freshly cracked cyclopentadiene was added and after 3 weeks at room temperature, another 9 ml. After a total of 65 weeks, the solution was concentrated at room temperature under reduced pressure. Addition of ether precipitated a crude brown solid, mp 200–208° dec. Recrystallization from acetonitrile–ethyl acetate yielded a brown, microcrystalline solid, mp 212° dec. NMR [$(CD_3)_2SO$] was complex and poorly defined, but there was no indication of resonance in the δ 9 region (iminium hydrogen).

Anal. Calcd for $C_{15}H_{18}BrNO$: C, 58.45; H, 5.89; N, 4.54. Found: C, 58.43; H, 5.92; N, 4.59.

***syn*-2-Methyl-5-nitro-1,4-(Δ^{12}-cyclopenteno)-1,4-dihydroisoquinolinium Hexafluorophosphate (18).** Freshly cracked cyclopentadiene (20 ml) was added to a solution of 5 g of 2-methyl-5-nitroisoquinolinium hexafluorophosphate (**16**) in 20 ml of anhydrous acetonitrile. After 17 hr was allowed for reaction at room temperature, the solution was concentrated under reduced pressure. On addition of ether to the residue, the salt precipitated as an oil which was washed with ether followed by removal under vacuum of all volatile materials. The solid residue remaining, 4.1 g (69%), was twice recrystallized from acetone–ethyl ether: mp 140° dec; NMR (CD_3CN) δ 1.47–2.87 (m, 2, C-11), 2.87–3.70 (m, 2, C-9, C-10), 3.82 (s, 3, Me), 5.33 (m, 2, C-12, C-13), 5.67 (d, 1, C-1), 5.85 (q, 1, C-4), 7.37–8.27 (m 3, aromatic), 8.94 ppm (m, 1, C-3 iminium). Spin decoupling experiments confirmed the assignment of the multiplet at δ 8.94 to the proton at position 3.

Anal. Calcd for $C_{15}H_{15}F_6N_2O_2P$: C, 45.01; H, 3.78; N, 7.00. Found: C, 45.02; H, 3.70; N, 6.90.

Addition Product (19) from Reaction of 2 Mol of 1-Methoxycyclohexene with 1 Mol of 16. To a solution of 4 g (12 mmol) of 2-methyl-5-nitroisoquinolinium hexafluorophosphate (**16**), 12 g (107 mmol) of 1-methoxycyclohexene was added and the mixture was allowed to stand for 30 days at room temperature. The solvents and excess methoxycyclohexene were romoved under reduced pressure. The product was precipitated by addition of ethyl ether and was collected and washed with ether, yield 5.8 g (87%). Twice recrystallized from acetonitrile–ethyl alcohol, it afforded colorless plates: mp >185° dec; NMR (CD_3CN, spectrum complex and not all resonances identified) δ 3.31 (s, 3, O-Me), 3.49 (s, 3, O-Me), 7.58–8.37 ppm (m, 3, aromatic).

Anal. Calcd for $C_{24}H_{33}F_6N_2O_4P$: C, 51.61; H, 5.96; N, 5.02. Found: C, 51.64; H, 6.07; N, 5.07.

Registry No.—**1b**, 54409-89-1; **1b** methosulfate analog, 54409-90-4; **1c**, 54409-92-6; **1c** iodide analog, 54409-93-7; **2b**, 54409-95-9; **2c**, 54446-45-6; **3**, 54409-97-1; **4**, 54409-99-3; **5**, 54410-01-4; **6**, 54410-03-6; **7**, 54446-47-8; **8**, 54446-49-0; **9**, 54410-05-8; **10**, 54410-07-0; **11**, 54410-09-2; **12**, 54446-51-4; **13a**, 54410-39-8; **13b**, 54482-30-3; **14**, 54446-53-6; **16**, 54410-10-5; **16** methosulfate analog, 54410-11-6; **17**, 54410-12-7; **18**, 54410-14-9; **19**, 54410-16-1; styrene, 100-42-5; *p*-methoxystyrene, 637-69-4; ethyl vinyl ether, 109-92-2; vinyl acetate, 108-05-4; 2,3-dimethylbutadiene, 513-81-5; β-pinene, 127-91-3; cyclopentadiene, 542-92-7; 1,3-cyclohexadiene, 592-57-4; 1-methoxycyclohexene, 931-57-7; indene, 95-13-6; norbornene, 498-66-8; 3-methyl-5-nitroisoquinoline, 18222-17-8; dimethyl sulfate, 77-78-1; hexafluorophosphoric acid, 16940-81-1; 3-methyl-5-aminoisoquinoline, 54410-17-2; acetic anhydride, 108-24-7; 2-ethoxypropene, 926-66-9; 5-nitroisoquinoline, 607-32-9; 2-methylisoquinolinium bromide, 54410-18-3.

References and Notes

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Cyclization of the Quaternary Salts of Some Heterocyclic Derivatives[1]

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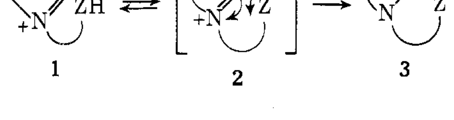
In the presence of a suitable base, certain aromatic or iminium quaternary salts having a nucleophilic group at an appropriate place of the N$^+$–R chain undergo nucleophilic cyclization. This cyclization has been applied to phenanthridinium, isoquinolinium, and 1,4-bridged 1,4-dihydroisoquinolinium salts using nucleophilic anions derived from the 4,4-dicarbethoxybutyl (e.g., **4** → **5**), the 2-mercaptoethyl (e.g., **10** → **12**), and 2-hydroxyethyl (**17** → **21**) groups.

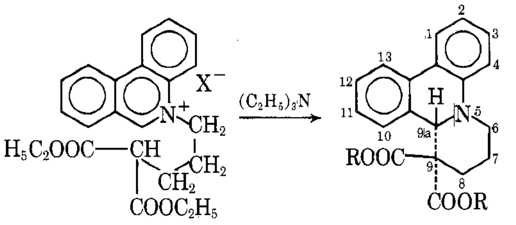
In 1962, Kröhnke and Zecher[2] showed that the quaternary salt formed by the reaction of phenacyl bromide and isoquinoline would condense with hydroxylamine hydrochloride and cyclize to yield a [2,1-*a*]imidazoisoquinoline derivative.[3] Later work[4–6] showed that the use of hydrazine on quaternary salts of the same general type led to triazino derivatives.

It was suggested[5] that there must exist several types of cyclization involving a nucleophilic attack on an electron-deficient carbon atom of an aromatic quaternary salt. A more general statement of this reaction may be seen in Scheme I, in which the quaternary salt might be either an iminium or a quaternary aromatic salt. The ZH group of **1** must be sufficiently more acidic than the α methylene group of the salt to prevent nonproductive ylide formation, and the base used should be of low nucleophilicity. The tendency of the anion to undergo cyclization (**2** → **3**) is a function of the size of the ring being formed, the nucleophilicity of Z, and the proportion of the total resonance energy lost in the transformation **1** → **3**.

Scheme I



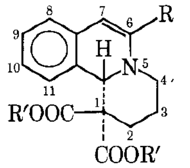
One possibility was the use of a carbanion as a nucleophile. The quaternary salt **4**, produced by the action of ethyl γ-bromopropyl malonate[7] on phenanthridine, was allowed to react for 2 hr at room temperature with triethylamine, affording, in 64% yield, a compound having the properties expected for the nucleophilic cyclization product (5). The new product (5) had not only a new benzylic hydrogen clearly identifiable by NMR but also *two* sets of signals corresponding to ethyl groups in different environments, a clear indication that cyclization had occurred as indicated. The cyclization product (5), when refluxed for 24 hr in methanol containing methoxide ion, underwent ester exchange, and the new product (6) clearly showed two methyl signals separated by δ 0.63. Attempts to aromatize **5** by the action of picric acid, ferric chloride, iodine, or trityl tetrafluoroborate all resulted in ring opening affording the appropriate salt of **4.** Ring opening was also effected by anhydrous or aqueous acids.



4

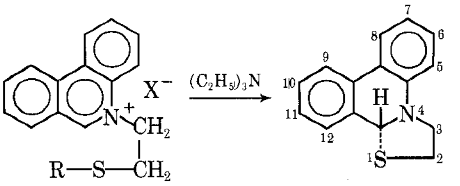
5, R = C_2H_5
6, R = CH_3

Isoquinolinium salts corresponding to 4 likewise underwent cyclization in the presence of triethylamine to yield products (**7, 8**) which were less stable than those from phenanthridine but could be purified for analysis. The dimethyl ester (**9**) showed only a δ 0.25 difference in the position of the two OMe signals in the NMR.



7, R = H; R′ = C_2H_5
8, R = CH_3; R′ = C_2H_5
9, R = H; R′ = CH_3

Another example of nucleophilic cyclization is afforded by the 5-(β-mercaptoethyl)phenanthridinium system (**10**). This cannot be prepared directly but is easily available through hydrolysis of the acetate ester **11.** Cyclization of the thiol **10** in the presence of triethylamine afforded 2,3-dihydro-12b*H*-thiazolo[3,2-*f*]phenanthridine (**12**) in 47% yield. The product was notable for giving NMR evidence of the lack of symmetry in the environment of the methylene protons at C-3.

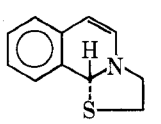


10, R = H
11, R = CH_3CO

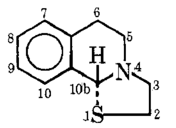
12

The isoquinolinium analog of **10** apparently underwent a similar type of cyclization, for the crude product gave an NMR spectrum compatible with **13**, but an attempted recrystallization appeared to undergo disproportionation affording the dihydro derivative (**14**).

A severe limitation of the application of this general type of nucleophilic cyclization to the quaternary salts of aromatic bases is the tendency of the cyclization products to undergo ring opening with resonance energy of the restored aromatic system providing the driving force. An ideal system for the application of the nucleophilic cyclization would be a nonaromatic iminium system which would be more reactive and would lead to more stable products.

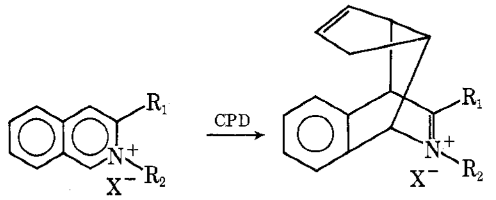


13



14

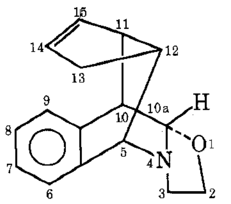
Recently it has been shown that quaternary isoquinolinium salts undergo cycloaddition (e.g., **15** → **18**) with the creation of iminium salts,[8-10] and that these can be made to undergo addition reactions[10,11] with a nucleophile. Present evidence indicates that iminium salts (e.g., **19**) derived from isoquinolinium salts (**16**) having no substituent at position 3 may be more reactive than those having such a substituent (e.g., **18**). Simple adducts of type **19** have proven elusive.[11]



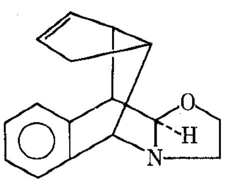
15, $R_1 = R_2$ = Me
16, R_1 = H; R_2 = Me
17, R_1 = H; $R_2 = CH_2CH_2OH$

18
19
20

Isoquinoline was quaternized with β-hydroxyethyl bromide, and the resulting salt (**17**, X = Br) was converted to the hexafluorophosphate (X = PF_4), which was allowed to react with cyclopentadiene. The adduct (presumably **20**) was allowed to react for several hours with aqueous potassium carbonate, affording a 60% yield of a base (**21**) which, on the basis of NMR evidence, is clearly a single geometrical isomer. Assuming only that the orientation of the cyclopentadiene during the cycloaddition is the same as that for the 2,3-dimethylisoquinolinium cation (**15**),[12] the product must have the endo (**21a**) or exo (**21b**) configuration. The endo configuration (**21a**) seems more attractive mechanistically, since cyclization to the exo isomer should be impeded by the cyclopenteno bridge. It is of interest that the addition of cyanide ion to an isoquinolinium adduct[10] has been found to occur most rapidly from the endo side.



21a



21b

Experimental Section

The elemental analyses were carried out by M-H-W Laboratories, Garden City, Mich. Melting points were determined in capillary tubes with a Thomas-Hoover apparatus and are uncorrected. Except as noted, proton magnetic resonance spectra were obtained at 60 MHz on Varian A-60 and T-60 spectrometers.

5-(4,4-Dicarboxybutyl)phenanthridinium Bromide Diethyl Ester (4, X = Br). A mixture of 7.2 g (0.04 mol) of phenanthridine[13] and 14 g (0.05 mol) of ethyl 3-bromopropylmalonate[7] was heated for 24 hr at 100°. The crude product which had solidified was crystallized from ethanol–hexane, yielding 15.2 g (83%) of colorless crystals, mp 136–142°. The analytical sample had mp 147–148° (from hot ethanol); NMR ($CDCl_3$) δ 1.20 (t, 6, *J* = 7 Hz, 2 CH_3), 2.35 (br s, 4, 2 CH_2), 3.57 (br t, 1, CH), 4.15 (q, 4, *J* = 7 Hz, 2 CH_2O), 5.67 (br t, 2, NCH_2), 8.62 (m, 8, aromatic), 11.53 ppm (s, 1, aromatic); ir (KBr) 1690, 1670 cm^{-1} (carbonyl).

Anal. Calcd for $C_{23}H_{26}BrNO_4$: C, 60.01; H, 5.69; N, 3.04. Found: C, 59.82; H, 5.55; N, 2.96.

Diethyl 7,8-Dihydro-6*H*-pyrido[1,2-*f*]phenanthridine-9,9(9a*H*)-dicarboxylate (5). To a solution of 2.3 g (5 mmol) of 5-(4,4-dicarboxybutyl)phenanthridinium bromide diethyl ester (4) in 500 ml of chloroform, 1.01 g (10 mmol) of triethylamine was added and the mixture was allowed to remain for 2 hr at room temperature. The chloroform and excess triethylamine were removed under reduced pressure, then 50 ml of water was added and the mixture was extracted three times with ether. The combined ether extracts were dried (Na_2SO_4) and concentrated and the residue was crystallized from hot hexane, affording 1.25 g (64%) of colorless prisms: mp 88–89°; NMR ($CDCl_3$) δ 0.66 (t, 3, *J* = 7 Hz, CH_3), 1.05 (t, 3, *J* = 7 Hz, CH_3), 2.17 (m, 3) 3.33 (m, 3), 4.12 (2 q, 4, *J* = 7 Hz, 2 CH_2O), 5.28 (s, 1, C-9a H), 7.22 (m, 8, aromatic).

Anal. Calcd for $C_{23}H_{25}NO_4$: C, 72.80; H, 6.64; N, 3.69. Found: C, 73.05; H, 6.58; N, 3.65.

The dimethyl ester (6) was obtained by suspending 1 g (2.6 mmol) of the diethyl ester 5 in 30 ml of methanol and adding a solution of sodium methoxide formed by dissolving 0.1 g (0.0043 g-atom) of sodium metal in 30 ml of methanol. The flask was protected from external moisture and refluxed for 24 hr. The methanol was evaporated and the residue was distributed between ether and water. The ethereal layer was dried (Na_2SO_4) and concentrated and the residue was crystallized from methanol: mp 64–65°; NMR ($CDCl_3$) δ 2.75 (m, 6, CH_2 at C-6, C-7, C-8), 2.88 (s, 3, CH_3), 3.52 (s, 3, CH_3), 5.22 (s, 1, C-9a H), 7.15 ppm (m, 8, aromatic).

Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.67; H, 6.16; N, 3.98. Found: C, 71.58; H, 6.10; N, 3.92.

Reactions of the Diethyl Ester (5). An attempt to dehydrogenate 5 by the action of trityl tetrafluoroborate in anhydrous acetonitrile at room temperature afforded the tetrafluoroborate of the open-chain product (4, X = BF_4), mp 170–171.5 (from ethanol).[14]

Other attempted dehydrogenations included the use of anhydrous ferric chloride for 1 hr at room temperature (in chloroform), iodine for 24 hr at room temperature (in anhydrous tetrahydrofuran), and picric acid, heating on a steam bath for 10 min (in 95% ethanol). With the exception of the last experiment, in which the product was isolated as the picrate,[14] mp 114–115°, all products were identified by conversion to the tetrafluoroborate (4, X = BF_4).

An attempt to isolate the hydrobromide of 5 by passing anhydrous hydrogen bromide into an ether solution of 5 afforded the ring-opened product (4, X = Br).

2-(4,4-Dicarboxybutyl)isoquinolinium Bromide Diethyl Ester. This was prepared by the action of ethyl 3-bromopropylmalonate on isoquinoline essentially as in the preparation of 4 (X = Br) except that the heating period was 3 days and a sample of the oily crude bromide (90% yield) was converted to the perchlorate by treating a methanol solution with a methanol–water solution of sodium perchlorate. Recrystallization from ethanol afforded colorless crystals of the perchlorate: mp 91–92°; NMR ($CDCl_3$) δ 1.20 (t, 6, *J* = 7 Hz, 2 CH_3), 2.13 (br s, 4, 2 CH_2), 3.50 (t, 1, *J* = 7 Hz, CH), 4.15 (q, 4, *J* = 7 Hz, 2 CH_2O), 4.88 (br t, 2, NCH_2), 8.27 (m, 6, aromatic), 9.95 ppm (s, 1, aromatic).

Anal. Calcd for $C_{19}H_{24}ClNO_8$: C, 53.09; H, 5.63; N, 3.26. Found: C, 53.21; H, 5.52; N, 3.11.

2-(4,4-Dicarboxybutyl)-3-methylisoquinolinium Bromide Diethyl Ester. This was made essentially as in the case of the lower homolog except that the bromide crystallized on addition of ether, affording 95% yield of bromide: mp 65–66°; ir (KBr pellet) 1717 cm^{-1} (carbonyl).

The perchlorate was prepared for analysis: white plates, mp 98–99.5°; uv max ($CHCl_3$) 349, 342, 279, 268, and 244 nm; NMR ($CDCl_3$) δ 1.20 (t, 6, *J* = 7 Hz, 2 CH_3), 2.10 (br s, 4, 2 CH_2), 2.90 (s, 3, CH_3), 3.47 (br t, 1, CH), 4.18 (q, 4, *J* = 7 Hz, 2 CH_2O), 4.80 (br t, 2, NCH_2), 8.15 (m, 5, aromatic), 9.83 ppm (s, 1, aromatic).

Anal. Calcd for $C_{20}H_{26}ClNO_8$: C, 54.12; H, 5.90; N, 3.15. Found: C, 54.17; H, 5.93; N, 3.16.

Diethyl 3,4-Dihydro-2*H*-benzo[*a*]quinolizine-1,1(11b*H*)-dicarboxylate (7). This was prepared essentially as was 5 except that 2-(4,4-dicarboxybutyl)isoquinolinium bromide diethyl ester was used, affording 1.19 g (36%) of yellow crystals: mp 95–96.5° (96.5–97° pure); NMR ($CDCl_3$) δ 0.82 (t, 3, *J* = 7 Hz, CH_3), 1.13 (t, 3, *J* = 7 Hz, CH_3), 1.86 (m, 4, 2 CH_2), 3.45 (m, 2, CH_2), 4.03 (2 q, 4, *J* = 7 Hz, 2 OCH_2), 5.03 (d, 1, *J* = 7 Hz, C-7 H), 5.28 (s, 1, C-11b H), 5.92 (d, 1, *J* = 7 Hz, C-6 H), 6.87 ppm (m, 4, aromatic).

Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.32; H, 7.16; N, 4.25.

Diethyl 3,4-Dihydro-6-methyl-2*H*-benzo[*a*]quinolizine-1,1(11b*H*)-dicarboxylate (8). This was prepared in 45% yield (mp 91–94°) essentially as was the lower homolog (7). The analytical sample was crystallized from hot methanol: mp 93.5–95°; NMR ($CDCl_3$) δ 0.88 (t, 3, *J* = 7 Hz, CH_3), 1.13 (t, 3, *J* = 7 Hz, CH_3), 1.90 (s, 3, CH_3), 2.58 (m, 6, CH_2, C-2, C-3, C-4), 4.13 (2 q, 4, *J* = 7 Hz, 2 OCH_2), 5.08 (s, 1, C-7 H), 5.37 (s, 1, C-11b H), 6.80 ppm (m, 4, aromatic); uv max ($CHCl_3$) 334, 246 nm.

Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.94; H, 7.33; N, 4.07. Found: C, 69.73; H, 7.39; N, 4.18.

Dimethyl 3,4-Dihydro-2*H*-benzo[*a*]quinolizine-1,1(11b*H*)-dicarboxylate (9). Ester interchange of the diethyl ester 7 was carried out in methanol as in the case of **5 → 6.** Recrystallization from methanol afforded a 55% yield of colorless prisms: mp 89–91.5°; NMR ($CDCl_3$) δ 1.22–3.80 (m, 6, 3 CH_2), 3.40 (s, 3, CH_3), 3.67 (s, 3, CH_3), 5.27 (d, 1, *J* = 7 Hz, C-7 H), 5.45 (s, 1, C-11b H), 6.10 (d, 1, *J* = 7 Hz, C-6 H), 7.10 ppm (m, 4, aromatic).

Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.60; H, 6.56; N, 4.52.

5-(2-Mercaptoethyl)phenanthridinium Bromide Acetate (11, X = Br). Heating 15 g (82 mmol) of *S*-(2-bromoethyl)thiolacetate[15] at 110° for 24 hr with 14.3 g (80 mmol) of phenanthridine resulted in the solidification of the melt. The crude product was suspended in ethyl acetate and collected. Recrystallization from methanol–ethyl acetate yielded 20 g (70%) of small, yellow plates: mp 206–208° (pure 210°); NMR [$(CD_3)_2SO$–D_2O] δ 1.93 (s, 3, CH_3), 3.23 (t, 2, *J* = 7 Hz, SCH_2), 4.93 (t, 2, *J* = 7 Hz, CCH_2), 8.05 (m, 8, aromatic), 9.50 ppm (s, 1, aromatic).

Anal. Calcd for $C_{17}H_{16}BrNOS$: C, 56.36; H, 4.45; N, 3.86. Found: C, 56.26; H, 4.35; N, 3.76.

The perchlorate,[14] mp 205.5–206.5°, was crystallized from methanol.

5-(2-Mercaptoethyl)phenanthridinium Chloride (10, X = Cl). Refluxing 15 g of the bromide acetate (11, X = Br) overnight with 125 ml of 6 *N* hydrochloric acid followed by concentration of the mixture under reduced pressure afforded an oil which solidified on standing. The crude product (11.5 g, 100%, mp 98–103°) was used directly in the cyclization, but a small sample of the hexafluorophosphate (10, X = PF_6) was prepared for analysis: mp 216–217°; NMR [$(CD_3)_2SO$–D_2O] δ 3.60 (s, 2, SCH_2), 5.43 (s, 2, CH_2), 8.65 (m, 8, aromatic), 10.08 ppm (s, 1, aromatic).

Anal. Calcd for $C_{15}H_{14}F_6NPS$: C, 46.76; H, 3.66; N, 3.63. Found: C, 46.60; H, 3.39; N, 3.42.

2,3-Dihydro-12b*H*-thiazolo[3,2-*f*]phenanthridine (12). To a suspension of 11 g (40 mmol) of 5-(2-mercaptoethyl)phenanthridinium chloride (10, X = Cl) in 500 ml of reagent-grade chloroform, the minimum quantity of methanol necessary to effect complete solution was added. The solution was stirred at room temperature while 8 g (80 mmol) of triethylamine was added dropwise, after which it was allowed to stand for 12 hr. The mixture was concentrated under vacuum to a volume of about 100 ml. The solution was extracted twice with water, the chloroform layer was dried (Na_2SO_4), the chloroform and excess triethylamine were removed, and the product was further purified by chromatography on neutral alumina, using ether as a solvent, yielding 4.6 g (47.5%) of colorless crystals: mp 127–128°; NMR ($CDCl_3$) δ 2.92 (m, 3, CH_2 and C-3 H), 4.50 (m, 1, C-3 H), 6.00 (s, 1, C-12b H), 7.35 ppm (m, 8, aromatic).

Anal. Calcd for $C_{15}H_{13}NS$: C, 75.26; H, 5.49; N, 5.85. Found: C, 75.04; H, 5.48; N, 5.75.

2-(2-Mercaptoethyl)isoquinolinium Bromide Acetate. This was prepared essentially as in the case of the analog (11, X = Br), except that the quaternization of isoquinoline by *S*-(2-bromoethyl)thiolacetate was carried out for 48 hr in the dark at room temperature. Recrystallization of the crude solid from ethanol–ethyl acetate afforded a 95% yield of colorless, hygroscopic crystals: mp 133–135°; NMR ($CDCl_3$) δ 2.20 (s, 3, CH_3), 3.72 (t, 2, *J* = 7 Hz, SCH_2), 5.41 (t, 2, *J* = 7 Hz, CCH_2), 8.57 (m, 6, aromatic), 11.1 ppm (s, 1, aromatic).

The perchlorate was crystallized from methanol: mp 117–118°; uv max ($CHCl_3$) 342, 335, 330, 285, 280, 278, 252 nm.

Anal. Calcd for $C_{13}H_{14}ClNO_5S$: C, 47.06; H, 4.25; N, 4.20. Found: C, 46.86; H, 4.15; N, 4.14.

2-(2-Mercaptoethyl)isoquinolinium Bromide. Hydrolysis of 16 g (50 mmol) of 2-(2-mercaptoethyl)isoquinolinium bromide acetate was carried out by refluxing it overnight in 100 ml of 48% hydrobromic acid. The excess acid was removed by evaporation under reduced pressure followed by heating for 12 hr under vacuum at 100°. The product consisted of light yellow, hygroscopic crystals (13.5 g, 100%): NMR [$(CD_3)_2SO$] δ 3.37 (t, 2, J = 7 Hz, SCH_2), 3.97 (s, 1, SH), 5.01 (t, 2, J = 7 Hz, CCH_2), 8.57 (m, 6, aromatic), 10.53 ppm (s, 1, aromatic).

Anal. Calcd for $C_{11}H_{12}BrNS$: C, 48.90; H, 4.48; N, 5.18. Found: C, 48.68; H, 4.36; N, 4.99.

2,3,6,10b-Tetrahydro-5*H*-thiazolo[2,3-*a*]isoquinoline (14). The cyclization of 2-(2-mercaptoethyl)isoquinolinium bromide (10 g, 37 mmol) was carried out under a nitrogen atmosphere essentially as in the cyclization of 10 (X = Cl). Worked up as usual, the residue remaining after removal of the chloroform solvent and excess triethylamine consisted of oily crystals (4.9 g, 70%), which decomposed on standing at room temperature. This substance was not analyzed, but, on spectroscopic evidence, appeared to be largely **13**: uv max ($CHCl_3$) 314, 248 nm; NMR ($CDCl_3$) δ 2.66 (t, 2, J = 6 Hz, SCH_2), 3.33 (t, 2, J = 6 Hz, CH_2), 5.55 (d, 1, J = 7 Hz, C-6 H), 5.80 (d, 1, J = 7 Hz, C-5 H), 6.00 (s, 1, C-10b H), 7.20 ppm (m, 4, aromatic).

The entire crude product (4.9 g) was placed in 50 ml of absolute ethanol, in which it rapidly dissolved, but after 1 min a crystalline substance began to precipitate from solution. The flask was warmed for 10 min and cooled and the product was collected, yielding 1.91 g (27% overall from mercaptan), mp 178–179°. The analytical sample was crystallized from chloroform–hexane: mp 179–180°; NMR ($CDCl_3$) δ 2.90 (br m, 8, aliphatic), 5.07 (s, 1, C-10b H), 7.20 ppm (m, 4, aromatic).

Anal. Calcd for $C_{11}H_{13}NS$: C, 69.06; H, 6.85; N, 7.32. Found: C, 69.26; H, 6.65; N, 7.33.

2-(β-Hydroxyethyl)isoquinolinium Bromide (17, X = Br). A solution containing 20 g of isoquinoline, 20 g of 2-bromoethanol, and 200 ml of acetonitrile was refluxed for 24 hr. On cooling, 26.8 g (68%) of colorless, hygroscopic plates was collected. Recrystallization from methanol–acetonitrile yielded the analytical sample, mp 154–155.5°.

Anal. Calcd for $C_{11}H_{12}BrNO$: C, 51.99; H, 4.74; N, 5.51. Found: C, 51.82; H, 4.81; N, 5.44.

The hexafluorophosphate (17, X = PF_6), mp 154–155.5°, prepared by addition of hexafluorophosphoric acid to an aqueous solution of the bromide salt (17, X = Br) was crystallized from methanol–ethyl acetate.[14]

***syn*-2,3,10,10a,12,13-Hexahydro-11*H*,5,10-[1′,2′]cyclopenta-5*H*-oxazolo[3,2-*b*]isoquinoline (21a).** To a solution of 5 g of 2-(β-hydroxyethyl)isoquinolinium hexafluorophosphate (17, X = PF_6) in 25 ml of acetonitrile, 25 ml of freshly cracked cyclopentadiene was added and the mixture was allowed to stand for 24 days. The solution was then concentrated under reduced pressure. The addition of cyclohexane caused the precipitation of 6 g of oil. To 2 g of the oil, a solution of 6 g of potassium carbonate in 20 ml of deionized water was added, and the mixture was stirred for a few hours at room temperature. The suspension was extracted with ether and the dried (potassium carbonate) solution was concentrated. The residue (1 g) was recrystallized from ethyl ether, affording 0.75 g (60%) of light pink prisms: mp 109–110°; NMR ($CDCl_3$) δ 7.14 (m, 4, aromatic H), 5.23 (s, 2, vinyl H), 4.96 (d, 1, J = 2.5 Hz, H-10a), 3.77 (d, 1, J = 3 Hz, H-5), 3.64–1.0 ppm (overlapping m, 9, aliphatic).

Anal. Calcd for $C_{16}H_{16}NO$: C, 80.64; H, 6.77; N, 5.88. Found: C, 80.84; H, 6.95; N, 5.75.

Registry No.—4 (X = Br), 54423-78-8; 4 (X = BF_4), 54424-04-3; 4 (X = picrate), 54423-80-2; **5**, 54423-85-7; **6**, 54423-86-8; **7**, 54423-87-9; **8**, 54423-88-0; **9**, 54423-89-1; **10** (X = Cl), 54423-81-3; **10** (X = PF_6), 54424-06-5; **11** (X = Br), 54423-82-4; **11** (X = perchlorate), 54423-84-6; **12**, 54424-03-2; **13**, 52131-57-4; **14**, 14692-38-7; **17** (X = Br), 54423-94-8; **17** (X = PF_6), 54423-96-0; **21a**, 54460-93-4; phenanthridine, 229-87-8; ethyl 3-bromopropylmalonate, 10149-21-0; 2-(4,4-dicarboxybutyl)isoquinolinium bromide diethyl ester, 54423-97-1; 2-(4,4-dicarboxybutyl)isoquinolinium perchlorate diethyl ester, 54423-99-3; 2-(4,4-dicarboxybutyl)-3-methylisoquinolinium bromide diethyl ester, 54424-00-9; 2-(4,4-dicarboxybutyl)-3-methylisoquinolinium perchlorate diethyl ester, 54424-02-1; *S*-(2-bromoethyl)thiolacetate, 927-70-8; isoquinoline, 119-65-3; 2-(2-mercaptoethyl)isoquinolinium bromide acetate, 54423-90-4; 2-(2-mercaptoethyl)isoquinolinium perchlorate acetate, 54423-92-6; 2-(2-mercaptoethyl)isoquinolinium bromide, 54423-93-7; 2-bromoethanol, 540-51-2; cyclopentadiene, 542-92-7.

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Periselectivity of Reactions of Fulvenes with Heterodienes and Heterodienophiles[1]

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The cycloaddition reactions of 6,6-dimethylfulvene, 6,6-diphenylfulvene, and 6-dimethylaminofulvene with tetrazine, diazacyclopentadienone, and azodicarboxylate are investigated. The periselectivity observed with the tetrazine is explained using the frontier orbital model where the fulvene HOMO–olefin LUMO interaction predominates. Thus, a novel 5,6-diazaazulene was prepared by the reaction of 6-dimethylaminofulvene with the tetrazine.

Previously we reported that 6,6-diphenylfulvene reacted with tropone to afford only a [4 + 2] adduct instead of an expected [6 + 4] adduct.[2] By contrast, the reaction of 6,6-dimethylfulvene with tropone resulted in the formation of a 2:1 [6 + 4] adduct.[3] The different behavior of these fulvenes indicates sensitivity to steric and electronic requirements of substitutents at the C-6 position of the fulvene. Recently, reactivity, regioselectivity, and periselectivity in cyloaddition reactions have been explained by employing quantitative perturbation molecular orbital theory.[4] These considerations led us to further investigation of the cycloaddition reaction of substituted fulvenes.