Condensation and Cyclization Catalyzed by Strong Bases. A New Route to Benzoquinolizine and Benzoquinolizinium Derivatives

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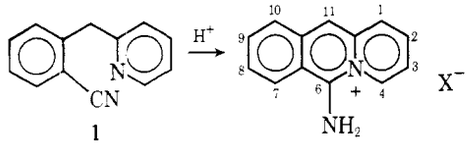
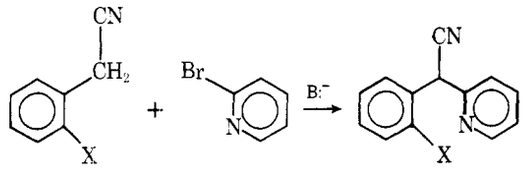
The base-catalyzed reaction of α-cyano-*o*-tolunitrile with 2-halopyridines (and analogues) affords 11-cyano-6*H*-benzo[*b*]quinolizin-6-one imine (**9**) and its congeners in modest yield. All of these imines are easily hydrolyzed to the corresponding quinolizinones (e.g., **10**). The action of hydrogen bromide on **9** converts it to the 6-amino-11-cyanoacridizinium ion (**11**).

Earlier research from this laboratory[1] showed that the acid-catalyzed cyclization of 2-(2-cyanobenzyl)pyridine (**1**) led to salts of the 6-aminoacridizinium (benzo[*b*]quinolizinium) ion. Unfortunately, the only known route to **1** involved ring opening of the acridizinium ion in the presence of hydroxylamine followed by dehydration of the resulting oxime. While such a reaction sequence should constitute a plausible route to derivatives of **2**, there appeared to be advantage in



1 **2**

seeking a more direct pathway. The patent literature[2-4] had reported that phenylacetonitrile (**3**) in the presence of sodium amide would undergo condensation with 2-bromopyridine in 30–58% yield. It appeared plausible that substitution of the commercially available α-cyano-*o*-tolunitrile (**4**) for phenylacetonitrile (**3**) would afford a 2-(2-cyanobenzyl)pyridine derivative (**6**) similar to **1** except for an extra nitrile function.



3, X = H
4, X = CN

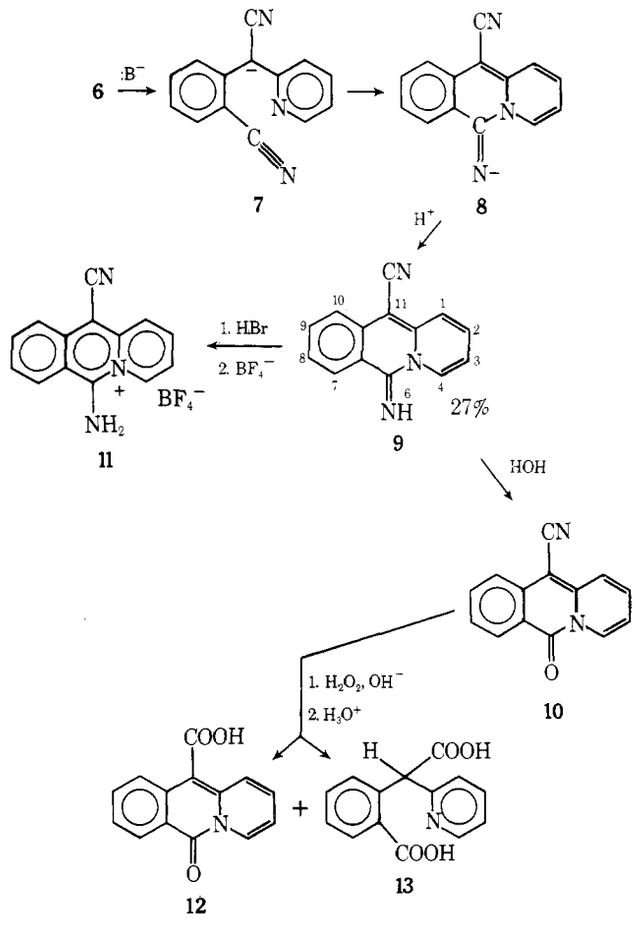
5, X = H
6, X = CN
(not isolated)

Since the anion from α-cyano-*o*-tolunitrile (**4**) is known to undergo self-condensation with great ease,[5] the anion was generated in the presence of an excess of the *o*-bromopyridine (or *o*-bromopyridine analogue) by addition of the mixture of bromopyridine and nitrile **4** in glyme to a solution of sodium ethoxide in the same solvent. The initial reaction mixture was yellow-orange, but after a 12-h reflux it had become dark brown. Although the product consisted of a complex mixture, extraction and crystallization procedures afforded an orange solid with physical properties which did not correspond to those of any known self-condensation product. Consistent with our expectations for the dinitrile **6** the low-resolution mass spectrum of the product exhibited a molecular ion at a *m/e* value of 219. However the IR suggested the presence of an imine as well as a nitrile function and the UV visible spectrum indicated the presence of more conjugation than would be possible with the dinitrile **6**.

These data plus reactions to be discussed later could be explained by assuming that any of the dinitrile **6** formed would immediately be converted to its ambident anion **7**, which could cyclize to anion **8** which, upon acidification, would afford 11-cyano-6*H*-benzo[*b*]quinolizin-6-one imine (**9**). A convincing argument for the correctness of **9** as the structural formula of the product isolated can be seen in Table I, where a direct comparison is made of the electronic spectral data for our new product with those of 6*H*-benzo[*b*]quinolizin-6-one imine prepared earlier by the addition of hydroxide ion to the 6-aminoacridizinium cation. The close agreement of the electronic spectrum of the new product **9** with that of the parent compound is remarkable and provides convincing evidence that the chromophores of the two systems are very similar.

Characteristic of a compound bearing an imine group the new product **9** is readily hydrolyzed, even by aqueous acetic acid. The hydrolysis is accompanied by a color change, the imine (**9**, Scheme I) being orange while the quinolizinone (**10**) is yellow. An attempt to separate the two compounds (**9** and **10**) chromatographically on alumina gave results that indicated that even alumina served as a catalyst for the hydrolysis. This catalysis was demonstrated by heating the pure imine

Scheme I



7 **8** **9** **11** **10** **12** **13**

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Table I. Comparison of Electronic Spectral Data of 6*H*-Benzo[*b*]quinolizin-6-one Imine with that of Its (presumed) 11-Cyano Derivative (9) in 95% Ethanol Solution

6*H*-benzo[*b*]-quinolizin-6-one imine[a]		11-cyano derivative (9)[b]	
λ_{max}, nm	log ϵ	λ_{max}, nm	log ϵ
475	3.30	478	3.62
450	3.66	454	3.90
429	3.84	426	3.93
403	4.01	298	4.05
387	3.98	378	3.99
337	3.58		
325	3.49	322	3.81
		309	3.74
		269	4.09
260	4.12	260	4.11
241	4.45	242	4.45
235	4.48	233	4.47

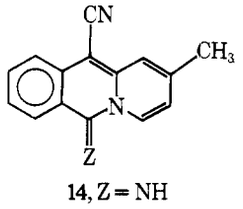
[a] Registry no.: 7561-83-3. [b] Registry no.: 66749-71-1.

9, mp 244–245 °C, in 95% ethanol with a small amount of suspended alumina. The product isolated in quantitative yield was the pure quinolizinone derivative (**10**), mp 284–285 °C.

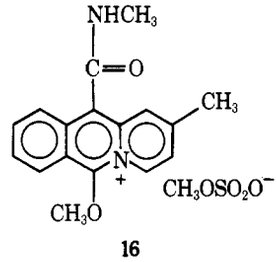
This facile hydrolysis has complicated the isolation of a pure acridizinium derivative (**11**). This could be accomplished by addition of hydrogen bromide to the imine **9** under essentially anhydrous conditions. A comparison of the electronic spectral data for **11** (as the tetrafluoroborate salt) with those obtained from 6-aminoacridizinium chloride (**2**) is shown in Table II. Again the spectral evidence appears to confirm our structural assignment.

Treatment of the cyanoquinolizinone **10** with alkaline hydrogen peroxide, followed by acidification, gave both the 11-carboxy-6*H*-benzo[*b*]quinolizine-6-one (**12**) and a dicarboxylic acid **13** formed by opening of the amide linkage. At least some of the carboxyquinolizinone **12** may be an artifact produced during the acidification process, since it is known that α-(2-pyridyl)toluic acid undergoes cyclization rapidly in the presence of a trace of mineral acid.[2]

Similar results were obtained in the condensation of α-cyano-*o*-tolunitrile (**4**) with 2-bromo-4-methylpyridine, a 29% yield of the expected imine (**14**) being obtained.



14, Z = NH
15, Z = O



16

Aside from the methyl signal at δ 2.23 the most notable feature in the proton NMR of **14** was a signal at δ 7.2–7.9 corresponding to a proton which exchanged on treatment with deuterium oxide. The unsubstituted imine **9** had an exchangeable proton at δ 8.67. There appears to be a paucity of NMR data for the imine signal in the literature: a value of δ 7.37 being reported[6] for the ketimine present in the polymer of malononitrile and δ 9.4 being listed for the imine resonance in diphenylketimine.[7] Perhaps accounting in part for the scarcity of data, Roberts[7] et al. have reported that the imine proton is rarely detectable in several common deuterated solvents. It was observed that the unsubstituted imine (**9**) underwent exchange in deuteriochloroform even in the absence of deuterium oxide, although several days were required for completion.

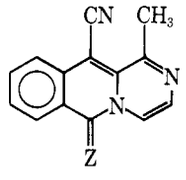
Table II. Comparison of Electronic Spectral Data of 6-Aminoacridizinium Ion with Those of 6-Amino-11-cyanoacridizinium Ion

6-aminoacridizinium ion[a] (**2**)		11-cyano-6-aminoacridizinium ion[b] (**11**)	
λ_{max}, nm	log ϵ	λ_{max}, nm	log ϵ
		450	2.93
427	3.88	426	3.81
405	4.04	412	4.01
380	4.06	379	4.16
340	3.68	362	4.03
257	4.25	257	4.38
241	4.56		
235	4.55	233	5.02

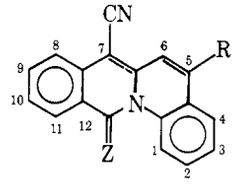
[a] In 95% ethanol as the chloride. Registry no.: 7547-90-2. [b] In acetonitrile as the tetrafluoroborate. Registry no.: 66749-73-3.

The amide (**15**) obtained by hydrolysis of the methylquinolizine imine (**14**) underwent an interesting reaction when heated at 150 °C with dimethyl sulfate. On the basis of spectral data and elemental analysis the new compound has been assigned as **16**.

2-Bromopyridine analogues which have been found to undergo the condensation–cyclization reaction with α-cyano-*o*-tolunitrile include 2-chloro-3-methylpyrazine, yielding **17** (7%), and 2-chloroquinoline and 2-chloro-4-methylquinoline, yielding **19** and **21** in yields of 44 and 49%, respectively.



17, Z = NH
18, Z = O



19, Z = NH; R = H
20, Z = O; R = H
21, Z = NH; R = CH_3
22, Z = O; R = CH_3

After completion of this project, but before completion of the manuscript, Douglass and Hunt[8] described an alternate route to 7-cyano-12*H*-dibenzo[*b*,*f*]quinolizin-12-one imine (**19**) via the reaction of quinoline 1-oxide with α-cyano-*o*-tolunitrile in the presence of acetic anhydride and triethylamine. Interestingly, the related dibenzoquinolizine derivative (**20**) which they obtained by hydrolysis of **19** had been prepared earlier[9] by a method similar to ours except that methyl α-cyano-*o*-toluate had been used instead of α-cyano-*o*-tolunitrile.

As a route to benzoquinolizine derivatives our method offers the advantages of being general yet requiring only a single operation using commercially available starting materials, advantages which may outweigh the modest yields obtained.

Experimental Section

The elemental analyses were carried out by M-H-W Laboratories, Garden City, Michigan. Melting points were determined in capillary tubes with a Thomas-Hoover melting point apparatus and are uncorrected. Ultraviolet absorption spectra were determined with a Beckman Model DB-G spectrometer and infrared spectra were taken in KBr disks with a Perkin-Elmer Model 237 spectrometer. ^{1}H NMR spectra were obtained at 60 MHz on a Varian T-60 spectrometer using tetramethylsilane as the internal standard.

Generalized Condensation–Cyclization Procedure. A three-neck flask is fitted with two reflux condensers, a glass-covered magnetic stir bar, and a glass stopper, all previously dried in an oven. Atop

one reflux condenser is placed a dropping funnel, and the entire system is protected with calcium chloride drying tubes and maintained under a static N_2 atmosphere.

The flask is charged with 1.1–1.2 equiv of NaH and about 100 mL of glyme freshly distilled from $LiAlH_4$. An excess of absolute ethanol was added dropwise to the NaH suspension ultimately resulting in a clear solution.

Commercial grade α-cyano-o-tolunitrile, purified by vacuum distillation and recrystallization from methanol (1 equiv), and 2 equiv of the 2-halopyridine (or analogue) were dissolved in dry glyme and added dropwise to the rapidly stirred mixture. Initially an orange solution is generated which turns to a brown suspension. After addition is complete the mixture, still under N_2 atmosphere, was refluxed for 12–24 h.

The reaction mixture was cooled to room temperature and poured into five volumes of water containing 1 equiv of NH_4Cl and a weighed amount of filter-aid. An immediate precipitation occurred. The precipitate was collected, washed with water, and dried in a vacuum oven at 50 °C. The dried solid was extracted in a Soxhlet extractor for 15 h with 200 mL of ethyl acetate. Concentration of the yellow or orange solution afforded the cyclized product, which frequently needed purification by column chromatography on alumina in addition to crystallization.

11-Cyano-6*H*-benzo[*b*]quinolizin-6-one Imine (9). Starting with 2-bromopyridine and following the standard procedure **9** was obtained, mp 237–242 °C, in 27% yield after an 18-h reflux. Without chromatography, but after recrystallization from 1-butanol, the analytical sample was obtained as long orange needles: mp 244–245 °C; UV_{max} (95% ethanol) 478 (sh) (log ε 3.62), 454 sh (3.90), 426 (3.93), 398 (4.05), 378 sh (3.99), 322 (3.81), 309 (3.74) 269 (4.09), 260 (4.11), 242 sh (4.45), 233 nm (4.47); IR (KBr) 3340 (C=NH), 2209 cm^{-1} (CN); ^1H NMR ($CDCl_3$) δ 6.70 (m, 1), 7.15–8.05 (m, 6), 8.67 (br s, 1, C=NH), 9.24 (d, 1, J = 8 Hz, C-4); mass spectrum m/e (rel intensity) 219 (70), 192 (10), 164 (6). Anal. ($C_{14}H_9N_3$) C, H, N.

6-Amino-11-cyanoacridizinium Tetrafluoroborate (11). Dry HBr was bubbled through a solution of 0.44 g of the imine **9** in 40 mL of dry glyme. The yellow precipitate was collected and dissolved in 15 mL of hot water. After filtration to remove a small amount of undissolved solid a concentrated aqueous solution of sodium tetrafluoroborate was added, precipitating 0.40 g (65%) of the expected salt **11**. The salt crystallized from acetonitrile as yellow needles: mp 247–249 °C; UV_{max} (CH_3CN) 450 sh (log ε 2.93), 426 (3.81), 412 (4.01), 379 (4.16), 362 sh (4.03), 268 sh (4.34), 257 sh (4.38), 233 nm (5.02); IR (KBr) 3355–3215 (NH_2), 2225 (CN), 1080 cm^{-1} (BF_4). Anal. ($C_{14}H_{10}BF_4N_3$) C, H, N.

11-Cyano-6*H*-benzo[*b*]quinolizin-6-one (10). To 5 mL of water in 45 mL of acetic acid 1.25 g of the imine **9** was added and the mixture was refluxed for 1 h. The solution was concentrated to 20 mL. The addition of 20 mL of water immediately precipitated 1.25 g (99%) of yellow solid, mp 283–285 °C. The analytical sample was obtained as long yellow needles: mp 284–285 °C; UV_{max} (95% ethanol) 452 (log ε 3.70), 427 (3.93), 394 sh (4.04), 384 (4.17), 363 sh (4.06), 309 (3.78), 296 (3.73), 265 (4.21) 238 (4.52), 235 nm (4.51); IR (KBr) 2208 (CN), 1690 cm^{-1} (C=O, amide); NMR (CF_3COOH) δ 7.10 (m, 1), 7.33–8.07 (m, 5), 8.30 (d, 1, J = 7 Hz), 8.98 (d, 1, J = 7 Hz). Anal. ($C_{14}H_8N_2O$) C, H, N.

Since the amide (**10**) is easily formed by hydrolysis of the imine (**9**) it appears as a byproduct in its preparation. When the preparation of 11-cyano-6*H*-benzo[*b*]quinolizin-6-one imine (**9**) was carried out essentially as described except that the unrecrystallized product was subjected to column chromatography on alumina, elution of the yellow band (amide) and orange band (imine) followed by hydrolysis with dilute acetic acid afforded the amide **10** in 32% yield, mp 283–285 °C.

A similar experiment carried out with 2-chloro instead of 2-bromopyridine afforded only a 21% yield of amide **10**.

11-Carboxy-6*H*-benzo[*b*]quinolizin-6-one (12). To a suspension of 0.2 g of amide **10** in 15 mL of 95% ethanol, 5 mL of 2 N NaOH was added along with 5 mL of 30% H_2O_2. After the mixture was stirred for 4 h at room temperature it was refluxed for an additional 2 h. The cooled mixture was acidified and diluted with water. Extraction with methylene chloride and evaporation of the solvent afforded 0.09 g (40%) of a dull yellow solid, which recrystallized to afford yellow microcrystals: mp 205–210 °C; IR (KBr) 2690–2490, (COOH, H-bonded), 1702–1680 (C=O, acid, amide), 1285 cm^{-1} (COOH). Anal. ($C_{14}H_9NO_3 \cdot \frac{1}{2}H_2O$) C, H, N.

α-(2-Pyridyl)-o-carboxyphenylacetic Acid (13). The hydrolysis was carried out as for **12** except that refluxing was continued for 18 h and the reaction mixture was carefully neutralized. The residue obtained by extraction with CH_2Cl_2 and evaporation of the solvent afforded 0.18 g (32%) of the diacid **13**. Pure **13** was obtained from ethanol as colorless needles: mp 217–222 °C; UV_{max} (95% ethanol) 266, 231 sh, 227 nm; IR (KBr) 2670–2470 (H-bonded COOH), 1705–1680 (C=O), 1280 cm^{-1} (COOH); ^1H NMR [$(D_3C)_2SO$] δ 7.41–8.27 (m, 7), 8.50 –8.67 (m, 1). Anal. ($C_{14}H_{11}NO_4 \cdot \frac{1}{4}H_2O$) C, H, N.

11-Cyano-2-methyl-6*H*-benzo[*b*]quinolizin-6-one Imine (14). The standard procedure was used with 2-bromo-4-methylpyridine and the orange chromatographic band was collected separately and the solvent was removed, affording 0.63 g (5.4%) of the imine **14**, mp 227–229 °C. Recrystallization from 1-butanol afforded orange platelets: mp 229–230; UV_{max} (95% ethanol) 473 sh (log ε 3.48), 443 sh (3.78), 394 (4.01), 322 (3.71), 309 (3.62), 269 sh (3.95), 256 sh (3.96), 236 sh (4.41), 232 nm (4.43); IR (KBr) 3310 (C=NH), 2210 cm^{-1} (CN); ^1H NMR ($CDCl_3$) δ 2.33 (s, 3, 2-Me), 6.47 (m, 1), 7.23–7.93 (m, 6, one H exchangeable with D_2O), 8.86 (d, 1, J = 8 Hz). Anal. ($C_{15}H_{11}N_3$) C, H, N.

11-Cyano-2-methyl-6*H*-benzo[*b*]quinolizin-6-one (15). The remaining orange-yellow and yellow chromatographic fractions from the preceding experiment were combined and the solute was subjected to hydrolysis in dilute acetic acid, affording 2.73 g (23.3%) of **15**, mp 263–265 °C. Recrystallization from acetic acid afforded yellow needles: mp 264.5–265 °C; UV_{max} (95% ethanol) 452 sh (log ε 3.76), 420 sh (3.87), 382 (4.21), 364 sh (4.18), 309 (3.72), 297 (3.67), 262 sh (4.24), 232 nm (4.57); IR (KBr) 2210 (CN), 1685 cm^{-1} (C=O, amide); ^1H NMR (CF_3COOH) δ 2.39 (s, 3, 2-Me), 6.78 (d, 1, J = 7 Hz), 6.96–8.06 (m, 5) and 8.52 (d, 1, J = 7 Hz). Anal. ($C_{15}H_{10}N_2O$) C, H, N.

6-Methoxy-11-(*N*-methylcarbamoyl)-2-methylacridizinium Methylsulfate (16). A suspension of 0.86 g of the amide (**15**) in 10 mL of dimethyl sulfate was heated for 5 h at 150 °C and the cooled reaction mixture was poured into anhydrous ether. The ether layer was decanted from an oil which was fractionally crystallized from ethanol. From the more soluble fraction 0.25 g (18%) of a yellow solid, mp 255–259 °C, was obtained. The analytical sample was recrystallized from acetonitrile: mp 259–262 °C; UV_{max} (95% ethanol) 426 sh, 342, 312, 242 sh, 222 nm; IR (KBr) 1657 cm^{-1} (C=O, amide); ^1H NMR (CF_3COOH) δ 2.58 (s, 3, 2-Me), 3.86 (s, 3, CONHMe), 3.95 (s, 3, $MeSO_2O^-$), 4.25 (s, 3, OMe), 7.03–7.37 (m, 1), 7.70–8.27 (m, 4), 8.47–9.00 (m, 2). Anal. ($C_{18}H_{20}N_2O_6S$) C, H, N.

11-Cyano-1-methyl-2-aza-6*H*-benzo[*b*]quinolizin-6-one Imine (17). Using 2-chloro-3-methylpyrazine in the general procedure there was obtained from the ethyl acetate extract a solid which did not completely dissolve in methylene chloride. Recrystallization of this residue from 1-butanol yielded 2.8% of the imine **17** as deep orange needles: mp 240–242 °C; UV_{max} (95% ethanol) 458 sh (log ε 3.98), 437 (3.90), 392 (3.91), 373 (3.88), 303 sh (3.71), 291 sh (3.77), 237 nm (4.44); IR (KBr) 3325 (C=NH), 2198 cm^{-1} (CN); ^1H NMR (CF_3COOH) δ 3.63 (s, 3, 1-Me), 7.90–9.10 (m, 7). Anal. ($C_{14}H_{10}N_4$) C, H, N.

11-Cyano-1-methyl-2-aza-6*H*-benzo[*b*]quinolizin-6-one (18). Chromatography of the methylene chloride solution and slow elution with benzene afforded a yellow solid which once recrystallized from 10:1 acetic acid/water afforded 0.51 g (4.35 %) of **18**: mp 270–272 °C dec; UV_{max} (95% ethanol) 438 sh (log ε 3.88), 424 sh (3.97), 383 (405), 364 sh (4.00), 270 sh (4.08), 236 nm (4.44); IR (KBr) 2208 (CN), 1690 cm^{-1} (C=O, amide); ^1H NMR (CF_3COOH) δ 3.67 (s, 3, 1-Me), 7.68 (d, 1, J = 6 Hz, C-4), 8.01–8.64 (m, 3), 8.86 (m, 1), 9.27 (d, 1, J = 6 Hz, C-3). Anal. ($C_{14}H_9N_3O$) C, H, N.

Condensation–Cyclization with 2-Chloroquinoline and 2-Chloro-4-methylquinoline. The standard procedure was followed.

For imine **19** the yield was 44% of yellow solid, mp 208–212 °C, which was recrystallized from 1-butanol: mp 210–212 °C [lit.[8] 214–215 °C]; UV_{max} (95% ethanol) 464 (log ε 3.77), 438 (4.04), 417 (4.03), 398 (3.95), 314 (4.09), 301 (4.01), 279 (4.07), 238 nm (4.50); IR (KBr) 3250 (C=NH), 2198 cm^{-1} (CN). Anal. ($C_{18}H_{11}N_3$) C, H, N.

Imine **21** was obtained (before chromatography) as a yellow solid, mp 215–218 °C, in 49% yield, but this was probably contaminated with the higher melting amide **22**. A sample was purified by chromatography and recrystallization from 1-butanol: mp 211–212 °C; UV_{max} (95% ethanol) 464 sh (log ε 3.84), 438 (4.08), 414 (4.08), 392 sh (4.02), 311 (4.16), 301 (4.17), 279 sh (4.12), 236 nm (4.51); IR (KBr) 3245 (C=NH), 2203 cm^{-1} (CN); ^1H NMR δ 2.81 (s, 3, Me), 7.67–9.30 (m, 10).

7-Cyano-12*H*-dibenzo[*b*,*f*]quinolizin-12-one (20) and its 5-Methyl Derivative (22). As reported by Douglass and Hunt[8] the imine **19** undergoes hydrolysis to the amide **20**, mp 191–192 °C (lit.[8,9] 189–190, 190 °C). Anal. ($C_{18}H_{10}N_2O$) C, H, N.

The hydrolysis of the homologous imine **21** gave the expected amide **22**, which crystallized from acetic acid: mp 231–232 °C; UV_{max} (95% ethanol) 420 (4.05), 404 (4.26), 386 (4.24), 306 (4.08), 295 (4.11), 279 sh (4.12), 236 (4.55), 232 nm sh (4.54); IR (KBr) 2213 (CN), 1676 cm^{-1}

(C=O, amide); ^{1}H NMR (CF_3COOH) δ 2.19 (s, 3, Me), 6.76 (s, 1), 7.03–7.63 (m, 6), 7.88–8.02 (m, 1), 8.70 (m, 1). Anal. ($C_{19}H_{12}N_2O$) C, H, N.

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Registry No.—**4,** 3759-28-2; **10,** 66749-74-4; **12,** 66749-75-5; **13,** 66749-76-6; **14,** 66749-77-7; **15,** 66749-78-8; **16,** 66749-80-2; **17,** 66749-81-3; **18,** 66749-82-4; **19,** 63702-24-9; **20,** 63702-25-0; **21,** 66749-83-5; **22,** 66749-84-6; 2-bromopyridine, 109-04-6; 2-bromo-4-methylpyridine, 4926-28-7; 2-chloro-3-methylpyrazine, 95-58-9; 2-chloroquinoline, 612-62-4; 2-chloro-4-methylquinoline, 634-47-9.

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A Convenient Synthesis of Azidothiophenes and Some of Their Reactions

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Several azidothiophenes have been prepared by treatment of lithium thiophene derivatives with *p*-toluenesulfonyl azide and subsequent fragmentation of the intermediate triazene–lithium salts. High yields have been obtained for all 3-azido compounds; conversely, yields are low in the case of 2-azido derivatives. 2-Azido- and 3-azidothiophene have been converted to the corresponding 1-(thienyl)-1,2,3-triazoles by reaction with acetylene or dimethyl acetylenedicarboxylate. Thermal decomposition of 3-azidothiophene and 3-azidobenzo[*b*]thiophene in acetic anhydride or in a mixture of acetic and polyphosphoric acids has been investigated as a possible route to thienooxazoles.

The azido group represents a very attractive starting group in organic synthesis.[1] Heteroaromatic azides derived from five- and six-membered rings containing nitrogen can be obtained by nucleophilic displacement of a suitable leaving group by azide ion.[1,2] Heteroaromatic azides derived from five-membered rings containing sulfur and oxygen have received only scant attention. For example, Gronowitz and coworkers[3] reported the preparation of 3-azido-2-formylfurano and -thiophen by nucleophilic displacement of the corresponding 3-bromo derivatives with azide ion. However, no azides could be obtained from 2- and 4-bromo-3-formylthiophene, 5-bromo-2-formylthiophene, and bromothiophenes carrying electron withdrawing groups thus limiting the scope of this reaction. Moreover this method is unsuited for the preparation of the parent azides or those carrying electron releasing groups.

We wish to report a convenient synthesis of azidothiophenes and some of their reactions. We have found that azidothiophenes can be obtained by treatment of the corresponding lithium derivatives with *p*-toluenesulfonyl azide and subsequent fragmentation of the resulting triazene salts.[4] Thus, treatment of an ethereal solution of 3-lithium thiophene with tosylazide at −70 °C for 4–5 h and decomposition of the resulting triazene salt with an aqueous solution of tetrasodium pyrophosphate at room temperature afforded 3-azidothiophene (**1**) in 85% yield.

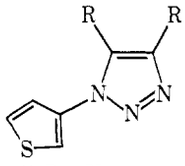
The azides **2–6, 9,** and **10** reported in Table I were prepared analogously; 3-azido-2-formylthiophene (**7**) and 4-azido-3-formylthiophene (**8**) were obtained by hydrolysis with 2 N HCl of the corresponding acetals (**3** and **4**).

All 3-azidothiophenes (**1** and **3–8**) and 3-azidobenzo[*b*]-thiophene (**10**) are stable compounds which showed no sign of decomposition on standing in the dark at room temperature for several days; 2-azidothiophene (**2**) and 2-azidobenzo[*b*]-thiophene (**9**) are somewhat unstable at room temperature but can be stored in the dark at low temperature for some days. The low yields obtained in the preparation of these two latter azides are attributed in part to some decomposition taking place during the fragmentation of the intermediate triazene salt and workup of the reaction mixture.[6]

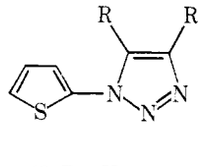
All azido compounds prepared in this work were characterized by spectra (IR, NMR, MS) and, when possible, elemental analysis.

The IR spectra showed the expected N_3 asymmetric stretching absorption in the region 2080–2100 cm^{-1}. The mass spectra showed, in addition to the parent ion, the expected peaks corresponding to loss of a nitrogen molecule [M − 28] and peaks due to subsequent loss of HCN. In particular, in the mass spectra of 2-azidothiophene (**2**) and 2-azidobenzo[*b*]-thiophene (**9**), the molecular ion peaks were noticeably less intense than the corresponding peaks of the 3-azido derivatives; this trend is in line with the reduced stability observed with 2-azido compounds.

Azides **1** and **2** were allowed to react with acetylene and dimethyl acetylenedicarboxylate at room temperature for 48–56 h affording the 1-(3-thienyl)-1,2,3-triazoles, **11** and **12,**



11, R = H
12, R = $COOCH_3$



13, R = H
14, R = $COOCH_3$

and 1-(2-thienyl)-1,2,3-triazoles, **13** and **14,** respectively, in almost quantitative yield.

On the other hand reaction of 3-azidothiophene (**1**) with acetic anhydride under reflux gave 3-diacetylamino-2-acetoxythiophene (**16**) in 52% yield as the only identifiable product. The formation of compound **16** is not unexpected

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