6-Chloro-2-dimethylamino-4-phenylquinoline (5), Prepared from 2,6-Dichloro-4-phenylquinoline.—The dichloroquinoline was prepared according to the procedure of Drukker and Judd.[12] A mixture of 13 g (47.5 mmol) of 2,6-dichloro-4-phenylquinoline, 100 ml of 25% dimethylamine in water, and 50 ml of ethanol was heated in a Parr bomb at 100–110° for 18 hr. After the solution was concentrated to a small volume, the residue was recrystallized from methanol to yield 12.1 g (90%) of **5** as pale yellow needles, mp 98–100°. The spectral data were identical with those for the compound obtained from the rearrangement of **2**.

Anal. Calcd for $C_{17}H_{15}ClN_2$: C, 72.21; H, 5.35; N, 9.91. Found: C, 72.24; H, 5.50; N, 9.55.

Registry No.—**2**, 3693-14-9; **3**, 35337-03-2; **4**, 35337-04-3; **5**, 31576-98-4; **6**, 35337-06-5; **6** HBr, 35337-07-6; **7**, 35337-08-7; **8**, 35337-09-8; **9**, 24139-18-2.

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Reactions of Epimeric 2,2′-Diacetyl-1,1′,2,2′-tetrahydro-1,1′-biisoquinolines

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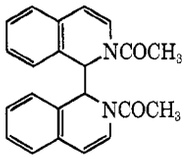
The title compounds are brominated by NBS to yield epimeric 2,2′-diacetyl-4,4′-dibromo-1,1′,2,2′-tetrahydro-1,1′-biisoquinolines rather than 1,1′-dibromo derivatives as reported previously. Cleavage of the 1,1′ bond characterizes attempts to aromatize these compounds by oxidative methods; *e.g.*, the dibromo derivatives are converted to 4-bromoisoquinoline in 90% yield by 5.3 *N* nitric acid at 30°. *dl*- and *meso*-4,4′-dibenzal-1,1′,4,4′-tetrahydro-1,1′-biisoquinolines are recovered in low yields when the title compounds are heated in ethanol with benzaldehyde and concentrated hydrochloric acid; extensive cleavage of the 1,1′ bond again occurs with the formation of 4-benzal-1,4- (and 3,4-) dihydroisoquinoline. 5,5′-Dinitro- and 5-nitro-1,1′-biisoquinoline are described.

Previously it was reported[1] that both epimers of 2,2′-diacetyl-1,1′,2,2′-tetrahydro-1,1′-biisoquinoline (**1a,b**)

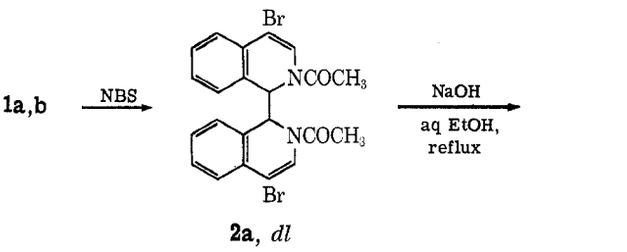


1a, *dl*
b, meso

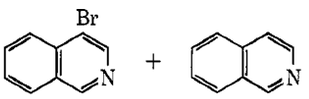
(prepared by the Dimroth reaction from isoquinoline, zinc, and acetic anhydride) and *N*-bromosuccinimide reacted in acetic acid to give epimeric dibromo compounds, $C_{22}H_{18}Br_2N_2O_2$. Alkaline hydrolysis of the latter gave mixtures of isoquinoline and a bromoisoquinoline (approximately equimolar). Based in part on the melting point of the bromoisoquinoline recovered by preparative glc, this compound was considered to be the 1-bromo isomer; the dibromo compounds were then considered to be epimeric 2,2′-diacetyl-1,1′-dibromo-1,1′,2,2′-tetrahydro-1,1′-biisoquinolines.

Subsequent work (mixture melting points, comparison of ir spectra, ^{1}H nmr) has shown that this bromoisoquinoline is actually the 4 isomer. Consequently, the dibromo compounds are reformulated as 2,2′-diacetyl-4,4′-dibromo-1,1′,2,2′-tetrahydro-1,1′-biisoquinolines (**2a,b**). This assignment is confirmed by the proton nmr spectrum[2] on the lower melting, more-soluble, *dl* isomer, **2a**.

Cleavage of the 1,1′ bond with formation of a mixture of isoquinoline and 4-bromoisoquinoline is also observed



2a, *dl*
b, meso



when **2a** and **2b** are oxidized by refluxing nitrobenzene. On the other hand, oxidation of **2a** with 5.3 *N* nitric acid at 30° gives 4-bromoisoquinoline in 90% yield.

Aromatization of **2a** without cleavage of the 1,1′ bond so as to recover 4,4′-dibromo-1,1′-biisoquinoline was attempted by the procedure of Knabe.[3] The latter had demonstrated that laudanosine could be oxidized to *N*-methylpapaverinium and *N*-methyl-3,4-dihydropapaverinium salts by mercuric acetate and disodium ethylenediaminetetracetate in aqueous acetic acid; other oxidation conditions had caused cleavage at the 1-methylene bond. However, even after prolonged heating at 80–85° only partial oxidation of **2a** had occurred; small amounts (<15%) of impure 4-bromoisoquinoline were isolated, suggesting that cleavage was still the preferred route.

The conversion of **1a,b** directly to 1,1′-biisoquinoline or derivatives has been further investigated beyond the results reported previously.[1] Extensive cleavage of the 1,1′ bond again characterizes most of the reactions.

(1) A. T. Nielsen, *J. Org. Chem.*, **35**, 2498 (1970).

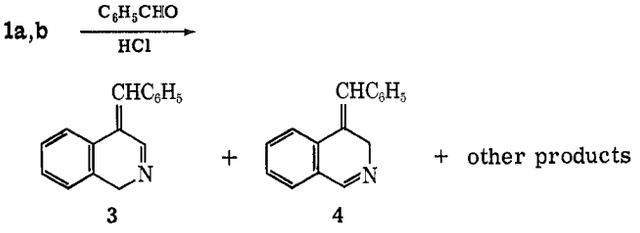
(2) ^{1}H nmr for *dl*-2,2′-diacetyl-4,4′-dibromo-1,1′,2,2′-tetrahydro-1,1′-biisoquinoline: τ ($CDCl_3$) 2.42 (dd, 1, J = 7.5, 1.5 Hz, H_5), 2.69 (td, 1, J = 7.5, 1.5 Hz, H_6), 2.94 (s, 1, H_3), 3.15 (td, 1, J = 7.5, 1.5 Hz, H_7), 4.02 (dd, 1, J = 7.5, 1.5 Hz, H_8), 4.15 (s, 1, H_1), 7.83 (s, 3, $COCH_3$).

(3) J. Knabe, *Arch. Pharm. (Weinheim)*, **292**, 416 (1959).

For example, isoquinoline (IQ) is formed from **1a** at room temperature with chloranil in aqueous acetic acid, with activated manganese dioxide in acetonitrile, and with cupric chloride in acetonitrile (the 1:1 complex, $CuCl_2$–IQ, precipitates). Oxidation of **1b** with either 5.3 *N* or 8 *N* nitric acid proceeds rapidly and exothermically at room temperature; isoquinoline is recovered in 90–95% yield. Nitration of **1a** in concentrated sulfuric acid at 3–7° furnishes 5-nitro- and 4,6-dinitroisoquinoline. Under the same conditions of nitration, 1,1′-biisoquinoline was converted to 5,5′-dinitro- and 5′-nitro-1,1′-biisoquinoline (73 and 21%, respectively).

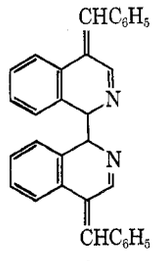
3,3′-Biisoquinoline was isolated in low yield from **1b** by refluxing in nitrobenzene with 10% palladium/charcoal catalyst; the principal product was isoquinoline. In the absence of Pd/C, no biisoquinoline was formed. It has been suggested by Carey and Sasse[4] that 3,3′-biisoquinoline is formed with 1,1′- and 1,3′-biisoquinolines when isoquinoline is heated with rhodium/carbon catalyst.

Since there is substantial evidence[5,6] that 1,2-dihydroisoquinolines are intermediates in the synthesis of 4-benzylisoquinolines from benzylaminoacetaldehyde dialkyl acetals, aromatic aldehyde and acid, the reaction of the 1,2-dihydroisoquinoline derivatives, **1a,b**, with benzaldehyde and hydrochloric acid was examined. A variety of products were formed; the principal one, which again arose from a cleavage of the 1,1′ bond, was a mixture (based on the nmr spectrum) of **3** and **4**.



3 **4**

Similar isomers have been found previously in this type of reaction.[6] More importantly, two other high-melting isomers were recovered in low yield; their molecular weights and mass spectral behavior indicated that they were derivatives of 1,1′-biisoquinoline. Because the ^1H nmr spectra showed methine but no benzyl methylene protons, the compounds are considered to be epimers **5a,b**. Other compounds, including some isoquinoline,



5a,b

were also isolated in low yield as their picrates, but were not characterized by nmr.

Experimental Section

Oxidation of 2a,b with Nitrobenzene. A.—The meso isomer (**2b**)[1] (4.0 g) was refluxed for 3 hr with 40 ml of nitrobenzene; the poorly soluble amide gradually dissolved to give a yellow solution which turned red, then dark brown. The cooled solution after dilution with 50 ml of 95% ethanol and 200 ml of diethyl ether was extracted with one 80 ml and one 25 ml portion of 3 *N* hydrochloric acid. The combined acid solutions were reextracted with 100 ml of fresh ether (discarded), made basic, and extracted with three 70-ml portions of ether. After drying over anhydrous potassium carbonate, the ether solution was evaporated to leave 2.5 g of red liquid. An analytical glc showed 12.0, 41.6, and 42.7 mol %, respectively, of nitrobenzene, isoquinoline, and 4-bromoisoquinoline (samples of the last two compounds, isolated by preparative glc, had ir spectra identical with those of authentic specimens): ^1H nmr for 4-bromoisoquinoline τ ($CDCl_3$) 0.85 (s, 1, H_1), 1.28 (s, 1, H_3), 1.7–2.5 (m, 4, H_5, H_6, H_7, H_8).

B.—A similar experiment with the *dl* isomer (**2a**) gave 2.66 g of product which contained 27.5 and 66.2 mol %, respectively, of isoquinoline and 4-bromoisoquinoline.

Oxidation of 2a with Nitric Acid.—**2a**[1] (1.5 g) was added with stirring to 30 ml of 5.3 *N* nitric acid at 29°. The temperature rose during 5 min to 31° and held for about 15 min; some oxides of nitrogen were evolved. Stirring was continued at 29° for 3.5 hr. Although the solid never dissolved completely, its character changed. After diluting with 10 ml of water and cooling to −15°, the solid was filtered, washed twice with 2–3 ml of cold water and dried, 1.36 g (84%). [From the mother liquors and washings after basification there was recovered 0.07 g (5.6%) of solid, mp 40–41°, whose ir spectrum was identical with that of 4-bromoisoquinoline.] Recrystallization of a small portion from dilute nitric acid gave felted, flat needles of 4-bromoisoquinolinium nitrate, mp 172–173° dec.

Anal. Calcd for $C_9H_7BrN_2O_3$: Br, 29.48; N, 10.34. Found: Br, 29.44; N, 10.28.

The balance of the salt in a minimum of cold water was made basic; white plates, mp 42–43°, separated upon cooling. Again the ir spectrum was identical with that for 4-bromoisoquinoline; mixture melting point was undepressed.

Oxidation of 1b with Nitrobenzene. A. Without Catalyst.—Refluxing 1.6 g of **1b**[1] with 15 ml of nitrobenzene under nitrogen for 3 hr followed by isolation of basic material in a conventional manner gave 1.13 g (95%) of isoquinoline (ir spectrum same as that of an authentic sample).

When the above reaction was attempted at 120–125° for 8 hr, under nitrogen and with stirring, the starting amide was recovered quantitatively.

B. With Catalyst.—A slurry of 2.0 g of **1b**, 1.0 g of 10% Pd/C, and 20 ml of nitrobenzene was flushed well with dry nitrogen, then stirred and heated at 120–130° for 3.5 hr. The cooled solution was diluted with 50 ml of benzene, filtered, and extracted with 50 ml of 2.4 *N* hydrochloric acid, followed by 25 ml of water. The combined aqueous extracts were reextracted once with benzene, made basic with concentrated ammonium hydroxide, and chilled overnight at 5°. The solid which separated was filtered, washed with water and dried, 0.4 g (27%). After two recrystallizations from cyclohexane–benzene (6:4) the melting point was 198–199°; the ir spectrum was the same as that for authentic 3,3′-biisoquinoline,[7] mp 197–198°.

Anal. Calcd for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72; N, 10.93; mol wt, 256. Found: C, 84.51; H, 4.71; N, 10.87; mol wt (vpo), 250.

From the basic aqueous mother liquors remaining after removal of the above solid product, there was isolated through ether extraction 0.91 g (61%) of isoquinoline (ir spectrum) and a few crystals of acetanilide, mp 113–116° (ir spectrum).

Formation of the 3,3′-biisoquinoline in this catalyzed oxidation was not reproducible; in many experiments only a trace or none of this compound was found. Cleavage to isoquinoline was consistently 65–70% under these same conditions; at 100–102° the yield of isoquinoline was only 9% after 6 hr; at 130–140° after 4 hr, it was 85%.

(4) J. C. Carey and W. H. F. Sasse, *Aust. J. Chem.*, **21**, 207 (1968). Compare, however, H. Rapoport, R. Iwamoto, and J. R. Tretter, *J. Org. Chem.*, **25**, 372 (1960), who reported that no biaryl was formed by catalytic dehydrogenation when isoquinoline was refluxed for 24 hr with 5% Pd/C.

(5) J. M. Bobbitt, D. P. Winter, and J. M. Kiely, *ibid.*, **30**, 2459 (1965), and references therein.

(6) D. W. Brown, S. F. Dyke, and M. Sainbury, *Tetrahedron*, **25**, 101 (1969); S. F. Dyke, M. Sainbury, D. W. Brown, M. N. Palfreyman, and D. W. Wiggins, *ibid.*, **27**, 281 (1971).

(7) F. H. Case, *J. Org. Chem.*, **17**, 471 (1952).

Oxidation of 1b with Nitric Acid.—The meso epimer **1b** (1.2 g) was slurried with 30 ml of 5.3 *N* nitric acid at 24°. Within 5 min the temperature had increased to 27° and oxides of nitrogen were being evolved. After 10 more min all of the solid had dissolved (temperature 26°). After standing overnight at 25°, the solution was cooled and made basic with concentrated ammonium hydroxide. Isoquinoline (0.85 g, 93%) separated as a pale yellow oil; the ir spectrum was identical with that for authentic isoquinoline.

With 8 *N* nitric the reaction was more rapid and exothermic; the yield of isoquinoline was 95%.

Nitration of 1a.—Compound **1a**[1] (3.44 g; 0.01 mol) was added during 5 min to 30 ml of 96% sulfuric acid at 10–15°. To the resulting slurry was added with stirring 4.5 g (0.044 mol) of powdered potassium nitrate over 1.75 hr while maintaining a temperature of 3–7°. The acetyl compound gradually dissolved, and the color changed from pale orange to dark amber; some frothing occurred. After 1 hr at 5°, the solution was poured over 100 g of ice and made basic with cold, concentrated ammonium hydroxide. The yellow solid was filtered, washed well with cold water and dried, 3.55 g, mp 100–130° (dec).

The crude product was separated into a poorly soluble fraction (1.5 g; mp 165–175°) and a soluble fraction by boiling with 100 ml of 95% ethanol and cooling to 5°. Recrystallization of the former from ethanol gave rosettes melting at 182–183°. The analyses and molecular weight indicate a dinitroisoquinoline.[8] The ^{1}H nmr spectrum is consistent with that required for **4,6-dinitroisoquinoline.** This structure was established unequivocally through use of the Eu(fod)$_3$ shift reagent[9] in $CDCl_3$. As expected, the singlet signals assigned to H_1 and H_3 showed the greatest downfield shift and were broadened. The protons on the benzo ring became well resolved: the signals assigned to H_8 shifted the most, since this proton is closest to the heteroatom, and showed only the splitting expected for ortho coupling (9 Hz); H_5 showed splitting due to meta coupling (2 Hz), whereas H_7, which was shifted the least, appeared as a doublet of doublets (both ortho and meta splitting). If this compound had been the 4,7 isomer, the H_8 signal would have again been shifted further downfield than those for the two other benzo protons but would have shown only meta splitting. Signals appeared at τ (Polysol-*d*[10]) 1.32 (6-line multiplet, 2, J_{78} = 9 Hz, J_{57} = 2 Hz, H_7 and H_8), 0.73 (m, 1, J_{57} = 2 Hz plus another 1 Hz splitting, H_5), 0.63 (s, 1, H_1 or H_3), 0.23 (s, 1, H_3 or H_1).

Anal. Calcd for $C_9H_5N_3O_4$: C, 49.32; H, 2.30; N, 19.17; mol wt, 219.15. Found: C, 49.32; H, 2.44; N, 18.93; mol wt (mass spectrum), 219.

From the alcohol soluble fraction, by incremental precipitation with water, there was ultimately recovered 0.9 g of off-white needles melting about 90°. Recrystallization from water gave long felted white needles, obviously hydrated, since they crumbled to a powder when vacuum dried, mp 107–108°. The ir spectrum was identical with that of authentic 5-nitroisoquinoline, whose melting point is reported[11] to be 110°; the ^{1}H nmr spectrum agrees with that expected for the 5-nitro isomer—τ ($CDCl_3$) 2.12 (t, 1, J = 8 Hz, H_7), 1.52 (d, 1, J_{67} = 8.5 Hz, J_{68} = 1 Hz, H_6), 1.38 (d, 1, J = 6.5 Hz, H_4), 1.27 (d, 1, J_{78} = 8.5 Hz, J_{68} = 1 Hz, H_8), 1.08 (d, 1, J = 6.5 Hz, H_3), 0.43 (s, 1, H_1).

Anal. Calcd for $C_9H_6N_2O_2$: C, 62.06; H, 3.47; N, 16.09; mol wt, 174.16. Found: C, 61.82; H, 3.18; N, 16.12; mol wt (mass spectrum), 174.

Reaction of Benzaldehyde and 1a.—A crude sample (mp 195–200°) of **1a** (3.5 g, 0.01 mol) was refluxed for 6 hr with 4.4 g (0.04 mol) of benzaldehyde, 50 ml of concentrated hydrochloric acid and 50 ml of 95% ethanol. After cooling and diluting with 100 ml of water, the solution was stored overnight at 5°; a small amount of yellow brown gum separated. The supernatant was decanted and saved (see below); the gum was heated with a few ml of ethanol and cooled. The white solid (0.04 g, mp >300°) was filtered and recrystallized from 90% ethanol containing several drops of hydrochloric acid: colorless, coarse prisms melting at 338–341°. This compound is the dihydrochloride of one of the epimers of 4,4′-dibenzal-1,1′,4,4′-tetrahydro-1,1′-biisoquinoline (see below).

Anal. Calcd for $C_{32}H_{26}Cl_2N_2 \cdot 2H_2O$: C, 70.45; H, 5.54; Cl, 13.00; N, 5.14. Found: C, 70.63; H, 5.27; Cl, 13.36, 13.07; N, 5.07, 5.17.

The picrate derived from this salt decomposed at 315–318° after recrystallization from ethanol as yellow felted needles.

Anal. Calcd for $C_{44}H_{30}N_8O_{14} \cdot H_2O$: C, 57.89; H, 3.53; N, 12.28. Found: C, 58.25; H, 3.52; N, 12.29.

The aqueous supernatant was extracted twice with 100-ml portions of diethyl ether to remove excess benzaldehyde, made basic with 25% aqueous sodium hydroxide, and extracted with three 50 ml portions of benzene. The combined benzene extracts were dried and evaporated to leave 4 g of gummy residue. The latter was triturated with 40 ml of ether–benzene (3:1); the white solid was then filtered, washed with more solvent and dried, 0.24 g (5.5%), mp 270–300°. The extracts were saved (C). This solid was next extracted with 15 ml of boiling benzene to separate the two isomers present.

A. Benzene-Soluble Isomer.—Evaporation of the benzene left a solid, mp 280–283°, which melted at 285–286° after recrystallization from 95% ethanol. The analyses, ^{1}H nmr spectrum, solubility behavior, and melting point suggest that this is the *dl* epimer of **4,4′-dibenzal-1,1′ 4,4′-tetrahydro-1,1′-biisoquinoline, 5a**: τ ($CDCl_3$) 4.39 (s, 1, H_1), 2.93 (s, 5, $H_{aromatic}$ in phenyl ring), 2.62–1.72 (m, 4, $H_{aromatic}$), 1.52 (s, 1, benzal methine), 1.06 (s, 1, H_3).

Anal. Calcd for $C_{32}H_{24}N_2$: C, 88.04; H, 5.54; N, 6.42. Found: C, 88.08; H, 5.52; N, 6.26; mol wt (mass spectrum), 436.

The picrate was obtained as plates after recrystallization from ethanol, mp 268–269° dec.

Anal. Calcd for $C_{44}H_{30}N_8O_{14}$: C, 59.06; H, 3.38; N, 12.52. Found: C, 58.97; H, 3.45; N, 12.66.

B. Benzene-Insoluble Isomer.—This compound was purified by dissolving in 20 ml of dimethylformamide, filtering, and adding 100 ml of diethyl ether. The white, microcrystalline powder was filtered, washed three times with ether, three times with water, and vacuum dried for several days at 68° (25 mm): mp 328–329° dec; absorptions due to NH and carbonyl stretching frequencies were absent in the ir spectrum; mass spectrum *m/e*, 436 (parent), 218 (M/2, base peak), the peak at *m/e* = 91 which would correspond to the loss of a benzyl fragment was very weak; τ (CF_3COOH) 3.72 (s, 1, H_1), 2.70 (s, 5, $H_{aromatic}$ phenyl ring), 1.15–2.05 (m, 4, $H_{aromatic}$), 1.01 (s, 1, benzal methine), 0.45 (s, 1, H_3).

The evidence is consistent with those expected for the meso epimer of **4,4′-dibenzal-1,1′,4,4′-tetrahydro-1,1′-biisoquinoline, 5b.**

Anal. Calcd for $C_{32}H_{24}N_2$: C, 88.04; H, 5.54; N, 6.42. Found: C, 87.84; H, 5.66; N, 6.46, 6.36.

Solutions of this compound have a blue-purple fluorescence. Its picrate, obtained from alcohol as long thin needles, decomposed at 317–320°.

C. 4-Benzal-1,4- (and 3,4-) dihydroisoquinoline.—The ether–benzene extract (see above) was diluted with 100 ml of *n*-hexane and chilled; a pale yellow solid (0.9 g, 20%, mp 90–110°) separated. Additional material was isolated as follows. The mother liquors were evaporated and the very gummy residue boiled with 25 ml of cyclohexane; the chilled solution was decanted from about 1 g of tar (discarded) and evaporated. Trituration of this residue with two small volumes of cold *n*-hexane to remove oily material left more crystalline solid. (The material in these hexane extracts gave a picrate melting at 223–225° after recrystallization from ethanol; a mixture melting point with isoquinoline picrate was not depressed; the ir spectra were identical.) Recrystallization of this solid from *n*-hexane gave a product melting at 99.5–100.5° (by way of comparison the melting point of 4-benzylisoquinoline is 119–120°[12]). The parent peak in the mass spectrum was 219; fragments of mass 128 (M − 91) and mass 91 (benzyl) were present but only had a very low intensity. The ^{1}H nmr spectrum confirmed the absence of a benzyl group (no benzyl methylene signal), but also suggested that the product was roughly a 2:1 mixture of isomers: τ ($CDCl_3$) 5.90, 5.62 (2 s, 2 total, protons of methylene group in the nitrogen bearing ring), 2.78 (s, 5, $H_{aromatic}$ in phenyl ring), 2.67–1.85 (m, 4, $H_{aromatic}$), 1.60 (s, 1, benzal methine), 0.84,

(8) A. Claus and K. Hoffmann, *J. Prakt. Chem.*, **47** (2), 252 (1893), prepared a dinitroisoquinoline, mp 283.5°, by the action of fuming nitric acid on isoquinoline in fuming sulfuric acid, but did not establish the position of the substituents.

(9) R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, **93**, 1522 (1971).

(10) A proprietary, deuterated solvent made by Stohler Isotope Chemicals, Azusa, Calif.

(11) F. Fortner, *Monatsh. Chem.*, **14**, 146 (1893).

(12) M. Avramoff and Y. Sprinzak, *J. Amer. Chem. Soc.*, **78**, 4090 (1956).

0.76 (2 s, 1 total, H_1 or H_8 in nitrogen ring, depending on isomeric form).

Anal. Calcd for $C_{16}H_{13}N$: C, 87.64; H, 5.97; N, 6.39. Found: C, 87.76; H, 5.98; N, 6.30.

The picrate after two recrystallizations from 95% ethanol melted at 190–192° (reported[12] for 4-benzylisoquinolinium picrate, 195–196°).

Anal. Calcd for $C_{22}H_{16}N_4O_7$: C, 58.93; H, 3.60; N, 12.50. Found: C, 58.62; H, 3.47; N, 12.17.

Small quantities of two other picrates were also isolated when the crude benzal dihydroisoquinoline was treated with picric acid and the salts were fractionally crystallized. One melted at 229–230° (dec) after recrystallization from ethanol; on admixture with isoquinoline picrate, the melting point was 200–210°.

Anal. Calcd for $C_{22}H_{14}N_4O_7$: C, 59.19; H, 3.16; N, 12.55. Found: C, 59.44; H, 3.22; N, 12.49, 12.47.

A hydrobromide prepared from this picrate decomposed at 308–312° after recrystallization from absolute ethanol; its elemental analyses, like that of the picrate, also suggested a lower hydrogen content than that demanded by a salt of **3** or **4**.

Anal. Calcd for $C_{16}H_{12}BrN$: C, 64.45; H, 4.06; Br, 26.80; N, 4.70. Found: C, 64.57; H, 4.04; Br, 26.63; N, 4.59.

The free base from the bromide partially melted, then resolidified at 157–159°, and finally remelted at 225–230°. The base peak (*m/e*) in the mass spectrum was 217; a small peak at 218 (M + 1) was present but there were no peaks at *m/e* 434–436 (coupled products). Fragments of mass 91 (benzyl) and M − 91 were not present.

The other picrate after recrystallization from acetonitrile decomposed at 266–267°; admixture with the picrate of dibenzal tetrahydrobiisoquinoline, mp 268–269° (see above), depressed the melting point to 245–250°. The ir spectra of these two compounds also differed. Perhaps this compound is the picrate of 4,4′-dibenzyl-1,1′-biisoquinoline, but it was not investigated further.

Anal. Calcd for $C_{44}H_{30}N_8O_{14}$: C, 59.06; H, 3.38; N, 12.52. Found: C, 58.95; H, 3.28; N, 12.49.

5,5′-Dinitro-1,1′-biisoquinolin eand 5-Nitro-1,1′-biisoquinoline.—1,1′-Biisoquinoline (8.7 g; 0.039 mol) was nitrated by the procedure of Le Fèvre and Le Fèvre[13] for making 5-nitroisoquinoline. The dried crude product (12.2 g) was dissolved in 2 l. of boiling xylene, filtered from 1.49 of inorganic salts, and chilled to 0°; 8.6 g (72.9%) of dinitro compound was recovered, decomposing at 265–270° after turning black at 250°. A portion was recrystallized from dimethylformamide as pinkish white, feathery needles, melting at 293–294° dec if plunged into a bath preheated to 290°. If heated from room temperature, the compound turned black at 265°, then decomposed at 270–280°: τ ($CF_3COCF_3 \cdot 1.6D_2O$) 2.37 (d, 2, H_7, H_8), 1.25 (m, 1, H_6), 1.05 (s, 2, H_3, H_4).

Anal. Calcd for $C_{18}H_{10}N_4O_4$: C, 62.43; H, 2.94; N, 16.18. Found: C, 62.76; H, 2.82; N, 15.78, 15.87.

Evaporation of the xylene left 2.2 g (20.6%) of solid which was recrystallized from 95% ethanol, mp 186–187° dec. The analyses and nmr are consistent with those required for **5-nitro-1,1′-biisoquinoline:** τ ($CF_3COCF_3 \cdot 1.6D_2O$) 2.65–1.79 (m, 6, H_7, $H_{7'}$, H_8, $H_{8'}$, $H_{5'}$, $H_{6'}$), 1.68–1.44 (m, 3, H_6, $H_{3'}$, $H_{4'}$), 1.28 (s, 2, H_3, H_4).

Anal. Calcd for $C_{18}H_{11}N_3O_2$: N, 13.95. Found: N, 14.04.

Registry No.—**1a**, 25080-52-8; **1b**, 25055-08-7; **2a**, 35202-34-7; **2b**, 35202-35-8; **3**, 35202-36-9; **3** picrate, 35249-61-7; **4**, 35202-37-0; **4** picrate, 35202-38-1; **5a**, 35202-39-2; **5a** picrate, 35202-40-5; **5b**, 35202-41-6; **5b** dihydrochloride, 35202-42-7; **5b** picrate, 35202-43-8; 4-bromoisoquinoline, 1532-97-4; 4-bromiisoquinolinum nitrate, 35202-45-0; 3,3′-biisoquinoline, 35202-46-1; 4,6-dinitroisoquinoline, 35202-47-2; 5-nitroisoquinoline, 607-32-9; 4,4′-dibenzyl-1,1′-biisoquinoline picrate, 35202-49-4.

Acknowledgment.—The assistance of Dr. R. L. Atkins in elucidating the structure of 4,6-dinitroisoquinoline is appreciated.

(13) C. G. La Fèvre and R. J. W. Le Fèvre, *J. Chem. Soc.*, 1470 (1935).

Synthesis and Reactions of 2-Alkylthio-s-triazolo[1,5-*b*]isoquinolin-5(10*H*)-ones

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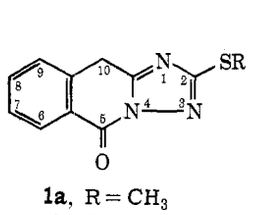
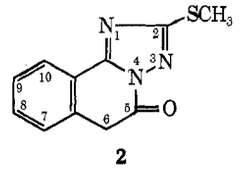
Homophthalic anhydride reacted with *S*-alkylisothiosemicarbazides to give 2-alkylthio-*s*-triazolo[1,5-*b*]isoquinolin-5(10*H*)-ones (**1**). Compounds **1** coupled with diazonium salts to give the 10-arylhydrazones of 5,10-dihydro-2-alkylthio-*s*-thiazolo[1,5-*b*]isoquinoline-5,10-diones (**6**) and condensed with aromatic aldehydes to form the 10-arylmethylene derivatives **11**. Compounds **1** also condensed with nitroso compounds to yield the 10-arylimino derivatives **17**, which on hydrolysis afforded 5,10-dihydro-2-alkylthio-*s*-triazolo[1,5-*b*]isoquinoline-5,10-diones (**18**). Formylation of **1a** gave 5,10-dihydro-2-methylthio-5-oxo-*s*-triazolo[1,5-*b*]isoquinoline-10-carboxaldehyde (**19**).

During investigation of the condensation reactions of homophthalic anhydride to obtain fused isoquinolines, we found that homophthalic anhydride reacts with *S*-methylisothiosemicarbazide in refluxing dimethylformamide to give a product which can be formulated as either 2-methylthio-*s*-triazolo[1,5-*b*]isoquinolin-5(10H)-one (**1a**) or the isomeric compound, 2-methylthio-*s*-triazolo[5,1-*a*]isoquinolin-5(6*H*)-one (**2**). The 2-ethylthio (**1b**) and 2-benzylthio (**1c**) analogs were similarly prepared.



1a, R = CH_3
b, R = C_2H_5
c, R = $CH_2C_6H_5$



2

The available data are compatible with the linear structure **1**, rather than the angular structure **2**. Homophthalic anhydride has been reported to react with hydrazine to yield *N*-aminohomophthalimide,[1] and to condense with *o*-phenylenediamine to give mainly the linear product **3** and not **4**.[2-5]

The ir spectrum of **1a** shows carbonyl absorption at 1720 cm^{-1}. For a comparison between the ir spectra

(1) G. Rosen and F. D. Popp, *J. Heterocycl. Chem.*, **6**, 9 (1969).
(2) A. Bistrzycki and K. Fassler, *Helv. Chim. Acta*, **6**, 519 (1923).
(3) M. F. Sartori, A. Oken, and H. E. Schroeder, *J. Org. Chem.*, **31**, 1498 (1966).
(4) E. Schefczik, *Justus Liebigs Ann. Chem.*, **729**, 83 (1969).
(5) A. Mustafa, M. I. Ali, and A. A. El-Sayed, *ibid.*, **739**, 68 (1970).