Tricyclic Heteroaromatic Ring Systems II (1). A Convenient Synthesis of 1*H*-Pyrrolo[3,2-c]quinolines (2a,b)

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Various quinol-4-yl hydrazones on heating in high boiling solvents undergo cyclizations to give 1*H*-pyrrolo[3,2-c]quinolines in good yields. Some of these pyrroloquinolines were alkylated to provide their *N*-alkyl derivatives.

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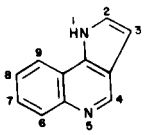
Although various derivatives of 1*H*-pyrrolo[3,2-c]quinoline (I) have been previously reported in the literature (3-9), only a handful of derivatives of the completely aromatic system exist. Thus, within our program of the synthesis of tricyclic heteroaromatic ring systems and the study of their chemical and biological activities, we decided to synthesize a number of derivatives of I. After our work on the synthesis was essentially completed (2b), a publication describing some derivatives of I, also obtained by us, appeared (10) and this prompts us to report our results

FORMULA I

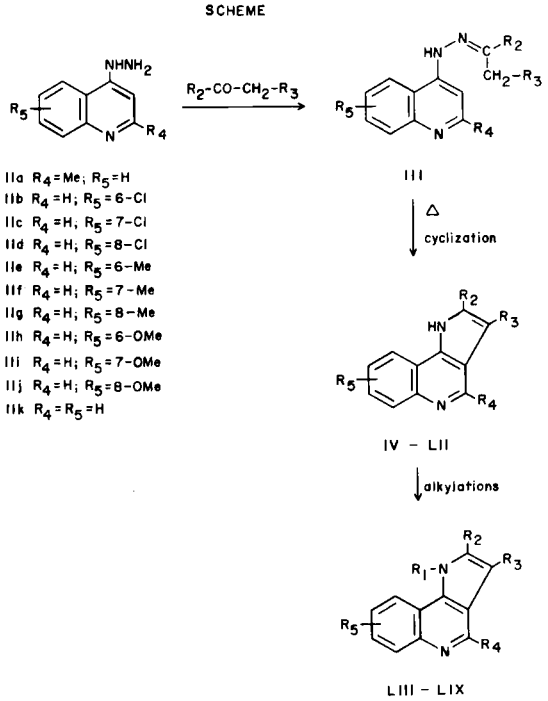


For our synthesis we decided first to employ the Fischer indole cyclization (Scheme). Various quinol-4-ylhydrazines (IIa-IIk), obtained from the corresponding 4-chloroquinolines, were treated with the appropriate carbonyl compounds to give the hydrazones IIIa-IIIk. Our initial attempts to cyclize some of these hydrazones using acids such as hydrochloric acid, sulfuric acid, polyphosphoric acid, acetic acid, and a mixture of hydrochloric and acetic acid, failed. Only traces of the desired product were obtained in these reactions. The failure of cyclization under similar conditions were earlier observed in the abortive attempts of the synthesis of azaindoles (11).

Thermal cyclization procedures previously used in the Fischer indole synthesis (12) were next attempted. Heating quinol-4-yl-hydrazones under reflux in Dowtherm, we were able to isolate the desired 1*H*-pyrrolo[3,2-c]quinolines (XII, XXXI, XLIII, and XLIX, see Table I). Later, Dowtherm was replaced by diethylene glycol and the pyrroloquinolines IV-LII were obtained in good to excellent yields by carrying out the cyclization in diethylene glycol under reflux over a short period (fifteen minutes to an hour). The products are presented in Tables I-III.

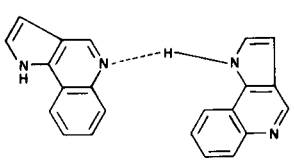
The *N*-alkylation of some of these products with alkyl iodides was carried out using potassium hydroxide in dimethyl sulfoxide (13) or sodium hydride in hexamethylphosphotriamide (14). In the absence of other confirmatory evidence we have tentatively assigned the structures LIII-LIX for these *N*-alkylated products.

SCHEME



In addition to elemental analyses (Table III), all the 1*H*-pyrrolo[3,2-c]quinolines (IV-LIX) were identified by spectral methods. The infrared absorption spectra of compounds IV-LII showed a broad absorption band between 3500 and 2500 cm^{-1} due to an intermolecular hydrogen bond (A). This band was, however, absent in the *N*-alkylated compounds LIII-LIX. In the pmr spectra of these

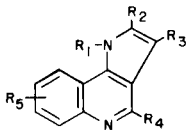
FORMULA A



compounds (Table II) the proton at the 4 position appears as a sharp singlet between δ 8.72 and 9.18. The NH of the pyrrole ring appears as a broad signal between δ 11.72 and 12.55, disappearing upon *N*-alkylation of the products.

Table I

1*H*-Pyrrolo[3,2-*c*]quinolines



Compound No.	R_1	R_2	R_3	R_4	R_5	Carbonyl Compound (a)	Reaction Time (hour)	Yield (%)	M.p.°
IV	H	-(CH$_2$)$_4$-		Me	H	A	0.25	82	270-271 dec. (b)
V	H	Me	Me	Me	H	B	0.25	70	267-268 dec. (c)
VI	H	Me	Ph	Me	H	C	0.5	83	278-279 dec.
VII	H	-(CH$_2$)$_4$-		H	6-Cl	A	0.75	84	>300
VIII	H	Me	Me	H	6-Cl	B	1	66	>300
IX	H	Me	Ph	H	6-Cl	C	0.5	87	297-298
X	H	-(CH$_2$)$_3$-		H	6-Cl	D	0.25	29	>300
XI	H	H	Me	H	6-Cl	E	1	80	>300
XII	H	-(CH$_2$)$_4$-		H	7-Cl	A	0.5	95	>300
XIII	H	Me	Me	H	7-Cl	B	0.5	81	>300
XIV	H	Me	Ph	H	7-Cl	C	0.5	84	>300
XV	H	H	Me	H	7-Cl	E	0.5	78	225-226
XVI	H	-(CH$_2$)$_4$-		H	8-Cl	A	0.5	80	>300
XVII	H	Me	Me	H	8-Cl	B	0.75	88	>300
XVIII	H	Me	Ph	H	8-Cl	C	0.5	58	>300
XIX	H	-(CH$_2$)$_3$-		H	8-Cl	D	0.25	79	>300
XX	H	H	Me	H	8-Cl	E	0.25	71	>300
XXI	H	Et	Me	H	8-Cl	F	0.5	80	>300
XXII	H	H	Et	H	8-Cl	G	0.5	80	299-300 dec.
XXIII	H	-(CH$_2$)$_4$-		H	6-Me	A	0.5	76	>300
XXIV	H	Me	Me	H	6-Me	B	1	60	281-282
XXV	H	Me	Ph	H	6-Me	C	1	90	237-238
XXVI	H	H	Me	H	6-Me	E	0.5	83	276-277
XXVII	H	-(CH$_2$)$_4$-		H	7-Me	A	0.5	77	>300
XXVIII	H	Me	Me	H	7-Me	B	0.5	64	>300
XXIX	H	Me	Ph	H	7-Me	C	0.25	87	297-298
XXX	H	H	Me	H	7-Me	E	0.5	51	>300
XXXI	H	-(CH$_2$)$_4$-		H	8-Me	A	0.75	78	>300
XXXII	H	Me	Me	H	8-Me	B	0.75	76	296-297 dec.
XXXIII	H	Me	Ph	H	8-Me	C	1	58	>300
XXXIV	H	H	Me	H	8-Me	E	0.5	78	>300
XXXV	H	Et	Me	H	8-Me	F	0.75	88	298-299
XXXVI	H	-(CH$_2$)$_4$-		H	6-OMe	A	0.5	76	>300
XXXVII	H	Me	Me	H	6-OMe	B	1	71	>300
XXXVIII	H	Me	Ph	H	6-OMe	C	0.5	74	>300

Table I (continued)

1*H*-Pyrrolo[3,2-*c*]quinolines

Compound No.	R_1	R_2	R_3	R_4	R_5	Carbonyl Compound (a)	Reaction Time (hour)	Yield (%)	M.p.°
XXXIX	H	H	Me	H	6-OMe	E	0.75	67	>300
XL	H	Et	Me	H	6-OMe	F	0.75	57	>300
XLI	H	-$(CH_2)_4$-		H	7-OMe	A	0.5	89	279-280 dec.
XLII	H	Me	Me	H	7-OMe	B	0.25	40	288-294
XLIII	H	Me	Ph	H	7-OMe	C	0.5	86	275-276 dec.
XLIV	H	H	Me	H	7-OMe	E	0.5	54	263-265 dec.
XLV	H	-$(CH_2)_4$-		H	8-OMe	A	0.5	84	291-293 dec.
XLVI	H	Me	Me	H	8-OMe	B	0.5	53	285-290 dec.
XLVII	H	Me	Ph	H	8-OMe	C	0.5	84	289-291 dec.
XLVIII	H	H	Me	H	8-OMe	E	0.25	90	249-250 dec.
XLIX	H	-$(CH_2)_4$-		H	H	A	0.5	78	294-295 (d)
L	H	Me	Me	H	H	B	0.5	59	303-304 dec. (e)
LI	H	Me	Ph	H	H	C	0.5	71	298-299
LII	H	H	Me	H	H	E	0.5	76	288-289 dec.
LIII	Me	H	Me	H	6-Cl	---	1.5	90	154-155
LIV	Me	Me	Me	H	6-Cl	---	2.25	89	224-225
LV	Me	-$(CH_2)_4$-		H	6-Cl	---	3	89	221-222
LVI	Et	H	Me	H	6-Cl	---	3	88	138-139
LVII	Me	Me	Ph	H	6-Cl	---	2.25	89	207-208
LVIII	Me	-$(CH_2)_4$-		H	7-Cl	---	3	90	219-220
LIX	Me	-$(CH_2)_4$-		H	H	---	2	88	>300

(a) A, cyclohexanone; B, 2-butanone; C, 1-phenyl-2-propanone; D, cyclopentanone; E, propanal; F, 3-pentanone; G. butanal. (b) Lit. 284-285° (10). (c) Lit. 270-271° (10). (d) Lit. 291-292° (10). (e) Lit. 318-319° (10).

This data provided the evidence for the ring closure at the β position of the quinoline ring as was expected.

EXPERIMENTAL

All melting points are uncorrected. Pmr spectra were taken on a 60 MHz Hitachi Perkin-Elmer R-20b using tetramethylsilane as an internal standard. Ir absorption spectra were measured on a Perkin-Elmer analyzer model 240.

The following starting materials were prepared according to the literature method: 4-chloroquinoline, oil (16), 4,6-dichloroquinoline, m.p. 103.5-104° (15,16); 4,7-dichloroquinoline, m.p. 85-86° (17); 4,8-dichloroquinoline, m.p. 84-85° (lit. m.p. 105° (16)); 4-chloro-2-quinaldine, m.p. 42-43° (18); 4-chloro-6-methylquinoline, m.p. 55° (21); 4-chloro-7-methylquinoline, m.p. 48-49° (lit. m.p. 28° (20)); 4-chloro-8-methylquinoline, m.p. 99° (21); 4-chloro-6-methoxyquinoline, m.p. 79-80° (15); 4-chloro-7-methoxyquinoline, m.p. 85-87° (22); and 4-chloro-8-methoxyquinoline, m.p. 77-78° (22).

Quinol-4-ylhydrazines.

General procedure.

A mixture of 0.1 mole of a 4-chloroquinoline, 0.1 mole of 85%

Table II

Pmr Spectra of 1*H*-Pyrrolo[3,2-*c*]quinolines
(Solvent DMSO-d_6; Chemical Shifts in δ; J in Hz)

Compound No.	H-1/R_1	H-2/R_1	H-3/R_3	H-4/R_4	H-6/R_5	H-7/R_5	H-8/R_5	H-9/R_5
VI	12.25 (br.)	2.28 (s)	7.20-7.70 (m)	2.28 (s)	7.20-7.70 (m)	7.70-8.00 (m)	7.20-7.70 (m)	8.15-8.50 (m)
VII	11.98 (br.)	1.60-2.10 (m) and 2.40-3.05 (m)		8.84 (s)	-----	7.10-7.70 (m)	7.10-7.70 (m)	8.10 (q) J = 2.25 and 7.50
VIII	12.06 (br.)	2.23 (s)	2.35 (s)	9.00 (s)	-----	7.65 (q) J = 2.25 and 7.50	7.43 (q) J = 7.50	8.22 (q) J = 2.25 and 7.50
IX	12.55 (br.)	2.60 (q)	7.20-7.85 (m)	9.15 (s)	-----	7.20-7.85 (m)	7.20-7.85 (m)	8.35 (q) J = 2.25 and 7.50
X	12.32 (br.)	2.30-3.00 (m)		8.95 (s)	-----	7.62 (q) J = 1.50 and 7.50	7.40 (q) J = 7.50	8.22 (q) J = 1.50 and 7.50
XI	12.35 (br.)	7.40 (s)	2.46 (s)	9.18 (s)	-----	7.78 (q) J = 2.25 and 7.50	7.53 (q) J = 7.50	8.36 (q) J = 2.25 and 7.50
XII	11.78 (br.)	1.50-2.10 (m) and 2.50-2.95 (m)		8.83 (s)	8.25 (d) J = 2.25	-----	7.33 (q) J = 2.25 and 9.00	7.87 (d) J = 9.00
XIII	12.00 (br.)	2.24 (s)	2.35 (s)	8.93 (s)	8.33 (d) J = 2.25	-----	7.41 (q) J = 2.25 and 9.00	7.98 (d) J = 9.00
XIV	12.49 (br.)	2.50 (s)	7.30-7.70 (m)	9.00 (s)	7.98 (d) J = 2.25	-----	7.30-7.70 (m)	8.34 (d) J = 9.00
XV	12.20 (br.)	7.27 (br.)	2.37 (s)	9.05 (s)	8.00 (d) J = 2.25	-----	7.54 (q) J = 2.25 and 9.00	8.33 (d) J = 9.00
XVI	12.05 (br.)	1.50-2.10 (m) and 2.55-3.00 (m)		8.88 (s)	8.25 (d) J = 9.00	7.48 (q) J = 2.25 and 9.00	-----	7.95 (d) J = 2.25
XVII	11.87 (br.)	2.30 (s)	2.41 (s)	8.98 (s)	8.29 (d) J = 9.00	7.49 (q) J = 2.25 and 9.00	-----	8.00 (d) J = 2.25
XVIII	12.45 (br.)	2.52 (s)	7.10-7.70 (m)	8.98 (s)	8.32 (d) J = 9.00	7.10-7.70 (m)	-----	7.98 (d) J = 2.25
XIX	(a)	2.05-3.20 (m)		8.84 (s)	7.91 (d) J = 9.00	7.35 (q) J = 2.25 and 9.00	-----	8.27 (d) J = 2.25
XX	12.15 (br.)	7.27 (br.)	2.37 (s)	9.03 (s)	7.98 (d) J = 9.00	7.47 (q) J = 2.25 and 9.00	-----	8.40 (d) J = 2.25
XXI	11.92 (br.)	1.22 (t); 2.74 (q) J = 7.50	2.25 (s)	8.95 (s)	7.93 (d) J = 9.00	7.41 (q) J = 2.25 and 9.00	-----	8.39 (d) J = 2.25
XXII	12.15 (br.)	7.25 (br.)	1.26 (t); 2.80 (q) J = 7.50	9.05 (s)	7.97 (d) J = 9.00	7.45 (q) J = 2.25 and 9.00	-----	8.39 (d) J = 2.25
XXIII	11.89 (br.)	1.65-2.05 (m) and 2.40-3.00 (m)		8.79 (s)	2.40-3.00 (m)	6.90 (q) J = 1.50 and 7.50	7.33 (t) J = 7.50	7.78 (q) J = 1.50 and 7.50

Table II (continued)

Pmr Spectra of 1*H*-Pyrrolo[3,2-*c*]quinolines
(Solvent DMSO-d_6; Chemical Shifts in δ; J in Hz)

Compound No.	H-1/R_1	H-2/R_2	H-3/R_3	H-4/R_4	H-6/R_5	H-7/R_5	H-8/R_5	H-9/R_5
XXIV (b)	11.80 (br.)	2.12 (s)	2.34 (s)	8.89 (s)	2.60 (s)	7.26 (m)	8.05 (m)	7.26 (m)
XXV	12.39 (br.)	2.59 (s)	7.25-7.75 (m)	9.10 (s)	2.75 (s)	7.25-7.75 (m)	8.26 (t) J = 5.25	7.25-7.75 (m)
XXVI	11.90 (br.)	7.22 (br.)	2.42 (s)	9.08 (s)	2.79 (s)	7.40 (m)	8.20 (t) J = 5.25	7.40 (m)
XXVII	(c)	1.40-2.00 (m) and 2.55-3.00 (m)		8.80 (s)	7.72 (br.) (e)	2.42 (s)	7.21 (q) J = 1.50 and 8.25	8.07 (d) J = 8.25
XXVIII	11.80 (br.)	2.23 (s)	2.34 (s)	8.85 (s)	7.73 (br.) (e)	2.44 (s)	7.29 (q) J = 1.50 and 8.25	8.11 (d) J = 8.25
XXIX	12.30 (br.)	2.52 (s)	7.05-7.65 (m)	8.98 (s)	7.79 (br.) (e)	2.45 (s)	7.05-7.65 (m)	8.23 (d) J = 8.25
XXX	11.96 (br.)	7.15 (br.)	2.34 (s)	8.96 (s)	7.77 (br.) (e)	2.45 (s)	7.30 (q) J = 1.50 and 8.25	8.18 (d) J = 8.25
XXXI	11.85 (br.)	1.55-2.00 (m) and 2.55-2.90 (m)		8.80 (s)	7.82 (d) J = 8.25	7.25 (q) J = 2.25 and 8.25	2.45 (s)	8.00 (br.) (e)
XXXII	(a)	2.22 (s)	2.32 (s)	8.81 (s)	8.08 (d) J = 9.00	7.24 (q) J = 2.25 and 9.00	2.43 (s)	7.71 (br.) (e)
XXXIII	12.45 (br.)	2.48 (s)	7.20-7.70 (m)	9.00 (s)	8.34 (d) J = 9.00	7.20-7.70 (m)	2.48 (s)	7.98 (d) J = 2.25
XXXIV	12.24 (br.)	7.27 (br.)	2.37 (s)	9.04 (s)	8.32 (d) J = 9.00	7.53 (q) J = 2.25 and 9.00	2.37 (s)	7.98 (d) J = 2.25
XXXV	11.78 (br.)	1.23 (t); 2.73 (q) J = 7.50	2.25 (s)	8.89 (s)	7.87 (d) J = 9.00	7.26 (q) J = 2.25 and 9.00	2.45 (s)	8.08 (br.) (e)
XXXVI	11.80 (br.)	1.65-2.10 (m) and 3.02-3.50 (m)		8.79 (s)	3.89 (s)	6.90 (q) J = 1.50 and 8.25	7.35 (t) J = 8.25	7.77 (q) J = 2.25 and 8.25
XXXVII	(d)	2.40 (s)	2.30 (s)	8.90 (s)	3.98 (s)	6.94 (q) J = 1.50 and 8.25	7.37 (t) J = 8.25	7.82 (q) J = 1.50 and 8.25
XXXVIII	12.35 (br.)	2.51 (s)	7.27-7.65 (m)	8.92 (s)	3.89 (s)	6.95 (q) J = 1.50 and 8.25	7.27-7.65 (m)	7.85 (q) J = 1.50 and 8.25
XXXIX	11.98 (br.)	7.19 (br.)	2.35 (s)	8.92 (s)	3.89 (s)	6.92 (q) J = 1.50 and 8.25	7.38 (t) J = 8.25	7.82 (q) J = 1.50 and 8.25
XL	11.75 (br.)	1.21 (t); 2.75 (q) J = 7.50	2.24 (s)	8.84 (s)	3.89 (s)	6.90 (q) J = 1.50 and 8.25	7.37 (t) J = 8.25	7.84 (q) J = 1.50 and 8.25
XLI	11.78 (br.)	1.35-2.10 (m) and 2.55-2.90 (m)		8.81 (s)	7.38 (d) J = 2.25	3.84 (s)	7.14 (q) J = 2.25 and 9.00	8.15 (d) J = 9.00

Table II (continued)

Pmr Spectra of 1*H*-Pyrrolo[3,2-*c*]quinolines
(Solvent DMSO-d_6; Chemical Shifts in δ; J in Hz)

Compound No.	H-1/R_1	H-2/R_2	H-3/R_3	H-4/R_4	H-6/R_5	H-7/R_5	H-8/R_5	H-9/R_5
XLII	11.76 (br.)	2.22 (s)	2.33 (s)	8.83 (s)	7.37 (d) J = 2.25	3.83 (s)	7.13 (q) J = 2.25 and 9.00	8.13 (d) J = 9.00
XLIII	12.20 (br.)	2.50 (s)	7.35-7.80 (m)	8.92 (s)	7.35-7.80 (m)	3.85 (s)	7.20 (q) J = 2.25 and 9.00	8.24 (d) J = 9.00
XLIV	11.92 (br.)	7.05-7.20 (m)	2.35 (s)	8.95 (s)	7.05-7.20 (m)	3.85 (s)	7.35 (q) J = 2.25 and 9.00	8.22 (d) J = 9.00
XLV	11.83 (br.)	1.43-2.05 (m) and 2.52-3.00 (m)		8.72 (s)	7.82 (d) J = 9.00	7.05 (q) J = 3.00 and 9.00	3.85 (s)	7.66 (d) J = 3.00
XLVI	11.80 (br.)	2.22 (s)	2.35 (s)	8.75 (s)	7.85 (d) J = 9.00	7.05 (q) J = 3.00 and 9.00	3.85 (s)	7.65 (d) J = 3.00
XLVII	12.25 (br.)	2.52 (s)	7.20-7.77 (m)	8.83 (s)	7.85 (d) J = 9.00	7.12 (q) J = 3.00 and 9.00	3.87 (s)	7.75 (d) J = 3.00
XLVII	12.01 (br.)	7.10-7.27 (m)	2.35 (s)	8.87 (s)	7.90 (d) J = 9.00	7.12 (q) J = 3.00 and 9.00	3.87 (s)	7.75 (d) J = 3.00
LI	12.43 (br.)	2.54 (s)	7.00-7.77 (m)	9.03 (s)	7.87-8.10 (m)	7.00-7.77 (m)	7.00-7.77 (m)	8.27-8.44 (m)
LII	12.11 (br.)	7.20 (br.)	2.38 (s)	9.05 (s)	7.87-8.10 (m)	7.35-7.65 (m)	7.35-7.65 (m)	8.25-8.45 (m)
LIII	4.07 (s)	6.77 (br.)	2.37 (s)	9.07 (s)	-----	7.65 (q) J = 1.50 and 7.50	7.36 (q) J = 7.50 and 9.00	8.14 (q) J = 1.50 and 7.50
LIV	3.92 (s)	2.25 (s)	2.25 (s)	8.97 (s)	-----	7.65 (q) J = 2.25 and 7.50	7.45 (q) J = 7.50	8.35 (q) J = 2.25 and 7.50
LV	3.90 (s)	1.60-2.20 (m) and 2.60-3.10 (m)		8.90 (s)	-----	7.62 (q) J = 2.25 and 7.50	7.33 (q) J = 7.50	8.20 (q) J = 2.25 and 7.50
LVI	1.45 (t); 4.30 (q) J = 7.50	6.77 (s)	2.35 (s)	9.05 (s)	-----	7.60 (q) J = 1.50 and 7.50	7.33 (q) J = 7.50	7.92 (q) J = 1.50 and 7.50
LVII (b)	4.28 (s)	2.56 (s)	7.10-7.60 (m)	9.13 (s)	-----	7.60-8.00 (m)	7.60-8.00 (m)	8.50-8.90 (m)
LVIII	3.85 (s)	1.50-2.35 (m) and 2.64-3.00 (m)		8.90 (s)	7.20-7.50 (m)	-----	7.20-7.50 (m)	8.17 (d) J = 7.50
LIX	3.92 (s)	1.52-2.10 (m) and 2.20-2.90 (m)		8.82 (s)	7.88-8.15 (m)	7.30-7.60 (m)	7.30-7.60 (m)	8.20-8.50 (m)

(a) Taken at 100°. (b) Taken in acetic acid-d_4. (c) Taken at 130°. (d) Taken at 150°. (e) A broad signal with a possible coupling.

Table III

Elemental Analyses

Compound No.	Formula	Calcd. %			Found %		
		C	H	N	C	H	N
VI	$C_{19}H_{16}N_2$	83.79	5.92	10.28	83.59	5.79	10.31
VII	$C_{15}H_{13}ClN_2$	70.17	5.10	10.91	70.10	5.03	10.70
VIII	$C_{13}H_{11}ClN_2$	67.67	4.77	12.14	67.38	4.75	11.93
IX	$C_{18}H_{13}ClN_2$	73.84	4.44	9.57	73.80	4.49	9.28
X	$C_{14}H_{11}ClN_2$	69.48	4.53	11.54	69.50	4.58	11.32
XI	$C_{12}H_9ClN_2$	66.48	4.18	12.92	66.25	4.11	12.71
XII	$C_{15}H_{13}ClN_2$	70.17	5.10	10.91	69.80	5.02	10.81
XIII	$C_{13}H_{11}ClN_2$	67.67	4.77	12.14	67.59	4.86	11.93
XIV	$C_{18}H_{13}ClN_2$	73.84	4.44	9.57	73.77	4.55	9.34
XV	$C_{12}H_9ClN_2$	66.48	4.18	12.92	66.52	4.35	12.68
XVI	$C_{15}H_{13}ClN_2$	70.17	5.10	10.91	70.00	5.10	10.67
XVII	$C_{13}H_{11}ClN_2$	67.67	4.77	12.14	67.78	4.80	11.79
XVIII	$C_{18}H_{13}ClN_2$	73.84	4.44	9.57	73.54	4.53	9.30
XIX	$C_{14}H_{11}ClN_2$	69.48	4.53	11.54	69.31	4.51	11.34
XX	$C_{12}H_9ClN_2$	66.48	4.18	12.92	66.42	4.26	12.71
XXI	$C_{14}H_{13}ClN_2$	68.71	5.32	11.47	68.72	5.31	11.21
XXII	$C_{13}H_{11}ClN_2$	67.67	4.77	12.14	67.76	4.65	11.98
XXIII	$C_{16}H_{16}N_2$	81.35	6.78	11.86	81.60	6.87	11.81
XXIV	$C_{14}H_{14}N_2$	79.96	6.71	13.32	79.90	6.71	13.54
XXV	$C_{19}H_{16}N_2$	83.79	5.92	10.28	83.57	6.04	10.13
XXVI	$C_{13}H_{12}N_2$	79.59	6.12	14.28	79.54	6.28	14.14
XXVII	$C_{16}H_{16}N_2$	81.35	6.78	11.86	81.16	6.83	11.87
XXVIII	$C_{14}H_{14}N_2$	79.96	6.71	13.32	80.17	6.62	13.41
XXIX	$C_{19}H_{16}N_2$	83.79	5.92	10.28	83.51	5.90	10.13
XXX	$C_{13}H_{13}N_2$	79.59	6.12	14.28	79.45	6.04	14.02
XXXI	$C_{16}H_{16}N_2$	81.35	6.78	11.86	81.19	6.72	11.57
XXXII	$C_{14}H_{14}N_2$	79.96	6.71	13.32	79.88	6.73	13.08
XXXIII	$C_{19}H_{16}N_2$	83.79	5.92	10.28	83.62	6.05	10.24
XXXIV	$C_{13}H_{12}N_2$	79.59	6.12	14.28	79.34	6.04	13.90
XXXV	$C_{15}H_{16}N_2$	80.35	7.14	12.50	80.20	7.21	12.47
XXXVI	$C_{16}H_{16}N_2O$	76.19	6.34	11.11	76.09	6.30	11.11
XXXVII	$C_{14}H_{14}N_2O$	74.33	6.19	12.38	74.60	6.25	12.08
XXXVIII	$C_{19}H_{16}N_2O$	79.16	5.55	9.72	78.97	5.67	9.58
XXXIX	$C_{13}H_{12}N_2O$	73.58	5.66	13.20	73.30	5.76	12.96
XL	$C_{15}H_{16}N_2O$	75.00	6.66	11.66	74.80	6.58	11.90
XLI	$C_{16}H_{16}N_2O$	76.19	6.34	11.11	76.14	6.35	10.98
XLII	$C_{14}H_{14}N_2O$	74.33	6.19	12.38	74.28	6.46	12.28
XLIII	$C_{19}H_{16}N_2O$	79.16	5.55	9.72	79.00	5.53	9.54
XLIV	$C_{13}H_{12}N_2O$	73.58	5.66	13.20	73.59	5.84	12.92
XLV	$C_{16}H_{16}N_2O$	76.19	6.34	11.11	75.96	6.33	10.97
XLVI	$C_{14}H_{14}N_2O$	74.33	6.19	12.38	74.37	6.21	12.20
XLVII	$C_{19}H_{16}N_2O$	79.16	5.55	9.72	79.17	5.60	9.61
XLVIII	$C_{13}H_{12}N_2O$	73.58	5.66	13.20	73.41	5.64	12.94
LI	$C_{18}H_{14}N_2$	83.62	5.42	10.85	83.49	5.43	10.65
LII	$C_{12}H_{10}N_2$	79.12	5.49	15.38	79.30	5.61	15.27
LIII	$C_{13}H_{11}ClN_2$	67.67	4.77	12.14	67.65	4.92	11.94
LIV	$C_{14}H_{13}ClN_2$	68.71	5.35	11.45	68.51	5.28	11.18

Table III (continued)

Elemental Analyses

Compound No.	Formula	Calcd. % C	Calcd. % H	Calcd. % N	Found% C	Found% H	Found% N
LV	$C_{16}H_{15}ClN_2$	70.98	5.58	10.35	70.87	5.58	10.24
LVI	$C_{14}H_{13}ClN_2$	68.71	5.35	11.45	68.51	5.15	11.29
LVII	$C_{19}H_{15}ClN_2$	74.38	4.89	9.13	74.28	4.98	8.94
LVIII	$C_{16}H_{15}ClN_2$	70.98	5.58	10.35	70.71	5.64	10.10
LIX	$C_{16}H_{16}N_2$	81.35	6.78	11.86	81.52	6.90	11.66

hydrazine hydrate and 125 ml. of ethanol was heated under reflux for a period of 12 to 24 hours. The mixture was allowed to cool down to the room temperature and then filtered, washed with ice-cooled ethanol (3 x 10 ml.). The quinol-4-ylhydrazine hydrochloride thus obtained was dissolved in water and the free base was liberated by treatment with ammonia. The precipitate was filtered, washed with water and then crystallized from ethanol. Using this procedure, the following hydrazines were prepared from the corresponding 4-chloroquinolines.

2-Methylquinol-4-ylhydrazine (IIa).

This compound had a m.p. of 200°; hydrochloride m.p. 306° (23).

6-Chloroquinol-4-ylhydrazine (IIb).

This compound had a m.p. of 195-196°.

Anal. Calcd. for $C_9H_8ClN_3$: C, 55.82; H, 4.16; N, 21.70. Found: C, 55.62; H, 4.17; N, 21.50.

7-Chloroquinol-4-ylhydrazine (IIc).

This compound had a m.p. of 208-209°.

Anal. Calcd. for $C_9H_8ClN_3$: C, 55.82; H, 4.16; N, 21.70. Found: C, 55.71; H, 4.06; N, 21.50.

8-Chloroquinol-4-ylhydrazine (IId).

This compound had a m.p. of 202-203°

Anal. Calcd. for $C_9H_8ClN_3$: C, 55.82; H, 4.16; N, 21.70. Found: C, 56.32; H, 4.29; N, 21.48.

6-Methylquinol-4-ylhydrazine (IIe).

The hydrochloride of this compound had a m.p. of 288-290°.

Anal. Calcd. for $C_{10}H_{12}ClN_3$: C, 57.28; H, 5.77; N, 20.04. Found: C, 57.02; H, 5.73; N, 19.78.

7-Methylquinol-4-ylhydrazine (IIf).

This compound had a m.p. of 170-173°; hydrochloride m.p. 270-272°.

Anal. Calcd. for $C_{10}H_{12}ClN_3$: C, 57.28; H, 5.77; N, 20.04. Found: C, 57.50; H, 5.88; N, 19.81.

8-Methylquinol-4-ylhydrazine (IIg).

This compound had a m.p. of 198-200°.

Anal. Calcd. for $C_{10}H_{11}N_3$: C, 69.43; H, 6.40; N, 24.26. Found: C, 69.46; H, 6.36; N, 24.00.

6-Methoxyquinol-4-ylhydrazine (IIh).

This compound had a m.p. of 151-153° (25); hydrochloride m.p. 270-272°.

7-Methoxyquinol-4-ylhydrazine (IIi).

This compound had a m.p. of 195-198° (26); hydrochloride m.p. 268-269°.

8-Methoxyquinol-4-ylhydrazine (IIj).

The hydrochloride of this compound had a m.p. of 268-270°.

Anal. Calcd. for $C_{10}H_{12}ClN_3O$: C, 53.22; H, 5.36; N, 18.62. Found: C, 52.81; H, 5.62; N, 18.98.

Quinol-4-ylhydrazine (IIk).

This compound had a m.p. of 134-136°; hydrochloride m.p. 298-301° (24).

1*H*-Pyrrolo[3,2-*c*]quinolines (IV-LII).

General method.

A mixture of 0.005 mole of a quinol-4-ylhydrazine, 0.005 mole of an appropriate carbonyl compound, 1.18 g. of sodium acetate, 7.5 ml. of water and 4 ml. of ethanol was heated under reflux for 1 hour. After this period the reaction mixture was diluted with 50 ml. of water and extracted with chloroform (4 x 10 ml.). After drying, the solvent was evaporated off *in vacuo* to give the hydrazone.

The hydrazone from the above was, without purification, taken up in 5 ml. of diethylene glycol and heated slowly to 100° and kept at this temperature for 10 minutes to drive off any vestiges of volatile materials. Afterwards the temperature was allowed to rise and the reaction mixture was heated under reflux for a further period of 10 minutes to 1 hour, cooled and diluted with 10 ml. of water. The precipitate was filtered and thoroughly washed with water to remove the solvent and dried in an oven at 100° and then crystallized from aqueous ethanol. The samples for elemental analyses were prepared by sublimation at 210-260°/2 mm.

The 1*H*-pyrrolo[3,2-*c*]quinolines (IV-LII) thus prepared are presented in Table I, their spectral properties in Table II, and their elemental analyses in Table III.

Thermocyclizations in Dowtherm.

As an alternative method for the cyclizations of hydrazones from the above procedure, Dowtherm was used in place of diethylene glycol. The hydrazones were taken up in 5 ml. of Dowtherm and heated under reflux for a period of 40 minutes. The reaction mixture was allowed to cool down to the room temperature and was diluted with 50 ml. of petroleum ether (b.p. 40-60°). The precipitate was filtered off and washed free of Dowtherm by using petroleum ether (b.p. 40-60°) and crystallized from aqueous ethanol. In this manner compounds XII, XXXI, XLIII, and XLIX were prepared in yields of 77, 54, 69, and 43%, respectively.

Alkylations.

General method (13).

To 2.6 ml. of dry dimethyl sulfoxide containing 0.35 g. of pulverized potassium hydroxide was added 1.3 millimoles of the 1*H*-pyrrolo[3,2-*c*]quinoline to be alkylated and the mixture was allowed to stir on a magnetic stir-plate until all the pyrroloquinoline is dissolved (1 hour). Afterwards, the mixture was cooled down to 0° and 1.6 millimoles of an alkyl iodide was added and left stir at the room temperature for 0.75 to 2 hours, diluted with 10 ml. of water and the precipitate filtered off and crystallized from aqueous ethanol. The *N*-alkylated products LIII-LIX were prepared in this manner and are listed in Table I, their spectra in Table II, and the elemental analyses in Table III.

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