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Cycloaddition Reactions of Some 5-Substituted Isoquinolinium Salts[1]

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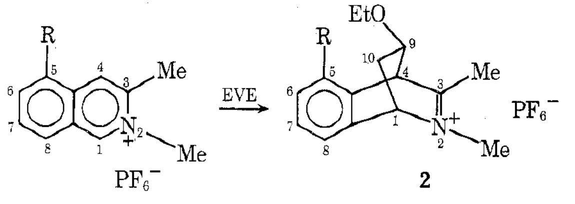
The reactivity of the 2,3-dimethylisoquinolinium nucleus (1) toward 1,4 cycloaddition with alkenes is greatly enhanced by the introduction of a nitro group at position 5, making possible new synthetic applications. The reactivity of the 2-methylisoquinolinium ion (15) is also enhanced by introduction of a nitro group into position 5, and the product (18) with cyclopentadiene is the first simple 1,4 adduct obtained from an isoquinolinium salt with no substituent at position 3.

The discovery that 2,3-disubstituted isoquinolinium salts (**1a**) would undergo cycloaddition reactions with alkyl vinyl ethers[2-4] and cyclopentadiene[4,5] offered the promise of easy access to a host of benzisoquinuclidine derivatives.



1

2

a, R = H
b, R = NO_2
c, R = NHCOMe

Unfortunately, the sluggishness of the cycloaddition at room temperature and the easy reversibility at higher temperatures have greatly limited the usefulness of the reaction. For example, 2,3-dimethyl-1,3-butadiene, which stands next below cyclopentadiene in reactivity toward the acridizinium ion,[6] does not react noticeably with **1a** in 3 months at room temperature.

In earlier work[7] it was shown that the introduction of the electron-withdrawing nitro group at position 9 of the acridizinium nucleus resulted in a 21-fold increase in the rate of cycloaddition toward styrene. This led us to examine the reactivity of 5-nitro-2,3-dimethylisoquinolinium ion (**1b**) toward activated alkenes. As measured by its reactivity with ethyl vinyl ether, the nitro derivative (**1b**) reacted approximately 120 times faster than the parent compound (**1a**). The magnitude of this rate enhancement raised the question whether the enhancement was entirely electronic in its origin or whether steric acceleration of cycloaddition[8] must play some part. A group at position 5 would tend to crowd the adjacent peri hydrogen, which is constrained further by the flanking methyl at position 3. Much of the resulting steric strain should be relieved during the cycloaddition, since the peri hydrogen moves out of plane. That some steric contribution is involved is suggested by the observation that the analog (**1c**) having an electron-releasing acetylamino group at position 5 is still twice as reactive as the parent compound (**1a**).

The 5-nitro-2,3-dimethylisoquinolinium ion (**1b**) reacts in good to excellent yield with a variety of the less reactive alkenes, including styrene, vinyl acetate, β-pinene, and norbornene (Table I). For none of the adducts was there any indication in the NMR spectrum of the presence of mixtures of regioisomers (always one set, rather than two, of bridgehead hydrogens). This is in conformity with all reported cycloadditions of unsymmetrical alkenes with quaternary aromatic salts.[9] Assignment of structure of the adducts has been made by analogy to the addition of unsymmetrical addends to the 2,3-dimethylisoquinolinium ion (**1a**) and to the acridizinium ion.[6] Direct assignment of the regiochemistry of the adducts on the basis of NMR evidence, following the method of Fields et al.,[6] was not possible. As usual, the quaternary nitrogen caused a characteristic deshielding of the adjacent bridgehead proton attached to C-1, but the nitro group at position 5 had a similar effect on the other bridgehead hydrogen at position 4, making the usual distinction between the bridgehead hydrogens on the basis of differences in chemical shift impossible.

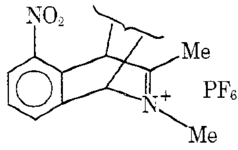
At least four of the addends appeared to afford only a single geometrical isomer. Three of these, the ethyl vinyl ether (**2b**), the cyclopentadiene (**8**), and the norbornene (**12**) adducts, can definitely be assigned as syn (with respect to the phenylene ring). The first two of these (**2b** and **8**) had NMR spectra similar to those of the unnitrated prototype (e.g., **2a**) and in both of these cases, the structure of

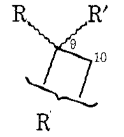
Table I
Reaction of Some Alkenes with 5-Nitro-2,3-dimethylisoquinolinium Hexafluorophosphate (1b) in Acetonitrile at Room Temperature

	Adduct		Concn, mmol/l.		Time,	Yield,		^{1}H NMR chemical shifts, δ (multiplicity)				
Addend	Compd	Formula[a]	1b	Addend	days	%	Mp, °C	Solvent	H-1	H-4	CH_3C[c]	CH_3N[c]
Styrene	**3**	$C_{19}H_{19}F_6N_2O_2P$	0.14	1.24	35	97	222[b]	CD_3CN	5.90 (q)	5.63 (d)	2.70	3.70
p-Methoxystyrene	**4**	$C_{20}H_{21}F_6N_2O_3P$	0.33	1.23	2	94	261–263.5	CF_3CO_2H	5.92 (q)	5.85 (d)	2.89	3.92
Ethyl vinyl ether	**2b**	$C_{15}H_{19}F_6N_2O_3P$	0.20	1.20	0.04	95	167[b]	CD_3CN	5.73 (q)	6.13 (d)	2.64	3.67
Vinyl acetate	**5**	$C_{15}H_{17}F_6N_2O_4P$	0.50	14.50	60	63	253[b]	CD_3CN	5.79 (q)	5.96 (d)	2.62	3.62
2,3-Dimethylbutadiene	**6**	$C_{17}H_{21}F_6N_2O_2P$	0.50	2.38	25	51	171[b]	CF_3CO_2H	5.81 (q)	5.97 (d)	2.91	3.92
β-Pinene	**7**	$C_{21}H_{27}F_6N_2O_2P$	0.25	1.23	34	74	195[b]	CF_3CO_2H	5.68 (q)	6.07 (d)	2.67	3.80
Cyclopentadiene	**8**	$C_{16}H_{17}F_6N_2O_2P$	0.94	4.04	2	82	200[b]	CD_3CN	5.80 (d)	5.67 (d)	2.87	3.98
1,3-Cyclohexadiene	**9**	$C_{17}H_{19}F_6N_2O_2P$	0.38	1.67	12	81	192[b]	CF_3CO_2H	6.02 (d)	5.63 (d)	2.82	3.88
1-Methoxycyclohexene	**10**	$C_{18}H_{23}F_6N_2O_3P$	0.28	26.80	24	98	191[b]	CD_3CN	5.60 (d)	6.05 (s)	2.65	3.77
Indene	**11**	$C_{20}H_{19}F_6N_2O_2P$	0.25	2.33	0.29[d]	56	223–224	CF_3CO_2H	6.42 (d)	5.72 (d)	2.94	3.94
Norbornene	**12**	$C_{18}H_{21}F_6N_2O_2P$	0.17	1.24	33	68	224–225	$(CD_3)_2CO$	6.03 (d)	5.83 (d)	2.83	3.90

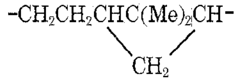
[a] Satisfactory analyses were submitted for all compounds listed in this table. Ed. [b] Decomposes. [c] All resonances in this column appeared as singlets. [d] This cycloaddition was carried out at 65°.

the prototype had been proved by single-crystal X-ray crystallography.[3,5]

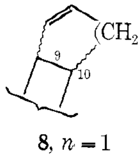




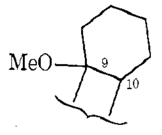
	R	R′
3	C_6H_5	H
4	*p*-$MeOC_6H_4$	H
5	MeCOO	H
6	$CH_2{=\!=}CMe$	CH_3
7	$-CH_2CH_2CHC(Me)_2CH-$	



$-CH_2CH_2\underset{\diagdown\;CH_2\;\diagup}{CHC(Me)_2CH}-$



8, $n = 1$
9, $n = 2$



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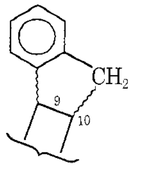

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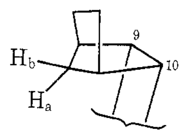
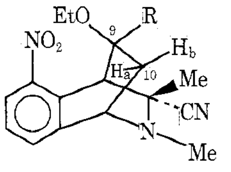


12

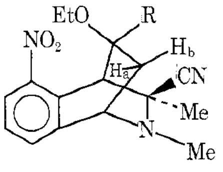
The structure of the norbornene adduct (**12**) follows from the very strong shielding of one of the methylene protons (δ −0.77) arising from its exposure to the diamagnetic ring current of the phenylene group. Despite the possibility that some of the stereoisomeric anti isomer might have been formed in the cycloaddition but lost in the recrystallization, the isolation of a 68% yield of the syn form indicates that the reaction is more stereoselective than the addition of norbornene to the acridizinium ion, which shows only a 60:40 preference for the syn configuration.[10]

The remaining case of stereoselectivity, that of the 1-methoxycyclohexene adduct (**10**), has been assigned the anti configuration (with the cyclohexane ring turned away from the phenylene ring on the basis of the coulombic repulsion rule).[5] Unfortunately, the NMR signal for the methine proton at C-10 is lost in the envelope arising from the methylene protons; hence there is no evidence whether it is directed toward or away from the quaternary nitrogen atom.

Earlier[4] it was shown that the initial attack of the cyanide ion on the unnitrated ethyl vinyl ether adduct (**2a**) is from the endo side, but when equilibrium is ultimately reached, the concentration of the endo and exo cyano compounds is essentially equal. Similar behavior has been observed with the nitro adduct (**2b**), affording at first mostly **13a** which isomerized to **13b**. When the cycloaddition of **1b** was carried out with 2-ethoxypropene, the adduct could not be crystallized but was converted directly to the nitrile by action of cyanide. Interestingly, a single geometrical isomer was obtained, but in a yield of only 20%. On the basis of the expected polarization, the charge repulsion rule,[5] and the NMR spectrum, as well as spin-decoupling experiments, the most likely structure appears to be **14**.

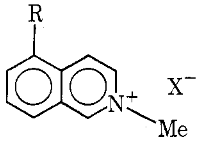


13a, R = H
14, R = Me

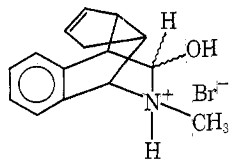


13b, R = H

Although some of our initial experiments were directed toward the cycloaddition of alkenes with isoquinolinium salts having no substituent at position 3, these were frustrated almost certainly by the great reactivity of the cycloadduct first obtained, resulting in complicating nucleophilic attacks by the solvent or excess alkene. An illustration is the reaction of 2-methylisoquinolinium bromide with cyclopentadiene, which gave, in 80% yield, a poorly defined product, probably **17**, corresponding to the addition of 1 mol of cyclopentadiene plus 1 mol of water. When 5-nitro-2-methylisoquinolinium hexafluorophosphate (**16**) was allowed to react with cyclopentadiene at room temperature, the simple adduct **18** was obtained in 69% yield. The iminium hydrogen of the adduct appeared as a multiplet centered at δ 8.94. This is the first example of the simple cycloaddition of an isoquinolinium salt having no substituent at position 3. Simple cycloaddition is not always characteristic of the 5-nitro-2-methylisoquinolinium salt (**16**), for addition to an excess of 1-methoxycyclohexene afforded an adduct which, from elemental analysis and NMR, clearly had 2 mol of the alkene incorporated. From mechanistic considerations and NMR evidence, it appears that the structure can best be represented as **19**.



15, R = H; X = Br
16, R = NO$_2$; X = PF$_6$



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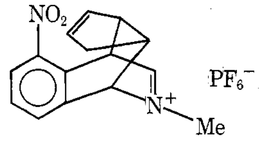

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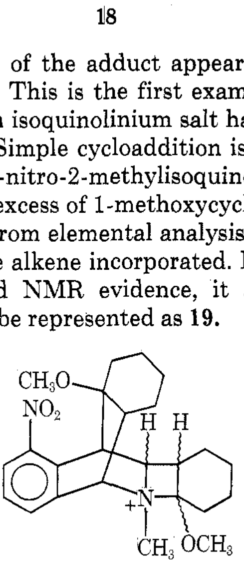

19

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 melting point apparatus and are uncorrected. Infrared spectra were determinded on a Perkin-Elmer Model 137 or Model 237 using KBr disks. Proton magnetic resonance spectra were obtained at 60 MHz on Varian A-60 and T-60 spectrometers.

2,3-Dimethyl-5-nitroisoquinolinium Methosulfate. Refluxing 15 g of 3-methyl-5-nitroisoquinoline[11] and 10 g of dimethyl sulfate for 24 hr in 100 ml of acetonitrile followed by concentration under reduced pressure and addition of ethyl acetate afforded the salt as a yellow solid, 22.6 g (90%). It crystallized from methanol as light yellow needles, mp 178°.

Anal. Calcd for $C_{12}H_{14}N_2O_6S$: C, 45.86; H, 4.49; N, 8.91. Found: C, 45.78; H, 4.42; N, 8.83.

The hexafluorophosphate (1b) was prepared (76%) by addition of hexafluorophosphoric acid to an aqueous solution of the methosulfate salt. Recrystallization from methanol afforded colorless needles, mp 195–196°.

Anal. Calcd for $C_{11}H_{11}F_6N_2O_2P$: C, 37.94; H, 3.18; N, 8.04. Found: C, 37.72; H, 3.01; N, 7.81.

2,3-Dimethyl-5-acetylaminoisoquinoline Hexafluorophosphate (1c). 3-Methyl-5-aminoisoquinoline (10 g) was dissolved in 50 ml of acetic anhydride and the mixture was allowed to stand at room temperature for 2 hr. The semisolid mixture was poured into ice–water and made basic by addition of sodium bicarbonate. The solid (9 g) was collected and treated with 15 g of methyl iodide to afford 13.5 g of the salt. This was dissolved in hot methanol and treated with 8 g of hexafluorophosphoric acid to yield 9.2 g (40%) of crude product, mp 254–257. The analytical sample, mp 259–261°, was crystallized from methanol–acetonitrile.

Anal. Calcd for $C_{13}H_{15}N_2OPF_6$: C, 43.33; H, 4.17; N, 7.78. Found: C, 43.07; H, 4.29; N, 7.56.

General Procedure for Preparation of Cycloadducts. To a solution of the isoquinolinium salt 1 in acetonitrile, a large excess of the alkene plus a small quantity of hydroquinone were added. Except as noted, the solution was allowed to stand at room temperature until the uv or NMR spectrum showed that the isoquinolinium ring system was no longer present. The solution was then concentrated to a small residue to which ether was added. The resulting precipitate was collected and washed with ether. All adducts were crystallized from methanol containing a small quantity of acetonitrile.

5-Acetamino-2,3-dimethyl-9-ethoxy-1,4-dihydro-1,4-ethanoisoquinolinium Hexafluorophosphate (2c). This was prepared in 63% yield from **1c**: mp 258–259°; NMR[12] (CD_3CN) δ 2.62 (s, C-3 CH_3), 3.58 (s, NCH_3), 5.14 (d, H-4), 5.54 ppm (q, H-1).

Anal. Calcd for $C_{17}H_{23}F_6N_2O_2P$: C, 47.22; H, 5.32; N, 6.48. Found: C, 47.37; H, 5.45; N, 6.34.

Reaction Rates for Cycloaddition of 1a–c. The comparison of reaction rates was carried out at 34.6 ± 0.5° in an acetonitrile solution that was 0.1 *M* in salt and 3.5 *M* in ethyl vinyl ether. Disappearance of the salt was measured by observing the disappearance of the long-wavelength absorption in the ultraviolet.

9-Ethoxy-1,2,3,4-tetrahydro-2,3-dimethyl-3-cyano-5-nitro-1,4-ethanoisoquinoline (13). To a solution of 1.5 g (4.6 mmol) of **2b** in a mixture containing 11 ml of acetonitrile and 4 ml of water, a solution of 0.25 g (1.5 mmol) of potassium cyanide in 1 ml of water was added dropwise. The solution was concentrated under reduced pressure and the crystalline residue was collected and washed with water. The crude product, 1.05 g (98%), mp 109–111°, was recrystallized from methanol–water as yellow microcrystals, mp 113°. The NMR suggested a mixture of geometrical isomers with the major isomer having the resonance at H-9 appearing at δ 4.12 (with methyl groups as singlets at δ 2.39 and 1.72). The H-9 resonance for the minor isomer appeared at δ 4.48 (with methyl groups as singlets at δ 2.55 and 1.28). Assignment of the major isomer as the endo cyano compound (**13a**) was based upon the long-range shielding effects[4,13] of the nitrile group on the H-9 resonance. In the endo isomer (**13a**) H-9 is approximately in the direction of the principal axis of the cyano group; hence it should be shielded. In the exo isomer (**13b**), H-9 is almost at right angles to the axis of the nitrile group; hence it should be deshielded. In a few days, the solution ($DCCl_3$) appeared to reach an equilibrium in which **13a** and **13b** were present in equal amounts: **13a** NMR ($CDCl_3$) δ 1.03 (t, 3, CH_3CH_2), 1.20 (m, 1, 10-H, syn), 1.72 (s, 3, 3-Me), 2.39 (s, 3, 2-Me), 2.62 (o, 1, 10-H, anti), 3.62 (m, 2, CH_3CH_2), 3.72 (q, 1, 1-H), 4.12 (m, 1, 9-H), 4.75 (d, 1, H-4), 7.30–8.30 (m, 3, aromatic).

Anal. Calcd for $C_{16}H_{19}N_3O_3$: C, 63.73; H, 6.36; N, 13.94. Found: C, 63.58,; H, 6.16; N, 13.65.

3-Cyano-9-ethoxyl-1,2,3,4-tetrahydro-2,3,9-trimethyl-5-nitroisoquinoline (14). The reaction for 1 day at room temperature of 5 g (14 mmol) of **1b** with 8 g (93 mmol) of 2-ethoxypropene[14] in 25 ml of acetonitrile, followed by removal of volatiles under reduced pressure, left a mixture of solid and oil. The solid, which was mainly starting material, was removed by dissolving the oil in cold methanol and filtering the solution. The solution was concentrated under reduced pressure and the oily residue was taken up in a mixture of 20 ml of acetonitrile and 4 ml of deionized water. To this solution, 1.2 g of potassium cyanide in 2 ml of water was added. The solvents were removed under reduced pressure, water was added to the residue, and the mixture was extracted with ether. The ether solution was dried (K_2CO_3) and concentrated and the solid product was twice recrystallized from ether, affording 1 g (20%) of colorless needles: mp 140–143°; NMR ($CDCl_3$) δ 0.98 (s, 3, 9-Me), 1.23 (t, 3, CH_3CH_2), 1.53 (d of d, 1, J_{gem} = 13, J_{vic} = 3 Hz, 10a), 1.93 (s, 3, 3-Me), 2.39 (s, 3+, MeN, 10b), 2.50 (d, J_{vic} = 3 Hz, 0.5, 10b), 3.56 (q, 2, CH_3CH_2), 3.79 (t, 1, 1 H), 4.51 (s, 1, 4 H), 7.53 (s, 1, aromatic), 7.58 (s, 1, aromatic), 8.14 (t, 1, 8 H).

Anal. Calcd for $C_{17}H_{21}N_3O_3$: C, 64.74; H, 6.71; N, 13.32. Found: C, 64.93; H, 6.51; N, 13.25.

2-Methyl-5-nitroisoquinolinium Hexafluorophosphate (16). A solution containing 17.8 g of 5-nitroisoquinoline,[15] 13 g of dimethyl sulfate, and 100 ml of acetonitrile was allowed to stand for 3 days at room temperature. Upon addition of ether, the methyl methosulfate salt separated as an oil. The oil was dissolved in 50 ml of methanol and added to 20 g of hexafluorophosphoric acid in a polypropylene beaker. The precipitate was collected and washed with methanol. The crude product, 21.2 g (62%), crystallized from hot methanol, afforded yellow microcrystals, mp 150°.

Anal. Calcd for $C_{10}H_9F_6N_2O_2P$: C, 35.94; H, 2.71; N, 8.38. Found: C, 35.82; H, 2.47; N, 8.18.

3-Hydroxy-2-methyl-1,4-Δ^{12}-cyclopenteno)-1,2,3,4-tetrahydroisoquinolinium Bromide (17). To a solution of 2.52 g of 2-methylisoquinolinium bromide[16] in 250 ml of acetonitrile, 9 ml of 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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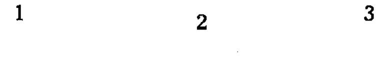
In the presence of a suitable base, certain aromatic or iminium quaternary salts having a nucleophilic group at an appropriate place of the N^+–R chain undergo nucleophilic cyclization. This cyclization has been applied to phenanthridinium, isoquinolinium, and 1,4-bridged 1,4-dihydroisoquinolinium salts 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 al-