N-Acetylphthalimide (7). Oxidation of 6.—Excess sodium dichromate dihydrate (50 mg., 2.7×10^{-4} mole) was added to **6** (10 mg., 5.2×10^{-5} mole) dissolved in glacial acetic acid (2 ml.) and acetic anhydride (1 ml.). After brief heating on a steam bath, the reaction mixture was allowed to stand in a dry air stream. The semisolid mass remaining was filtered, washed with water, and recrystallized from benzene to yield 5 mg. (53%) of **7**, m.p. 134–135° (lit.[18] m.p. 132–135°). The infrared spectrum of **7** was identical with that of an authentic sample prepared by a usual method.[18]

Formation of Phthalimide (8) from 6 and from 7.—Treatment of **6** or of **7** with excess aqueous acidic sodium dichromate followed by brief heating on a steam bath resulted in deposition of **8** which, when recrystallized from benzene, had m.p. 235–236° (lit.[5] m.p. 233.5°). Phthalimide thus obtained was shown by identical infrared spectra and an undepressed mixture melting point to be identical with that of an authentic sample (Eastman Kodak Co.).

Thermal Decomposition of 2.—Heating of **2** (0.6 g., 0.003 mole) in a test tube immersed in an oil bath at 167° for 10 min. yielded a dark brown tarry mass which was extracted with ligroin (b.p. 66–75°). Removal of solvent left 0.1 g. (25%) of **1**, m.p. 53–54° (lit.[18] m.p. 56°), identified by its infrared spectrum which was identical with that of an authentic sample.

α-Hydroxy-*o*-toluic Acid (9). Base-Catalyzed Hydrolysis of 2.—A mixture of **2** (1.0 g., 0.005 mole) and 40 ml. of aqueous sodium hydroxide (10% by weight) was heated at reflux for 3 hr. The hot solution was filtered, cooled in an ice bath, carefully acidified with 5 *N* hydrochloric acid, and extracted five times with ether. The ether extracts were dried over anhydrous sodium sulfate. Removal of the solvent on the steam bath left a white solid with a vinegar-like odor. Recrystallization from a benzene–ether mixture yielded 0.5 g. (66%) of **9**, m.p. 123.5–124.5° (lit.[19] m.p. 120°).

Anal. Calcd. for $C_8H_8O_3$: C, 63.16; H, 5.26; mol. wt., 152. Found: C, 63.34; H, 5.03; mol. wt., 150 ± 5.

An authentic sample of **9** was prepared using the method of Gardner and Naylor[20] for the preparation of the sodium salt of **9** and hydrolyzing this salt with 5 *N* hydrochloric acid at 0°. The product from base-catalyzed hydrolysis of **2** and the authentic sample of **9** were identical as shown by infrared spectra and mixture melting point behavior.

When **1** was allowed to react with 10% sodium hydroxide under the same conditions employed for base-catalyzed hydrolysis of **2**, **9** was obtained in nearly quantitative yield.

Phthalimidine (10). Acid-Catalyzed Hydrolysis of 2.—Treatment of **2** (1.34 g., 0.007 mole) with excess 3 *N* hydrochloric acid (30 ml.) at reflux for 30 hr. yielded a yellow solution containing a black semisolid. After filtration the mixture was reduced in volume on a rotary evaporator. The black gum remaining was recrystallized from acetone to yield 0.01 g. (11%) of **10**, m.p. 148–150° (lit.[21] m.p. 150°); **10** produced in this manner was shown to be identical with an authentic sample[21] by undepressed mixture melting point and identical infrared spectra.

Acknowledgment.—The authors wish to thank Mr. John C. Gilbert of Yale University for determination of the n.m.r. spectra.

(18) O. Aschan, *Ber.*, **19**, 1400 (1886).

(19) E. Hjelt, *ibid.*, **25**, 524 (1892).

(20) J. H. Gardner and C. A. Naylor, Jr., "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 526.

(21) C. Graebe, *Ber.*, **17**, 2598 (1884).

A Novel Synthesis of 2,3-Disubstituted Indoles. A Study of the Reductive Cyclizations of Some 3-Substituted 2-(4,5-Dimethoxy-2-nitrophenyl)acrylonitriles[1a]

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The reductive cyclizations of 3-substituted 2-(4,5-dimethoxy-2-nitrophenyl)acrylonitriles with iron and acetic acid constitute a rapid and convenient synthesis for many novel 2,3-disubstituted indoles. A reaction mechanism and the general scope of the new synthesis are presented.

The intramolecular cyclizations of aminoalkyl cyanides[2–4] and the reductive cyclizations of nitrophenylalkyl cyanides[5,6] have been extensively investigated for the syntheses of quinolizidines, 2-aminoindolenine,[7] and 3-substituted indoles. Generally these reactions involve intramolecular amidine formation by addition of an amino group to a nitrile function. Subsequent deamination of the amidine can occur under forcing hydrogenation conditions as shown by Boekelheide,[3] Walker,[5] Kebrle,[4] Heacock,[8] and other investigators.[9]

In connection with similar studies in these laboratories we wish to report a new synthesis for 2-substituted 5,6-dimethoxyindole-3-carbonitriles (Table II). The essential steps of this synthesis are (1) the condensation of 5,6-dimethoxy-2-nitrophenylacetonitrile with various aldehydes, and (2) reductive cyclization of the resulting β-substituted α-(4,5-dimethoxy-2-nitrophenyl)acrylonitriles (Table I) with iron and acetic acid. The second step of this synthesis proceeds smoothly by reduction of the nitro group followed by intramolecular Michael addition of the resulting basic nitrogen function to the α,β-unsaturated nitrile system (it is to be noted that most reductive cyclizations have been reported under the conditions of catalytic hydrogenation).

The proposed reaction mechanism[10a] is illustrated for the case of 3-(*p*-chlorophenyl)-2-(4,5-dimethoxy-2-

(1) (a) Presented at the 149th Meeting of the American Chemical Society, Detroit, Mich., April 1965. (b) To whom correspondence should be sent: Lakeside Laboratories, Division of Colgate-Palmolive Co., Milwaukee, Wis. 53201.

(2) R. Pschorr and G. Hoppe, *Ber.*, **43**, 2543 (1910).

(3) V. Boekelheide, W. J. Linn, P. O'Grady, and M. Lamborg, *J. Am. Chem. Soc.*, **75**, 3243 (1953).

(4) J. Kebrle and K. Hoffmann, *Helv. Chim. Acta*, **39**, 116 (1956).

(5) G. N. Walker, *J. Am. Chem. Soc.*, **77**, 3844 (1955).

(6) J. D. Loudon and I. Wellings, *J. Chem. Soc.*, 3470 (1960).

(7) C. A. Grob and O. Weissbach, *Helv. Chim. Acta*, **44**, 1748 (1961).

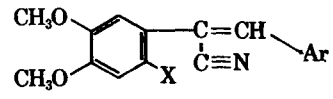
(8) R. A. Heacock, O. Hutzinger, B. D. Scott, J. W. Daly, and B. Witkop, *J. Am. Chem. Soc.*, **85**, 1825 (1963).

(9) H. Plieninger and I. Nógrádi, *Ber.*, **88**, 1961 (1955).

(10) (a) Although complete reduction to the amine followed by cyclization and oxidative dehydrogenation of dihydroindole by ferric ion is conceivable, the isolation of ferrous acetate from the reaction mixture and the extremely lower yield of indoles when less than 2 moles of iron was used for the reductive cyclization favor our proposed mechanism. (b) C. S. Marvel and O. Kamm, *J. Am. Chem. Soc.*, **41**, 278 (1919).

TABLE I

α,β-DISUBSTITUTED ACRYLONITRILES



Compd.	Ar	X	M.p., °C.	λ_{max}^{MeOH}, mμ (ε)	Yield, %	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N	Description
VI		NO_2	200–201	254 (20,000)	99	$C_{16}H_{13}N_3O_4$	61.73	4.21	13.50	61.51	4.42	13.46	Yellow crystals[a]
VII		NH_2	180–181	249 (14,750) 284 (15,600)	43.7	$C_{16}H_{15}N_3O_2$			14.94			15.11	Orange plates[b]
VIII		NO_2	204	247 (17,700) 291 (18,300)	94	$C_{16}H_{13}N_3O_4$	61.73	4.21	13.50	61.51	4.35	13.46	Yellow plates[a]
IX		NH_2	130–131.5	247 (14,750) 284 (15,200)	55	$C_{16}H_{15}N_3O_2$			14.94			14.74	Orange plates[b]
X		NO_2	187–188	245 (12,300) 322 (21,800)	85.4	$C_{15}H_{12}N_2O_4S$	56.83	3.82	8.86	57.01	3.97	8.91	Yellow plates[b]
XI		NO_2	181–182	244 (12,900) 316 (25,600)	85	$C_{15}H_{12}N_2O_5$	60.00	4.03	9.33	59.79	3.96	9.65	Gold needles[b]
XII		NO_2	200–201	237 (16,700) 319 (24,000)	90.5	$C_{18}H_{16}N_2O_5$	63.52	4.74	8.23	63.68	4.96	8.29	Yellow plates[a]
XIII		NO_2	213–214	246 (14,200) 289 (26,600)	95.5	$C_{18}H_{13}N_3O_4$	64.47	3.91	12.53	64.37	4.02	12.66	Yellow plates[b]
XIV		NO_2	123–124	223 (17,600) 244 (16,500) 328 (11,750)	75.5	$C_{21}H_{23}N_3O_4$	66.12	6.08	11.02	65.94	6.15	11.11	Orange needles[a]
XV		NH_2	147–148	239 (16,800) 328 (7500) 360 (19,100)	46	$C_{21}H_{25}N_3O_2$	71.77	7.17	11.96	71.75	7.23	12.04	Yellow crystals[b]

XVI		NO_2	105	230 (18,800) 311 (28,700)	88	$C_{23}H_{27}N_3O_6$	64.92	6.40	9.88	64.98	6.40	9.88	Yellow needles[b]
I		NO_2	176.5–177	223 (18,700) 295 (25,800)	91	$C_{17}H_{13}ClN_2O_4$	59.22	3.80	8.12	59.20	3.89	8.32	Yellow needle[b]
XVII		NH_2	112–115	235 (15,500) 330 (12,800)	83	$C_{17}H_{15}N_2O_2$			8.90			8.65	Yellow plates[c]
XXVIII		NO_2	161	248 (12,400)	93	$C_{17}H_{28}N_2O_4$	64.54	6.37	8.86	64.15	6.43	8.92	Yellow plates[b]
XIX		NO_2	193–194	247 (11,100) 337 (24,400)	78.5	$C_{15}H_{13}N_3O_4$	60.19	4.38	14.04	60.29	4.55	13.76	Orange needles[b]
XX		NO_2	182–183	249 (11,300) 342 (21,400)	94.5	$C_{16}H_{15}N_3O_4$	61.33	4.83	13.14	61.41	4.77	13.34	Orange plates[b]

[a] From ethanol. [b] From methanol. [c] From benzene.

nitrophenyl)acrylonitrile (I). Presumably the first step involves the reduction of the nitro group to give the hydroxylamine II; the hydroxylamine then participates in an intramolecular Michael addition followed by dehydration to give the 2,3-disubstituted indole V (Chart I, p. 2258).

Treatment of 2-(2-amino-4,5-dimethoxyphenyl)-3-(*p*-chlorophenyl)acrylonitrile (XVII) with acetic acid and iron failed to yield the indole V, indicating that an amino group is not involved in the cyclization step. It is known that phenylhydroxylamine is an intermediate in the reduction of nitrobenzene,[10b] and that *o*-aminostyrene yields dihydroindole in the presence of an acid catalyst.[11] Therefore, it is postulated that the phenylhydroxylamine II is the intermediate for the Michael condensation rather than *o*-aminophenylacrylonitrile XVII.

In order to evaluate the general scope and limitations of our indole synthesis, the reductive cyclizations of substituted acrylonitriles containing various aromatic or cycloalkyl groups on the β-position, such as 4-pyridyl, 3-pyridyl, 2-thienyl, 2-furyl, 4-methoxyphenyl, 4-cyanophenyl, 4-dialkylaminophenyl, 4-diethylaminoethoxyphenyl, 4-chlorophenyl, and cyclohexyl, have been investigated.

Condensation of 4,5-dimethoxy-2-nitrophenylacetonitrile with various aldehydes in the presence of catalytic amounts of piperidine, according to the procedure of Walker,[5] gave excellent yields (over 75%) of the desired 3-substituted 2-(4,5-dimethoxy-2-nitrophenyl)-acrylonitriles. The ultraviolet absorption spectra and other physical properties of these new compounds are presented in Table I.

Our synthesis was carried out by adding 2 moles of iron powder to a refluxing solution of the nitrile in glacial acetic acid and allowing it to reflux gently for 2 to 5 hr. The solvent was distilled under diminished pressure, and a crude product was purified by recrystallization. The yields varied from 36 to 82% depending upon the groups on the β-position of the acrylonitriles. The elemental analyses as well as ultraviolet absorption, infrared, and n.m.r. spectra supported the assignment of the indole structures (see Table II).

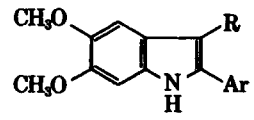
The influence of the substituents (β-position) on the cyclization step requires additional study. However, high yields (79–82.5%) were observed when the phenyl ring (β-position) contained a *p*-chloro or *p*-cyano group; whereas, lower yields (44.3–62.1%) were obtained when the phenyl ring had a *p*-methoxy, *p*-dimethylamino, or *p*-diethylaminoethoxy group. The reductive cyclization of 3-(2-furyl)-2-(4,5-dimethoxy-2-nitrophenyl)acrylonitrile (XI) gave the lowest yield (36%), presumably owing to the instability of the furan ring in the acid solution. The acrylonitriles containing the pyrrole rings (XIX and XX) failed to yield indoles under these conditions, apparently owing to low stability in acid.

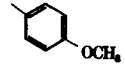
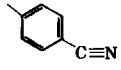
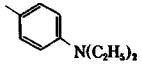
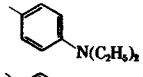
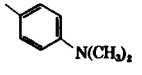
The selective hydrogenation of the nitro group of acrylonitrile XXXV in ethyl acetate with hydrogen (50 p.s.i.) at room temperature in the presence of 10% palladium on carbon gave fair yields (43.7–83%) of the β-substituted α-(2-amino-4,5-dimethoxyphenyl)-acrylonitrile XXXVI (also see Table I).

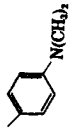
(11) P. Ruggli and O. Schmid, *Helv. Chim. Acta*, **18**, 1215 (1935).

TABLE II

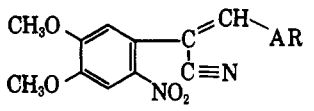
α,β-DISUBSTITUTED INDOLE



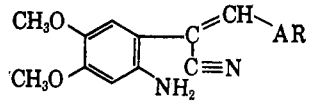
Compd.	Ar	R	M.p., °C.	λ_{max}^{MeOH}, mμ (ε)	Yield, %	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N	Description
XXI		—C≡N	321	224 (41,000) 354 (24,100)	72.5	$C_{16}H_{12}N_2O_2$	68.80	4.69	15.05	68.69	4.78	15.02	Yellow crystals
XXII		—C≡N	238–239	222 (35,000) 340 (21,900)	39	$C_{16}H_{12}N_2O_2$	68.80	4.67	15.05	68.70	4.88	15.01	Tan needles[a]
XXIII		—C≡N	207–208	234 (15,100) 344 (21,200)	50	$C_{15}H_{12}N_2O_2S$	63.36	4.25	9.85	63.33	4.57	9.55	White needles[a]
XXIV		—C≡N	180–181	237 (19,100) 336 (29,400)	36	$C_{15}H_{12}N_2O_3$	67.15	4.51	10.44	67.02	4.66	10.56	Tan crystals[a]
XXV		—C≡N	247–248	238 (22,800) 332 (27,600)	44.3	$C_{18}H_{16}N_2O_3$	70.11	5.23	9.09	69.83	5.32	9.26	Pink plates[a]
XXVI		—C≡N	283–284	219 (28,000) 242 (16,300) 359 (19,900)	79	$C_{18}H_{12}N_2O_2$	71.27	4.32	13.86	71.34	4.38	14.19	Pink crystals[a]
XXVII		—C≡N	254–255	225 (27,800) 330 (20,800)	55.5	$C_{17}H_{14}N_2O_2$	73.36	5.07	10.07	73.51	5.47	10.41	Yellow plates[b]
XXVIII		—C≡N	222–223	245 (14,000) 360 (31,500)	55	$C_{21}H_{23}N_3O_2$	72.18	6.63	12.03	72.16	6.39	12.03	Brown plates[a]
XXIX		—CH2NH—C(=O)—CH3	194	220 (31,200) 280 (12,400) 332 (37,000)	83.4	$C_{23}H_{29}N_3O_3$	69.85	7.39	10.63	69.74	7.48	10.82	White plates[c]
XXX		—C≡N	265–266	240 (20,300) 354 (36,800)	62.1	$C_{19}H_{19}N_3O_2$	71.01	5.96	13.08	71.34	6.17	13.22	White needles[a]

XXXI		$CH_2NH-\overset{O}{\overset{\|\|}{C}}-CH_3$	240–241	216 (26,900) 270 (10,000) 328 (27,800)	50	$C_{21}H_{25}N_3O_3$	68.64	6.86	11.44	68.35	6.80	11.31	White plates[d]
XXXII		—C≡N	165	233 (17,100)	45.8	$C_{23}H_{27}N_3O_3$	70.20	6.92	10.68	69.93	7.01	10.69	White needles[c]
V		—C≡N	284–285	236 (24,800) 331 (22,000)	82.5	$C_{17}H_{13}ClN_2O_5$	65.37	4.19	8.95	65.66	4.33	9.00	Yellow needles[c]
XXXIII		$CH_2-NH-\overset{O}{\overset{\|\|}{C}}-CH_3$	211	224 (37,000) 323 (33,200)	70	$C_{19}H_{19}ClN_2O_3$			7.80			7.87	White plates[d]
XXXIV		—C≡N	137–139	214 (39,500) 296 (12,500) 302 (11,900)	55.5	$C_{17}H_{20}N_2O_2$	71.80	7.01	9.85	71.47	7.12	9.72	Brown crystals[a]

[a] From methanol or dilute methanol. [b] From ethanol. [c] From benzene. [d] From benzene–ethanol.

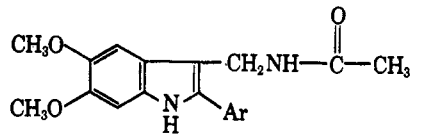


XXXV



XXXVI

When 2-substituted 3-cyano-5,6-dimethoxyindoles (V, XXVIII, and XXX) were subjected to hydrogenation in acetic anhydride over a nickel catalyst,[12] the method described by Gould, Johnson, and Ferris,[13] 3-N-acetamidomethylindoles (XXIX, XXXI, and XXXIII) were formed in good yield (50–92%).



XXXVII

By modification of the method of Whitmore and coworkers,[14] it was possible to effect cyanoethylation of V in 80% yield when dimethylformamide was used as a solvent. Hydrogenation of XXXVIII over nickel with acetic anhydride gave 80.6% yield of diacetamide XXXIX. The N-acylindole XL was obtained in 31.2% yield by allowing V to reflux with acetic anhydride for several hours (Chart II, p. 2258).

The versatility of the reaction has been demonstrated by the preparation of some 2-aryl-, 2-heterocyclic-, and 2-cycloalkyl-3-cyanoindoles, and appears to be of general utility for synthesizing 2,3-substituted indoles. As shown in Table II, it is possible by this method to prepare in relatively few steps novel indoles otherwise accessible only by fairly lengthy reaction schemes.

Experimental[15]

3-(*p*-Chlorophenyl)-2-(4,5-dimethoxy-2-nitrophenyl)acrylonitrile (I).—The procedure of Walker[5] was used. To a solution of 21 g. (0.094 mole) of 4,5-dimethoxy-2-nitrophenylacetonitrile in 200 ml. of refluxing methanol was added, in portions, 14 g. (0.1 mole) of *p*-chlorobenzaldehyde in 100 ml. of methanol and 5 ml. of piperidine. The reaction mixture was allowed to reflux for 4 hr. and cooled.

The reaction mixture was filtered and the yellow residue was recrystallized from methanol to yield 31 g. (91%) of 3-(*p*-chlorophenyl)-2-(4,5-dimethoxy-2-nitrophenyl)acrylonitrile (I) as yellow plates: m.p. 176.5–177°; λ_{max}^{MeOH} 223 mμ (ε 18,700) and 295 mμ (ε 25,800); λ_{max}^{KBr} 4.55 (conjugated —C≡N), 6.25, 6.38, and 6.63 μ.

Anal. Calcd. for $C_{17}H_{13}ClN_2O_4$: C, 59.22; H, 3.80; N, 8.12. Found: C, 59.20; H, 3.89; N, 8.32.

2-(2-Amino-4,5-dimethoxyphenyl)-3-(4-diethylaminophenyl)acrylonitrile (XV).—A solution of 3.74 g. (0.00983 mole) of 3-(4-diethylaminophenyl)-2-(2-nitro-4,5-dimethoxyphenyl)acryloni-

(12) Sponge nickel catalyst (approximately 50% solids) by W. R. Grace and Co., Cincinnati 29, Ohio.

(13) F. E. Gould, G. S. Johnson, and A. F. Ferris, *J. Org. Chem.*, **25**, 1658 (1960).

(14) F. C. Whitmore, R. R. Adams, R. B. Taylor, E. C. Chapin, C. Weisel, and W. Yanko, *J. Am. Chem. Soc.*, **66**, 725 (1944).

(15) Melting points are corrected. Infrared spectra were determined with a Perkin-Elmer Model 21 recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14, and n.m.r. spectra were determined on a Varian A-60 spectrometer at 60 Mc. and the values are reported in parts per million downfield from tetramethylsilane.

CHART I

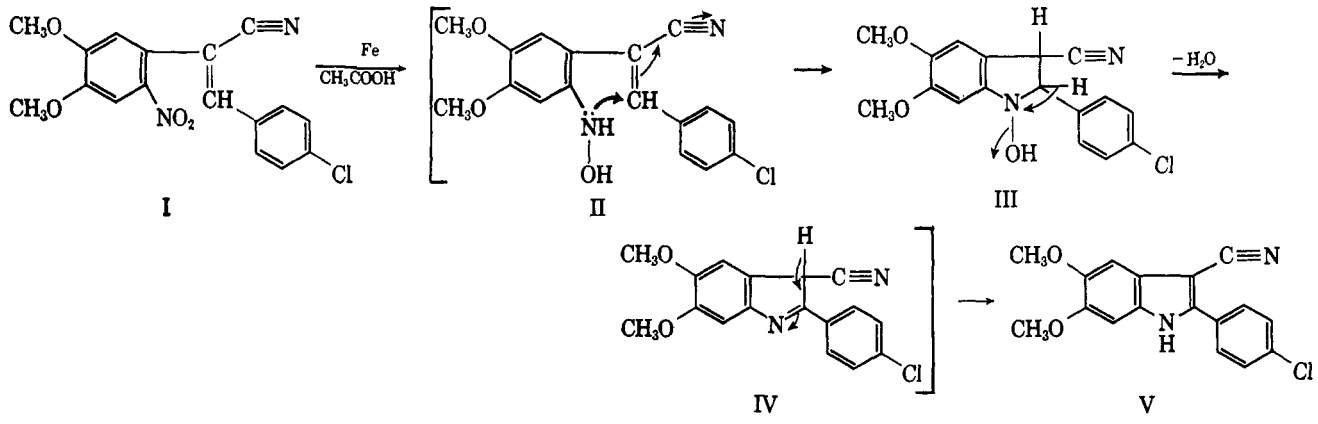
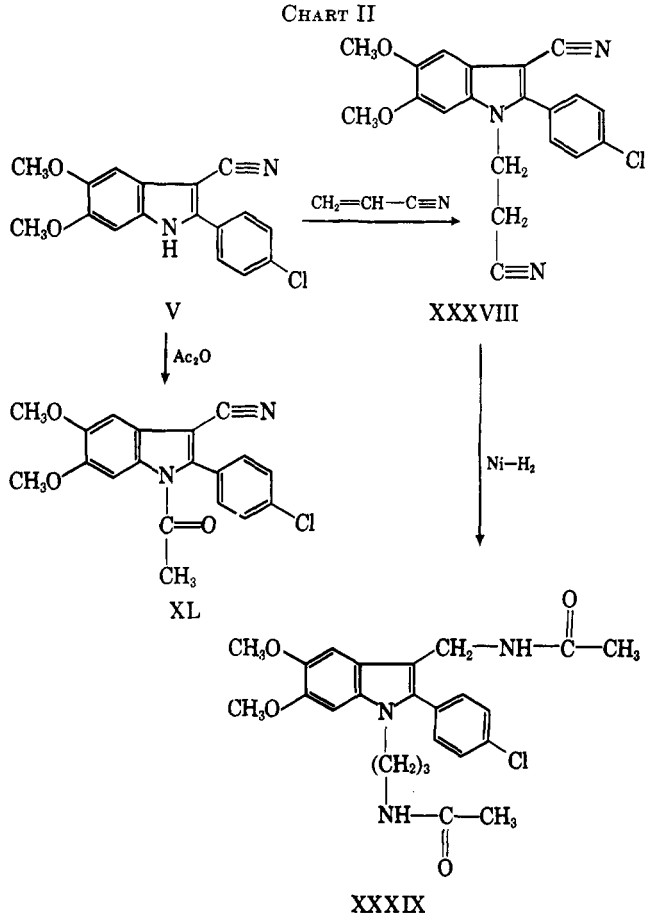


CHART II



trile in 150 ml. of ethyl acetate containing 1 g. of 10% palladium on carbon was shaken under hydrogen (35 lb.) at room temperature for 3.5 hr. The reaction mixture was filtered and the filtrate was distilled under diminished pressure. The residue was recrystallized from ethyl acetate to yield 1.57 g. (46%) of 2-(2-amino-4,5-dimethoxyphenyl)-3-(4-diethylaminophenyl)acrylonitrile (XV) as yellow crystals; m.p. 147–148°; λ_{max}^{MeOH} 239 mμ (ε 16,800), 328 (7500), and 360 (19,100); λ_{max}^{KBr} 4.56, 6.24, 6.33, and 6.60 μ; n.m.r. (10% in $CDCl_3$) 3.82 (OCH_3), 3.85 (OCH_3), 6.32 (vinyl H), 6.70, 6.75, 7.1, 7.3, 7.72, and 7.88 (6 aromatic H), 1.20 (CH_3, triplet, J = 7 c.p.s.), and 3.42 ($-CH_2-$, quartet, J = 7 c.p.s.) p.p.m.

Anal. Calcd. for $C_{21}H_{25}N_3O_2$: C, 71.77; H, 7.17; N, 11.96. Found: C, 71.75; H, 7.22; N, 12.04.

5,6-Dimethoxy-2-(4-pyridyl)indole-3-carbonitrile (XXI).—To a solution of 6 g. (0.0193 mole) of 2-(2-nitro-4,5-dimethoxyphenyl)-3-(4-pyridyl)acrylonitrile in 80 ml. of refluxing glacial acetic acid was added in portions 3.38 g. (0.0605 mole) of iron powder and the reaction mixture was allowed to reflux with stirring for 3 hr.

The reaction mixture was cooled and filtered, and the yellow residue was washed with water. The combined solution was treated with a saturated solution of $KHCO_3$ and the yellow product was filtered. The combined residue was recrystallized from methanol to yield 3.89 g. (72.5%) of 5,6-dimethoxy-2-(4-pyridyl)indole-3-carbonitrile (XXI) as yellow crystals: m.p. 321°; λ_{max}^{MeOH} 224 mμ (ε 41,000) and 354 mμ (ε 24,100); λ_{max}^{KBr} 3.43, 4.55 (conjugated —C≡N), and 6.23 μ; n.m.r. (10% in TFA) 4.09 (OCH_3), 4.12 (OCH_3), 7.19 (H-4 or H-7), 7.24 (H-4 or H-7), and 8.52–9.05 (broad unresolved pyridyl) p.p.m.

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.80; H, 4.69; N, 15.05. Found: C, 68.69; H, 4.78; N, 15.08.

2-(*p*-Chlorophenyl)-5,6-dimethoxyindole-3-carbonitrile (XXV).—To a refluxing solution of 24 g. (0.07 mole) of 3-(*p*-chlorophenyl)-2-(4,5-dimethoxy-2-nitrophenyl)acrylonitrile in 200 ml. of glacial acetic acid was added in portions 8 g. (0.14 mole) of iron powder and the reaction mixture was allowed to reflux with stirring for 4 hr.

The reaction mixture was cooled and filtered, and the residue was washed with hot methanol and water. After one recrystallization from methanol 18 g. (82.5%) of 2-(*p*-chlorophenyl)-5,6-dimethoxyindole-3-carbonitrile was obtained: as yellow needles, m. p. 284–285°; λ_{max}^{MeOH} 236 mμ (ε 24,800) and 331 mμ (ε 22,000); λ_{max}^{KBr} 3.05, 4.53 (conjugated —C≡N), 6.13, and 6.26 μ.

Anal. Calcd. for $C_{17}H_{13}ClN_2O_2$: C, 65.37; H, 4.19; N, 8.95. Found: C, 65.66; H, 4.33; N, 9.00.

N′-{[2-(*p*-Diethylaminophenyl)-5,6-dimethoxy-3-indolyl]-methyl}acetamide (XXIX).—A mixture of 7.6 g. (0.0217 mole) of 2-(*p*-diethylaminophenyl)-5,6-dimethoxyindole-3-carbonitrile, 6 g. of anhydrous sodium acetate, and 2 teaspoonfuls of nickel catalyst[11] in 150 ml. of acetic anhydride was shaken under hydrogen (50 lb.) at room temperature for 24 hr.

The reaction mixture was filtered and the filtrate was treated with ice water to hydrolyze the acetic anhydride. The resulting solution was neutralized with dilute sodium hydroxide solution and filtered, and the residue was recrystallized from benzene to give 7 g. (83.4%) of the amide XXIX as white plates: m.p. 194°; λ_{max}^{MeOH} 220 mμ (ε 31,200), 280 (12,400), and 332 (27,000); λ_{max}^{KBr} 3.03, 6.10, and 6.21 μ.

Anal. Calcd. for $C_{23}H_{29}N_3O_3$: C, 69.85; H, 7.39; N, 10.63. Found: C, 69.74; H, 7.48; N, 10.82.

2-(*p*-Chlorophenyl)-3-cyano-5,6-dimethoxy-1-indolepropionitrile (XXXVIII).—5,6-Dimethoxy-2-(*p*-chlorophenyl)indole-3-carbonitrile (5 g., 0.016 mole) was dissolved in a mixture of 145 ml. of dimethylformamide and 77 ml. of acrylonitrile while stirring in an ice bath. To the solution 6 ml. of 40% solution of benzyltrimethylammonium hydroxide was added, and the reaction mixture was allowed to stir 0.5 hr. with cooling and then was refluxed for 3 hr.

The reaction mixture was cooled and filtered, and the residue was recrystallized from dimethylformamide to yield 4.32 g. (74%) of the propionitrile XXXVIII as tan crystals: m.p. 262–264°; λ_{max}^{MeOH} 222 mμ (ε 30,100), 229 (12,900), and 317 (15,500); λ_{max}^{KBr} 4.50 (—C≡N) and 4.56 μ (conjugated —C≡N).

Anal. Calcd. for $C_{20}H_{16}ClN_3O_2$: C, 65.66; H, 4.41; N, 11.49. Found: C, 65.71; H, 4.58; N, 11.12.

3-Acetamidomethyl-1-acetamidopropyl-2-(*p*-chlorophenyl)-5,6-dimethoxyindole (XXXIX).—A mixture of 5 g. (0.0136 mole) of the above indolepropionitrile XXXVII, 10 g. of anhydrous sodium acetate, and 2 teaspoonfuls of nickel catalyst[11] in 200 ml.

of acetic anhydride was shaken under hydrogen (50 lb.) at room temperature for 6 hr.

The reaction mixture was filtered and the filtrate was distilled under diminished pressure. The residue was washed with water and recrystallized from dilute alcohol to yield 5.01 g. (80.6%) of the diamide XXXIX as white crystals: m.p. 226–227°; λ_{max}^{MeOH} 227 mμ (ε 37,900) and 313 mμ (ε 17,500); λ_{max}^{KBr} 3.06, 6.09, and 6.46 μ.

Anal. Calcd. for $C_{24}H_{28}ClN_3O_4$: C, 63.03; H, 6.16; N, 9.18. Found: C, 62.96; H, 6.16; N, 9.02.

1-Acetyl-2-(*p*-chlorophenyl)-5,6-dimethoxyindole-3-carbonitrile (XL).—A mixture of 5 g. (0.016 mole) of 2-(*p*-chlorophenyl)-5,6-dimethoxyindole-3-carbonitrile in 140 ml. of acetic anhydride was allowed to reflux for 5.5 hr., then stirred at room temperature for 19 hr. The reaction mixture was filtered, and the residue (the starting material and the desired product) was heated with benzene and filtered to separate the benzene-insoluble starting material. The filtrate, was cooled and 1.77 g. (31.2%) of 1-acetyl-2-(*p*-chlorophenyl)-5,6-dimethoxyindole-3-carbonitrile (XL) was obtained as tan plates: m.p. 266–267°; λ_{max}^{MeOH} 218 mμ (ε 10,800), 244 (10,800), and 327 (11,600); λ_{max}^{KBr} 4.42 (—C≡N), 5.83, and 6.22 μ.

Anal. Calcd. for $C_{19}H_{15}ClN_2O_3$: C, 64.32; H, 4.26; N, 7.89. Found: C, 64.43; H, 4.56; N, 7.89.

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Syntheses and Spectra of 7,7′-Bis(2,5-norbornadiene) and 7,7′-Bisquadricyclo[2.2.1.0^{2,6}.0^{3,5}]heptane[1,2]

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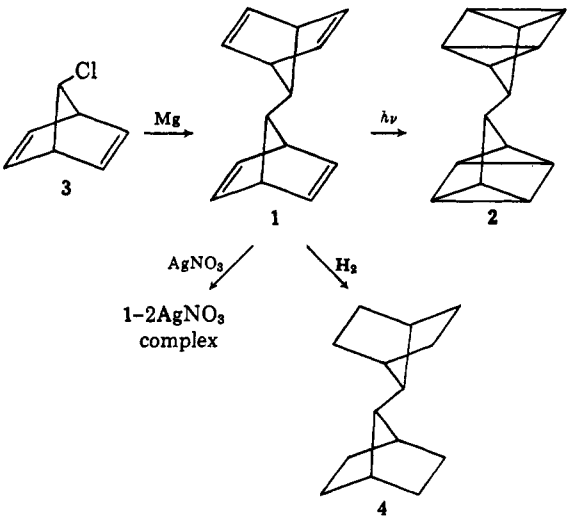
7,7′-Bis(2,5-norbornadiene) (1) and 7,7′-bisquadricyclo[2.2.1.0^{2,6}.0^{3,5}]heptane (2) were prepared. The detailed analysis of the first overtones of cyclopropyl CH stretching vibration in the near-infrared spectrum of 2 gave useful information on the structural investigations of cyclopropyl rings.

Whereas the chemistry of norbornadiene and its valence bond isomer, quadricyclene (quadricyclo[2.2.1.0^{2,6}.0^{3,5}]heptane),[3] has received considerable attention in recent years, that of their dimer appears to have not. During the course of study of the reactivity at the 7-position of norbornadiene system, we observed that treatment of 7-chloronorbornadiene with magnesium with the purpose of preparation of the Grignard reagent results in the instantaneous formation of the coupling product, 7,7′-bis(2,5-norbornadiene) (1). Preparation of 1 and its photochemical conversion to 7,7′-bisquadricyclo[2.2.1.0^{2,6}.0^{3,5}]heptane (2) are a part of this report. On the other hand, in connection with our other work,[6] we desired a powerful tool to demonstrate the presence of tertiary cyclopropyl hydrogens, in the case of which n.m.r. spectra can not usually provide good evidence, because the n.m.r. peaks of tertiary cyclopropyl hydrogens do not appear at high field characteristic of the cyclopropyl methylene protons.[7] It is known that the examination of near-infrared spectra provides a strong evidence for the presence of cyclopropyl hydrogens,[8–10] even in the case of a tertiary cyclopropyl hydrogen. In general, a cyclopropyl hydrogen is evidenced by the presence of carbon–hydrogen stretching vibration bands around 3000 cm.$^{-1}$ in the infrared region and by its first overtones in the near-infrared region. However, to our knowledge the detailed assignments and investigations of intensities of cyclopropyl hydrogens have not been reported so far. Since the compound 2 was purely isolable crystals[11] and thought to be a suitable model compound for the above kinds of investigations owing to the presence of abundant cyclopropyl hydrogens, we performed detailed analysis of the near-infrared spectrum of 2 and obtained useful information about the relative molecular extinction coefficients of aliphatic and cyclopropyl CH stretching vibrations,



(1) Part IX of a series on Bicyclic Systems. Part VIII: H. Tanida and Y. Hata, *J. Org. Chem.*, **30**, 977 (1965).

(2) Presented, in part, at the 17th Annual Meeting of the Chemical Society of Japan, Tokyo, April 1964.

(3) Quadricyclene was obtained in 1961 with the photoisomerization of norbornadiene by the two independent groups of investigators.[4,5]

(4) W. G. Dauben and R. L. Cargill, *Tetrahedron*, **15**, 197 (1961).

(5) G. S. Hammond, N. J. Turro, and A. Fisher, *J. Am. Chem. Soc.*, **83**, 4674 (1961); see also, G. S. Hammond, P. Wyatt, C. D. DeBoer, and N. J. Turro, *ibid.*, **86**, 2532 (1964).

(6) Part VIII. In this work, we had a compound, 2-cyanotricyclo[4.1.0.0^{3,7}]heptane, in which the presence of a cyclopropyl ring was demonstrated by the analysis of the near-infrared spectrum.

(7) L. M. Jackmann, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p. 52.

(8) W. H. Washburn and M. J. Mahoney, *J. Am. Chem. Soc.*, **80**, 504 (1958).

(9) J. Meinwald, A. Lewis, and P. G. Gassman, *ibid.*, **84**, 977 (1962).

(10) P. G. Gassman, *Chem. Ind.* (London), 740 (1962).

(11) Since the highly strained ring system of quadricyclene is thermodynamically less favored than the ring system of norbornadiene, the facile thermal reversion of quadricyclene to norbornadiene is usually observed.[4,5] Thus due to the labile nature of the ring system and the oily nature, the isolation of a pure sample of quadricyclene and thereby a program in the area of quadricyclene chemistry were often accompanied by some technical difficulties.