Benzologs of the Quinolizinium Ion

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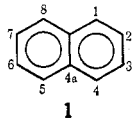
The interest in benzene and its benzologs which has prevailed since the beginning of organic chemistry has been intensified during the past few decades under the stimulus provided by quantum mechanics. It is in the area of condensed systems that theoretical chemists have made the closest approach to the goal of predicting reactivities and physical constants of organic compounds.

The occurrence of aromatic compounds formally related to the classical aromatic hydrocarbons by the replacement of a CH by N has long been recognized. The structural relationship of quinoline (**2**) to naphthalene (**1**) was understood nearly 100 years ago[1] while the relationship of isoquinoline[2] was recognized a few years later.



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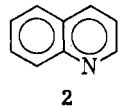

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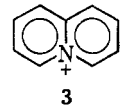

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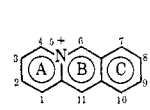
Despite the continuing attention devoted to simple aromatic systems, the first synthesis of the quinolizinium ion (**3**), in which the carbon at position 4a of the naphthalene (**1**) nucleus is replaced by a quaternary nitrogen, was not announced until 1954,[3] and this date may be regarded as the beginning of the *systematic* study of the quinolizinium ion and its benzologs.[4]

In our laboratory, interest in the synthesis of *benzologs* of the quinolizinium ion arose from a search for further tests of the general nature of the aromatic cyclodehydration[6] reaction and, with the development of interest in the chemistry of these new systems, other synthetic methods were devised. There are only three simple monobenzologs of the quinolizinium ion, one linear and two angular. As may be seen in Table I, the tricyclic systems are described as benzologs of the quinolizinium ion or *azonialogs*[7] of anthracene or phenanthrene, or (in two instances) have been given trivial names. The *Chemical Abstracts* numbering for the three systems (**4**–**6**) is shown in Table I and will be used throughout this Account.[8]

(1) A. Baeyer, *Ann.*, **155**, 321 (1870).
(2) S. Hoogewerf and W. A. van Dorp, *Rec. Trav. Chim.*, **5**, 305 (1886).
(3) V. Boekelheide and W. G. Gall, *J. Am. Chem. Soc.*, **76**, 1832 (1954); see also ref 18 of that publication.
(4) For references to earlier compounds (nearly all tetracyclic) believed or known to contain the quinolizinium nucleus, see ref 5.
(5) C. K. Bradsher and L. E. Beavers, *J. Am. Chem. Soc.*, **77**, 4812 (1955).
(6) C. K. Bradsher, *Chem. Rev.*, **38**, 447 (1946).
(7) It was proposed (R. E. Doolittle and C. K. Bradsher, *J. Heterocyclic Chem.*, **2**, 399 (1965)) that the izinium salt be referred to as an *azonialog* of the analogous hydrocarbon.
(8) In the azonia arene nomenclature (see Table I, footnote *b*) the numbering is that of the parent hydrocarbon.

Table I

Nomenclature of Quinolizinium Benzologs



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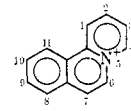

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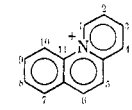

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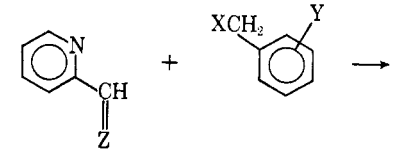
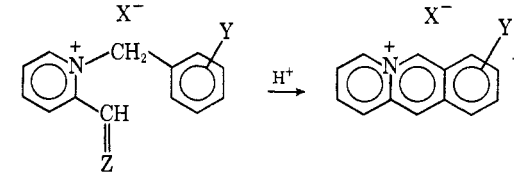
Ben o'og	Benzo[*b*]quinolizinium ion[a]	Benzo[*a*]quinolizinium ion	Benzo[*c*]quinolizinium ion
Azonia	4 :-Azonia-anthracene[b]	8a-Azonia-phenanthrene	4a-Azonia-phenanthrene
Trivial	Acridizinium ion[c]	Phenanthridizinium ion[d]	

[a] *Chem. Abstr.*, **50**, 366*s* (1956). [b] Report of the IUPAC Nomenclature Committee, *J. Am. Chem. Soc.*, **82**, 5545, 5572 (1960). [c] Reference 5. [d] C. K. Bradsher and K. B. Moser, *J. Am. Chem. Soc.*, **81**, 1940 (1959).

Synthesis of the Acridizinium Ion (4). Despite the fact that the acridizinium ion (**4**) was previously unknown both as a compound and as an aromatic system, its synthesis turned out to be remarkably simple. Benzyl bromide or a substituted benzyl bromide was allowed to react with 2-pyridinecarboxaldehyde (**7**) and the crude salt (**10**) cyclized in boiling hydrobromic



7, Z = O
8, Z = NOH
9, Z = $(OCH_2)_2$



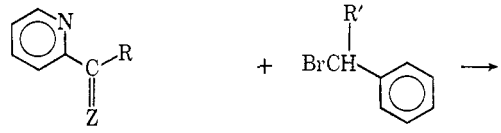
10, Z = O
11, Z = NOH
12, Z = $(OCH_2)_2$

acid to afford acridizinium derivatives.[5,9] The oxime **8** of 2-pyridinecarboxaldehyde, also commercially available, offers the advantages of greater stability and ease of quaternization, and, in addition, the intermediate salt **11** is more easily purified and cyclizes more rapidly

(9) C. K. Bradsher and L. E. Beavers, *Chem. Ind.* (London), 1394 (1954).

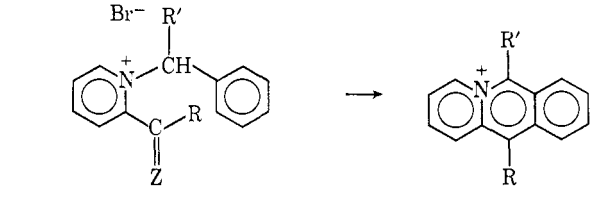
than the aldehyde salt **10**.[10] For benzyl halides that contain a substituent which deactivates the ring, best results are obtained using the cyclic acetal **9**, 2-(1,3-dioxolan-2-yl)pyridine, since the resulting intermediate salt **12** is well suited for cyclization in hot polyphosphoric acid.[11,12] Not only is the acridizinium ion one of the most readily prepared heterocyclic compounds, but due to the ready availability of substituted benzyl halides, systematically substituted acridizinium salts are more easily available than substituted anthracenes or azaanthracenes. It has also been shown how acridizinium benzologs can be prepared by replacement of the benzyl halides by naphthyl- or phenanthrylmethyl halides[13] or the pyridinecarboxaldehyde by isoquinoline 1-[14] or 3-carboxaldehydes.[15]

An alkyl or aryl group may be introduced into the *meso* positions of the acridizinium ion generally with better success in the 11 position than in the 6 position. With 2-benzoylpyridine (**13**), benzyl bromide afforded a crude salt (**19**) that cyclized in liquid hydrogen fluoride to afford 11-phenylacridizinium ion in 89.5%



13, Z = O; R = C_6H_5
14, Z = O; R = CH_3
15, Z = $(OCH_2)_2$; R = H
16, Z = $(OCH_2)_2$; R = CH_3

17, R′ = CH_3
18, R′ = C_3H_7

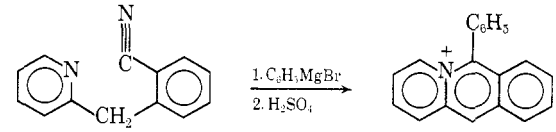


19, R′ = H; R = C_6H_5; Z = O
20, R′ = CH_3; R = C_6H_5; Z = O
21, R′ = H; R = CH_3; Z = $(OCH_2)_2$

22, R′ = H; R = C_6H_5
23, R′ = H; R = CH_3
24, R′ = CH_3; R = H
25, R′ = R = CH_3

yield.[16] It is not understood why under comparable conditions 2-acetopyridine (**14**) afforded only a poor yield (3%),[16] but this could be improved (35% yield) by use of the cyclic ketal **16**, carrying out the cyclization of the crude salt **21** in polyphosphoric acid.[11] 6-Methyl- (**24**) and 6-propylacridizinium salts[17] have been prepared by allowing α-bromoalkylbenzenes (**17** and **18**) to react with the cyclic acetal **15** followed by cyclization of the quaternary salt in hydrobromic acid. A small yield of 6,11-dimethylacridizinium (**25**) ion was obtained by starting with the ketal **16** and α-bromoethylbenzene (**17**).

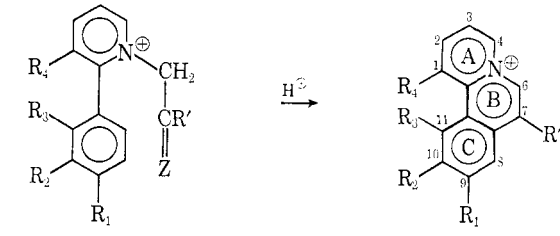
The 6-phenylacridizinium ion has been obtained by a route which is of theoretical interest only.[18] *o*-(2-Pyridylmethyl)benzonitrile (**26**) was treated with



26 **27**

an excess of phenylmagnesium bromide and, after suitable hydrolysis to crude ketone, was cyclized in concentrated sulfuric acid. Published[11] and unpublished[19] work seems to indicate that the synthesis of acridizinium derivatives having substituents in ring A is limited only by the availability of the substituted 2-pyridinecarboxaldehyde derivatives and their ability to undergo quaternization with benzyl bromide.

Synthesis of the Benzo[*a*]quinolizinium System 5. The first general[20] method for the synthesis of simple phenanthridizinium derivatives (**32**, **33**) involved the quaternization of 2-phenylpyridine or a derivative with an appropriate α-halo carbonyl derivative, after which the resulting salts (**28–31**) were usually cyclized in boiling hydrobromic acid.[21–23] The presence of a methyl group on the phenyl ring did not appear to interfere with the cyclization except when in the *ortho*



28, R′ = CH_3; Z = O
29, R′ = C_6H_5; Z = O
30, R′ = H; Z = NOH
31, R′ = $(CH_2)_2COOCH_3$

32, R′ = CH_3
33, R′ = C_6H_5
34, R′ = H
35, R′ = $(CH_2)_2COOH$

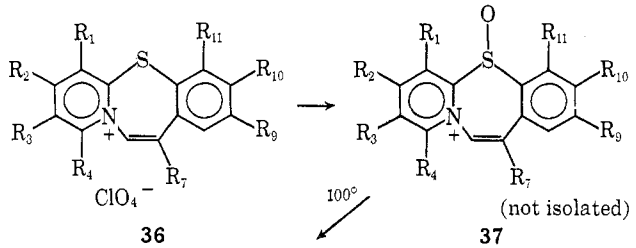
position (**28**, R_3 = CH_3),[21] in which case the low yield could be anticipated because rings A and C have difficulty in attaining coplanarity.

The discovery, in this laboratory,[24] of the use of chloroacetaldoxime as a quaternizing agent to yield (ultimately) phenanthridizinium derivatives (**34**) with no substituents on ring B was not made until after the

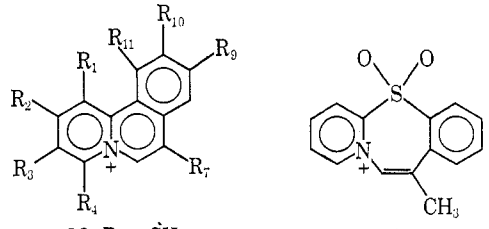
(10) C. K. Bradsher, T. W. G. Solomons, and F. R. Vaughan, *J. Org. Chem.*, **25**, 757 (1960).
(11) C. K. Bradsher and J. C. Parham, *ibid.*, **28**, 83 (1963).
(12) C. K. Bradsher and J. C. Parham, *J. Heterocyclic Chem.*, **1**, 30 (1964).
(13) C. K. Bradsher and L. E. Beavers, *J. Am. Chem. Soc.*, **78**, 2459 (1956).
(14) C. K. Bradsher and J. H. Jones, *J. Org. Chem.*, **23**, 430 (1958).
(15) C. K. Bradsher and T. W. G. Solomons, *J. Am. Chem. Soc.*, **82**, 1808 (1960).
(16) C. K. Bradsher and T. W. G. Solomons, *ibid.*, **81**, 2550 (1959).
(17) C. K. Bradsher and J. C. Parham, *J. Heterocyclic Chem.*, **1**, 121 (1964).
(18) C. K. Bradsher and J. P. Sherer, *J. Org. Chem.*, **32**, 733 (1967).
(19) J. E. Boliek, M.A. Thesis, Duke University, 1964.
(20) The route used by O. Diels and J. Harms (*Ann.*, **525**, 73 (1936)) for the synthesis of a tetracarbomethoxybenzo[*a*]quinolizinium salt does not appear promising as a route to simple analogs, *cf.* R. M. Acheson and G. A. Taylor, *J. Chem. Soc.*, 1691 (1960).
(21) See Table I, footnote *d*.
(22) C. K. Bradsher and L. A. Beavers, *J. Am. Chem. Soc.*, **77**, 453 (1955).
(23) C. K. Bradsher and N. L. Yarrington, *J. Org. Chem.*, **28**, 78 (1963).
(24) R. W. L. Kimber and J. C. Parham, *ibid.*, **28**, 81 (1963).

synthesis of the unsubstituted quinolizinium ion had been made by Glover and Jones[25] and by Akaboshi and Kato[26] using other methods.

Another route to the phenanthridizinium ion, less interesting from the preparative than from the theoretical point of view, is the ring contraction by pyrido[2,1-*b*]benzo[*f*][1,3]thiazepinium perchlorates (**36**) when these substances are oxidized and the resulting crude sulfoxide is heated at 100°.[27-30] Yields of 24-



36 **37**

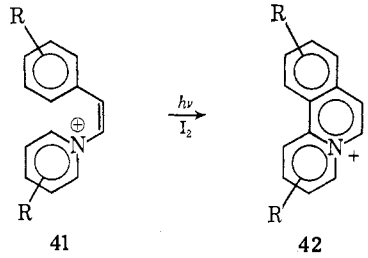


38, $R_7 = CH_3$
39, $R_7 = H$

40

45% were obtained for a variety of dimethylphenanthridizinium salts, and it was likewise shown that the unsubstituted derivative **39** could be prepared in 65% yield by this method.[30] Synthesis of the *sulfone* **40** showed that this was not an intermediate in the sulfur extrusion reaction.[30]

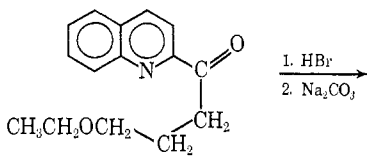
The most recent method for the synthesis of phenanthridizinium derivatives is not only extremely versatile but is probably the most convenient for the preparation of the unsubstituted cation. Styrylpyridinium salts (**41**) (probably *trans*) on irradiation with ultraviolet light give yields averaging about 50% of



41 **42**

derivatives of the phenanthridizinium ion.[31,32] While this is but one of several successful attempts made to extend the photocyclization observed with stilbene[33] to the synthesis of heterocyclic systems[34] it is believed to be the first such instance involving a quaternary salt.

Synthesis of Benzo[*c*]quinolizinium Salts. The first synthesis of the benzo[*c*]quinolizinium ion was accomplished by Glover and Jones[25] using their general method for the synthesis of the quinolizinium ion and its benzologs. The ketone **43** formed by the reaction of 2-cyanoquinoline with γ-ethoxypropylmagnesium bromide was heated with hydrobromic acid to cleave the alkoxyl group and the resulting halide was con-



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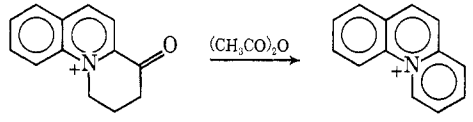
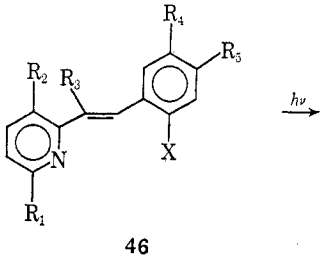


44 **45**

verted to the cyclic ketone **44**. The Jones dehydration carried out on the cyclic ketone led to the benzo[*c*]quinolizinium cation (**45**).

A new general synthesis has been devised[35,36] which makes the benzo[*c*]quinolizinium ion nearly as accessible as the benzo[*b*]. The stilbazoles (**46**) formed by the condensation of *o*-chlorobenzaldehyde with α-picoline (or a suitable derivative) were irradiated in



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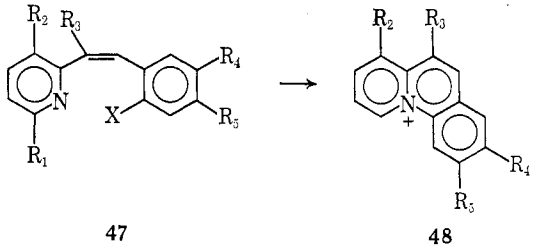


47 **48**

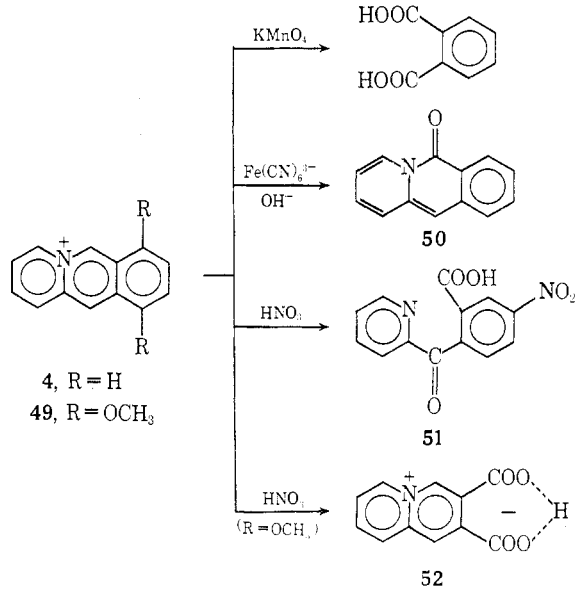
benzene solution and the mixture, consisting largely of the *cis* isomer, was heated for 1 hr at 170°. The average conversion to benzo[*c*]quinolizinium salts was 66% except when there was a methyl group at the 6 position of the pyridine ring ($R_1 = CH_3$), in which case steric hindrance is believed to be responsible for

(25) E. E. Glover and G. Jones, *J. Chem. Soc.*, 3021 (1958).
(26) S. Akaboshi and T. Kato, *Yakugaku Zasshi*, **83**, 1067 (1963).
(27) C. K. Bradsher and J. W. McDonald, *Chem. Ind.* (London), 1797 (1961).
(28) C. K. Bradsher and J. W. McDonald, *J. Org. Chem.*, **27**, 4475 (1962).
(29) C. K. Bradsher and J. W. McDonald, *ibid.*, **27**, 4478 (1962).
(30) C. K. Bradsher and D. F. Lohr, Jr., *ibid.*, **31**, 978 (1966).
(31) R. E. Doolittle and C. K. Bradsher, *Chem. Ind.* (London), 127 (1965).
(32) R. E. Doolittle and C. K. Bradsher, *J. Org. Chem.*, **31**, 2616 (1966).
(33) F. B. Mallory, C. S. Wood, and J. T. Gordon, *J. Am. Chem. Soc.*, **86**, 3094 (1964), and references cited therein.
(34) See footnote 4 of ref 33.
(35) A. Fozard and C. K. Bradsher, *Chem. Commun.*, 288 (1965).
(36) A. Fozard and C. K. Bradsher, *J. Org. Chem.*, **31**, 2346 (1966).

the failure of the internal quaternization reaction. Usually the internal quaternization reaction yielded reusable *trans*-stilbazoles as by-products. The participation of an aryl halide in a quaternization reaction is believed[37] to be due in large measure to the activation of the carbon bearing the halogen by the electron withdrawal of the pyridyl group, communicated through the conjugated system.

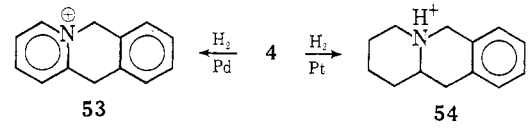
Reactions of the Benzoquinolizinium Systems. Acridizinium Ion. Of the benzoquinolizinium salts the acridizinium ion, probably because of its availability and reactivity, has been the most studied. Acridizinium salts are yellow, giving a fluorescent solution in water or polar solvents, and such solutions have an ultraviolet absorption spectrum[5] reminiscent of that of anthracene, except for a general shift to longer wavelengths and an intensified absorption at longer wavelengths. Acridizinium salts appear to be stable provided they are shielded from light.

Oxidation of the acridizinium ion (**4**) can occur in several ways. With permanganate, phthalic acid was formed,[5] while with alkaline ferricyanide a 9% yield of 6H-benzo[*b*]quinolizin-6-one (**50**) was reported.[38] If the acridizinium ion was heated with 12 *M* nitric acid, it yielded 2-(2-carboxy-4-nitrobenzoyl)pyridine (**51**), while a similar oxidation carried out on 7,10-dimethoxyacridizinium ion (**49**) afforded the betaine (**52**) of 2,3-dicarboxyquinolizinium hydroxide, the



first example of the transformation of an acridizinium derivative to a quinolizinium derivative.[39]

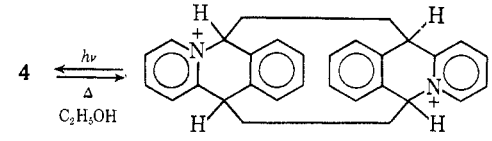
The reduction of the acridizinium nucleus can be made to occur stepwise. With a palladium catalyst the reduction may be interrupted after the addition of 1 mol of hydrogen, affording 6,11-dihydroacridizinium ion (**53**).[40] With a platinum catalyst, both rings



53 54

common to the nitrogen atom are reduced, affording benzo[*b*]quinolizidine salts (**54**).[5]

The acridizinium ion is more sensitive to light than is anthracene, but, like it, is believed to undergo photodimerization through the *meso* positions.[41] The photodimer **55** dissociated when refluxed in ethanol.



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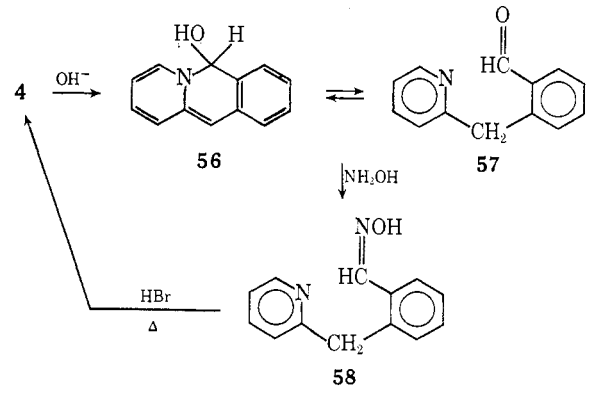
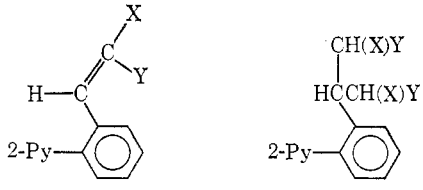
Action of Bases. The acridizinium ion is quite stable in acid solution but is sensitive to attack by bases. The addition of alkali caused a precipitate[18,42,43]



which could not be recrystallized and had approximately the composition expected for either the pseudo base **56** or 2-(α-picolyl)benzaldehyde (**57**). From nmr and infrared evidence the substance appeared to be a mixture of both compounds. If hydroxylamine was allowed to react with acridizinium ion in the presence of bicarbonate ion, high yields of the oxime **58** of the aldehyde **57** were obtained.[18] The oxime was readily cyclized back to acridizinium bromide.

The condensation product obtained by the reaction of phenylacetonitrile with acridizinium bromide in the presence of base[18,42] has been shown[18] to be the product expected from aldol condensation with 2-(α-picolyl)-benzaldehyde (**57**) followed by loss of water. It



59 61

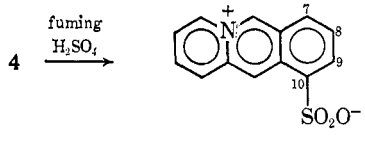
60, X = C_6H_5; Y = CN

(37) A. Fozard and C. K. Bradsher, *J. Org. Chem.*, **31**, 3683 (1966).
(38) L. A. Paquette, *Chem. Ind.* (London), 1292 (1962).
(39) C. K. Bradsher and M. W. Barker, *J. Org. Chem.*, **29**, 452 (1964).
(40) L. L. Braun and C. K. Bradsher, *ibid.*, **33**, 1296 (1968).
(41) C. K. Bradsher, L. E. Beavers, and J. H. Jones, *ibid.*, **22**, 1740 (1957).
(42) A. Richards and T. S. Stevens, *J. Chem. Soc.*, 3067 (1958).
(43) C. K. Bradsher and J. H. Jones, *J. Am. Chem. Soc.*, **81**, 1938 (1959).

seems likely that all of the products[42] obtained by reaction with active methylene groups have analogous structures or are Michael addition products (**61**) derived therefrom.

It has been demonstrated[42] that phenylmagnesium bromide, like the hydroxyl ion, attacks the acridizinium ion at the 6 position.

Action of Electrophilic Reagents. In the absence of activating groups, the quinolizinium ion does not appear to undergo electrophilic substitution. With the acridizinium ion, sulfonation occurs in the more remote (C) ring, in the 10 position, affording the betaine **62** in 82% yield.[44] This can be rationalized on the basis



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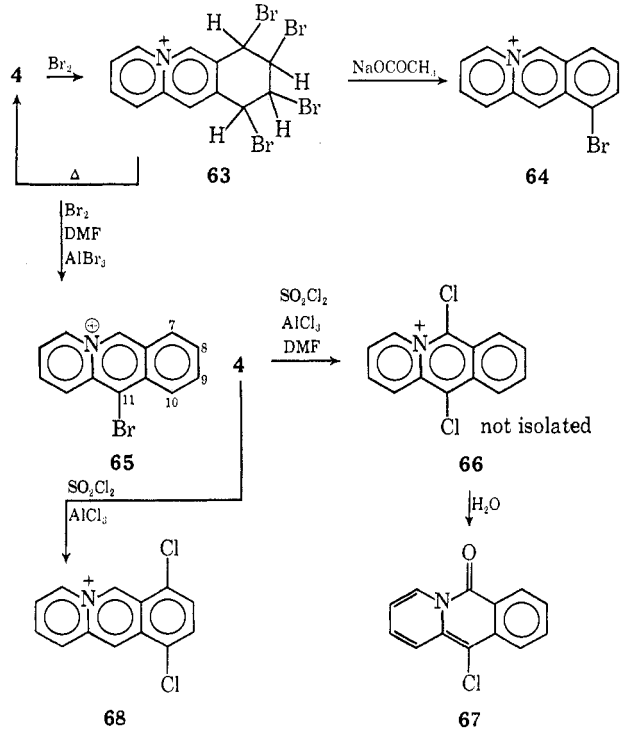
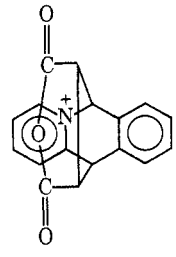
that the 10 position is an α rather than a β position and, unlike position 7, is not a position which bears a positive charge in the resonance hybrid.

The mechanism of halogenation of the acridizinium ion[45] appears less clear. It is certain that reaction with bromine in the absence of solvent affords an addition compound (**63**) in which it is probable that bromine has been added to the 7, 8, 9, and 10 positions. The new cation reverts to the acridizinium ion on heating and, with sodium acetate, affords the 10-bromoacridizinium ion (**64**). Dimethylformamide plays an unexplained role in promoting attack by



bromine and sulfuryl chloride at the *meso* positions. The bromination product is believed to be the 11-bromo derivative **65**, while from the chlorination, 11-chloro-6H-benzo[*b*]quinolizin-6-one (**67**), obviously an artifact, was isolated. The primary product was likely 6,11-dichloroacridizinium ion (**66**) which underwent hydrolysis during the isolation procedure. In the absence of dimethylformamide, sulfuryl chloride afforded the 7,10-dichloroacridizinium ion (**68**).

Transannular Addition of Substituted Ethylenes. Without question, the most interesting reaction of the acridizinium ion and its derivatives is the addition of substituted ethylenes across the *meso* positions of the nucleus. The first examples[46] involved the addition of the common dienophiles, maleic anhydride and maleate and fumarate esters. At the time, this was the unique



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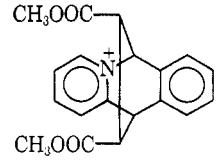

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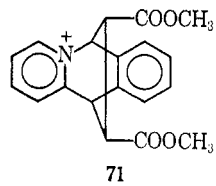
example of a Diels–Alder reaction in which the "diene" component bore a positive charge.

The *cis* dimethyl ester **70** derived from the maleic anhydride addition product **69** has been assigned the *anti* configuration with respect to the benzene ring since the infrared and nmr spectra give evidence of the proximity of one of the carbomethoxy groups to the quaternary nitrogen atom.[47] Such evidence was not to be found in the spectra of the *cis* dimethyl maleate adduct **71** which has been designated *syn*. *Diethyl* maleate gives almost exclusively a *trans* product (**72**)



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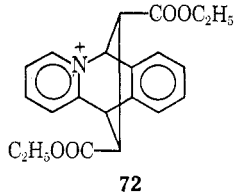

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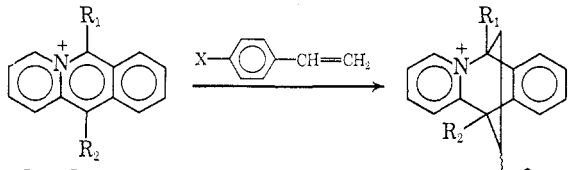
identical with that obtained when diethyl fumarate is used as the ethylenic reactant.

The classical paper of Sauer and Wiest[48] concerning the existence of Diels–Alder reactions with inverse electron demand first made it possible to understand how a *cation* could function as a "diene." *Synthetic*[49] as well as kinetic[46] evidence now shows definitely that the acridizinium ion functions as the electron-deficient

(44) C. K. Bradsher and J. D. Turner, *J. Org. Chem.*, **31**, 565 (1966).
(45) J. D. Turner and C. K. Bradsher, *ibid.*, **32**, 1169 (1967).
(46) C. K. Bradsher and T. W. G. Solomons, *J. Am. Chem. Soc.*, **80**, 933 (1958).
(47) C. K. Bradsher and J. A. Stone, *J. Org. Chem.*, **33**, 519 (1968).
(48) J. Sauer and H. Wiest, *Angew. Chem.*, **74**, 353 (1962).
(49) D. L. Fields, T. H. Regan, and J. C. Dignan, *J. Org. Chem.*, **33**, 390 (1968).

species. Rates of addition of *para*-substituted styrenes to the acridizinium ion follow the inverse electron demand pattern, *p*-nitrostyrene being slowest and *p*-



4, $R_1 = R_2 = H$
73, $R_1 = CH_3$; $R_2 = H$
74, $R_1 = H$; $R_2 = CH_3$
75, $R_1 = R_2 = CH_3$

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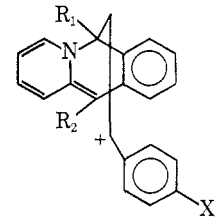
methoxystyrene being fastest in the series.

More recently,[50] the effect of the methyl groups at the *meso* positions of the acridizinium ring has been studied. It is known[51] that 9,10-dimethylanthracene reacts with maleic anhydride much more rapidly than does anthracene, and the observation is explicable in terms of electron release. The introduction of a methyl group at the 6 position of the acridizinium ion (**73**) does slow the reaction significantly. On the other hand, introduction of a methyl group into the other *meso* position, position 11 (**74**), results in a greater than tenfold *increase* in the rate of reaction. Reaction rates for the *meso* dimethyl derivative **75** are not as high as for the 11-methyl (**74**) but are significantly higher than for the acridizinium ion (**4**) itself. It is believed that these results can best be rationalized by assuming the intermediacy of a benzyl carbonium ion (**77**) in a reaction which involves two steps.

(50) J. A. Stone, Ph.D. Dissertation, Duke University, 1968.
(51) W. E. Bachmann and M. C. Kloetzel, *J. Am. Chem. Soc.*, **60**, 481 (1938).



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Reactions of the Benzo[*a*]- and Benzo[*c*]quinolizinium Ions. By comparison with the benzo[*b*]-quinolizinium (acridizinium) ion, very little has been published concerning the chemistry of the angular analogs. The initial paper[22] on the subject of the 7-substituted benzo[*a*]quinolizinium analogs reported that the 7-methyl derivative could be reduced catalytically, presumably to a methylbenzoquinolizidine derivative (**79**), and oxidized by permanganate to phthalic acid.

Richards and Stevens[42] have reported that, on standing in ammonia solution, 7-phenylbenzo[*a*]quinolizinium ion was converted to a pseudo base.

Although preliminary work[52] has been done on the reduction, electrophilic substitution, and ring opening of the benzo[*c*]quinolizinium system, there have as yet been no publications concerning the chemistry of this system.

I wish to acknowledge the support of the National Institutes of Health (National Cancer Institute and National Heart Institute), as well as the support of the National Science Foundation for certain parts of the earlier work in this area.

(52) A. Fozard and C. K. Bradsher, unpublished work.

The Polar Addition of Isocyanates to Carbon–Nitrogen Bonds

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The polar cycloaddition of isocyanates to a great variety of double-bond-containing substrates (dipolarophiles) is an exceedingly useful method of synthesis of heterocyclic molecules.[1] Often one reaction product is obtained in a kinetically controlled reaction, and the reported yields approach theory. However, in the case of slower reacting isocyanates heating is required, which tends to establish thermodynamically controlled equilibria. Some control over the product distribution can be exerted by the choice of reagents and reaction conditions or by removal of lower boiling species from the reaction mixture.

In isocyanates both the C=N and the C=O double bond can participate in polar cycloaddition reactions, but usually reaction products resulting from addition across the C=N double bond are isolated. I have selected the addition of isocyanates to carbon–nitrogen bonds for emphasis in this Account, because the complexities encountered best demonstrate the scope and the limitations of this versatile synthetic method.

(1) H. Ulrich, "Cycloaddition Reactions of Heterocumulenes," Academic Press, New York, N. Y., 1967, Chapters 1 and 4.

Scope and General Description

The reaction of an isocyanate with a double-bond-containing substrate A=B can occur stepwise or concerted with formation of the cycloadduct **4**, provided **4** is stable under the reaction conditions employed. In stepwise addition an acyclic polar adduct, **2**, is formed, which can be intercepted by either the isocyanate or A=B to yield a six-membered-ring 2:1 adduct,