyanide (13·0 g., 0·200 mole) in water (40 ml.) over 0·75 hr. and the mixture was stirred for a further 0·75 hr. The solid was filtered off and washed with water to give the *product* (24·2 g., 98%), m. p. 81·5—83° (ether) (Found: C, 82·8; H, 5·6. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·7%).

On treatment of this compound with ethanolic picric acid, hydrogen cyanide was evolved to give a yellow solid, m. p. 179—181° (ethanol) (Found: C, 59.0; H, 3.6; N, 12.5. $C_{22}H_{16}N_4O_7$ requires C, 58.9; H, 3.6; N, 12.5). Infrared spectroscopy and an undepressed mixed m. p. with an authentic specimen of 2-benzylisoquinolinium picrate showed that the two compounds were identical.

2-Benzyl-1-thiocyano-1,2-dihydroisoquinoline.—This compound was prepared, in quantitative yield, by substituting potassium thiocyanate for potassium cyanide in the above procedure; it was a low melting solid which could not be

14 F. D. Popp and W. Blount. Chem. and Ind., 1961, 550.

recrystallised. When treated with ethanolic picric acid a compound, m. p. $178-180^{\circ}$, was obtained which was identical with the picrate obtained above.

2-Ethyl-1,2-dihydroisoquinaldonitrile.—The quaternary salt obtained from isoquinoline and ethyl iodide was treated with potassium cyanide, as described above, to give a quantitative yield of oil. Treatment of this oil with ethanolic picric acid resulted in the evolution of hydrogen cyanide and the formation of a yellow compound, m. p. 181·5—183° (ethanol) (Found: C, 52·9; H, 3·7; N, 14·7. Calc. for $C_{17}H_{14}N_4O_7$: C, 52·85; H, 3·65; N, 14·5%). A mixed m. p. with 2-ethylisoquinolinium picrate was not depressed.

2-Benzoyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinaldo-

nitrile (VIII).—Reaction of 6,7-dimethoxy-3,4-dihydroisoquinoline, potassium cyanide, and benzoyl chloride by the methylene dichloride-water method ¹⁴ gave the title compound (96%), m. p. 78—86°. Recrystallisation from ethanol afforded an 18% yield, m. p. 212—213° (Found: C, 70·8; H, 5·7; N, 8·5. $C_{19}H_{18}N_2O_3$ requires C, 70·8; H, 5·6; N, 8·7).

H. W. G. acknowledges receipt of a N.D.E.A. Fellowship.

DEPARTMENT OF CHEMISTRY,

CLARKSON COLLEGE OF TECHNOLOGY,

POTSDAM, NEW YORK 13676,

U.S.A. [6/526 Received, May 2nd, 1966]