Cycloaddition Reactions of Heteroaromatic Six-Membered Rings

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Contents

I. Introduction

A. Previous Reviews

Parts of this subject have been extensively reviewed previously. Thus heterocyclic Diels–Alder reactions have been reviewed [83T2869, 86CRV781]. Six-membered aromatic betaines (mesoionic six-membered rings) have been covered [80AHC1].

The emphasis in the present treatment is on cycloaddition reactions of heteroaromatic six-membered betaines, especially our work on this topic. Our own work has previously been reviewed in [76AG(E)1] and [79MI290].

B. Organization of the Review

We deal first rather briefly with cycloaddition reactions of neutral and cationic six-membered rings, dividing our discussion into those in which the heterocycle is acting as a 2π component and those where it is acting as a 4π component.

The major emphasis of this review is on the cycloadditions of nitrogen heteroaromatic betaines with six-membered rings, particularly those of 3-oxidopyridiniums and related compounds. In this main section we deal first with dimerizations and then with reactions with 2π substrates followed by reactions with 4π and 6π substrates. This systematic survey leads into a treatment of the rationale of the regiochemistry, site chemistry, and stereochemistry. This section closes with an account of subsequent transformation of the adducts.

The final section of the review deals with cycloaddition reactions of six-membered heteroaromatic betaines containing ring oxygen or sulfur atoms.

Readers will notice that we are using an unconventional system of references in this work. This is the

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Alan R. Katritzky studied at Oxford and was on the Faculty at Cambridge before his appointment as Founding Dean of the School of Chemical Sciences at the University of East Anglia in 1963. He became Kenan Professor at the University of Florida in 1980. He is an honorary member of the Italian and Polish Chemical Societies and has received medals from the Free University of Brussels (Belgium), the Royal Chemical Society (UK), and Tartu State University (Estonia, USSR) and an Honorary D.Sc. from Madrid (Spain). He was nominated Cavaliere Ufficiale by the President of Italy and is a Fellow of the Royal Society (UK).

Nick Dennis was born near Brisbane, Australia, in 1940. He received a B.Sc. degree in chemistry in 1962, an M.Sc. degree in 1964, and a Ph.D. in organic chemistry in 1968 at the University of Queensland, Australia, under the supervision of Prof. Ray A. Carman. He carried out postdoctoral studies with Prof. W. Herz at Florida State University, Prof. E. L. Eliel at the University of Notre Dame, and Prof. A. R. Katritzky at the University of East Anglia, England. In 1974, he joined the Research and Development Unit of Dow Chemical Co., England. His research interests are pesticide design and synthesis, cycloaddition reactions, and heterocyclic chemistry. Nick has a wife, Janet, a daughter, Angela, and a son, Christopher, and in what little time he has available attends to his hobbies of photography and fossil collecting.

reference citation system previously used in the monographs *Heteroaromatic N-Oxides* (by A. R. Katritzky and J. M. Lagowski, Academic Press, 1971) and *Tautomerism of Heterocycles* (by J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, Academic Press, 1976), in *Comprehensive Heterocyclic Chemistry* (edited by A. R. Katritzky and C. W. Rees, Pergamon, 1984), and, starting with Volume 40, for *Advances in Heterocyclic Chemistry*. In this system, each time a reference is cited in the text there appears in brackets a two-letter code assigned to the journal being cited. This code is preceded by the year (tens and units only except for pre-twentieth century references) and followed by the page number. For example: "It was shown [80TL1327] that...." In this phrase, "80" refers to 1980, "TL" to *Tetrahedron Lett.*, and "1327" to the page number. For those journals that are published in parts or that have more than one volume number per year, the appropriate part or volume is indicated, e.g., as in [73J(P2)1594] or [78JM(162)611], where the first example refers to *J. Chem. Soc., Perkin Trans. 2*, p 1594 (1973), and the second to *J. Organomet. Chem.*, Vol. 162, p 611 (1978). Table references are designated by superscript letters, which will be given as footnotes to each table according to the same codes.

This reference system possesses several advantages over the conventional "superscript number" system. It enables the reader to go directly to the literature reference cited, without first having to consult the bibliography at the end of each chapter. A big advantage for authors is that it enables references to be added or subtracted at any time up to final submission of the manuscript without altering the numbering system.

The use of this system for this paper in *Chemical Reviews* is an experiment, and we are grateful to the Editor for his support.

II. Cycloaddition Reactions of Neutral and Cationic Six-Membered Rings

Neutral and cationic rings can enter into cycloaddition reactions either as 2π or as 4π components.

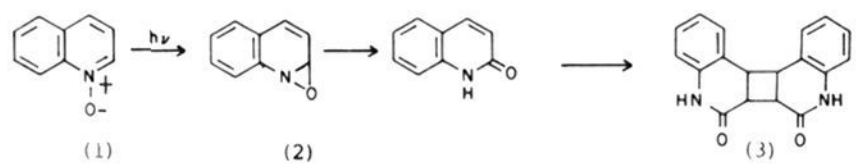
A. Heterocycle as 2π Component

The heterocycle acts as the 2π component in two major classes of reaction: [2 + 2] photoaddition to give four-membered rings, and [2 + 3]/[2 + 4] thermal reactions to give five- and six-membered rings.

1. In [2 + 2] Photochemical Cycloadditions

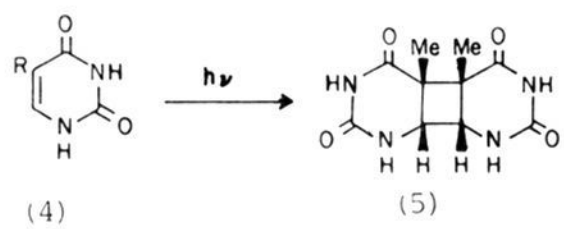
Irradiation of quinoline 1-oxide (**1**) leads (Scheme 1) to a single dimer (**3**) derived from the intermediate carbostyril (**2**) [76H(4)1391].

SCHEME 1



Of biological importance is the fact that thiamine (**4**) on irradiation in a frozen aqueous solution yields photodimers of the "cyclobutane" type (Scheme 2). The main constituent has been identified as the cis–syn dimer (**5**) [66JCS(C)2239]. Similar dimers are formed by the irradiation of frozen solutions of uracil [71B4283, 72MI479], cytosine [71MI365, 71MI357], and related pyrimidines.

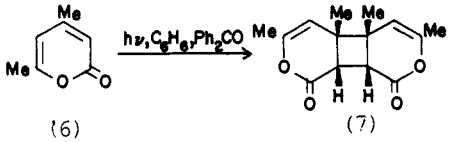
SCHEME 2



The irradiation of 4,6-dimethylpyran-2-one (**6**) (Scheme 3) in benzene in the presence of a sensitizer (benzophenone) yields a symmetrical dimer (**7**) [72TL2247]. The photodimerization of coumarin (**9**) (Scheme 4) in polar solvents such as methanol produces only the cis head-to-head isomer (**10**); however, in benzene the main product is the trans head-to-head

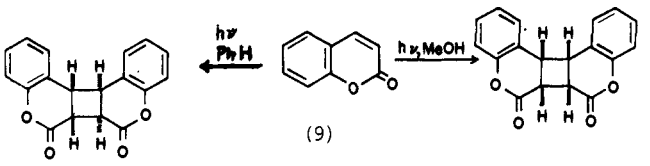
dimer (8). Small quantities of the head-to-tail isomer (11) are found in nonpolar solvents [66JA5415].

SCHEME 3

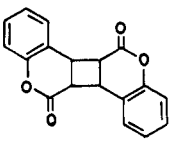


(6) (7)

SCHEME 4



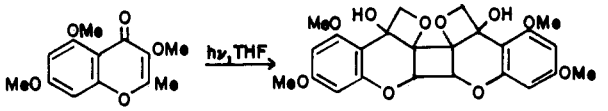
(8) (9) (10)



(11)

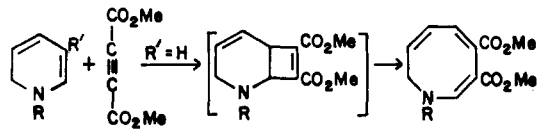
Simple chromones are less susceptible to photolysis, but 3,5,7-trimethoxy-2-methylchromone (12) is converted (Scheme 5) into a dimer 13 [73TL5073]. 1,2-Dihydropyridines (14) undergo [2 + 2] cycloaddition with alkynes to yield azacyclooctatrienes (15) (Scheme 6).

SCHEME 5



(12) (13)

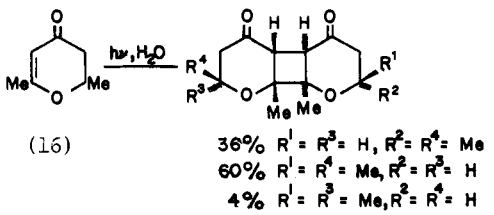
SCHEME 6



(14) (15)

Irradiation of reduced pyran-4-ones forms dimeric products: thus 2,6-dimethyl-2,3-dihydropyran-4-one (16) (cf. Scheme 7) in water solution gives a 96% yield of a mixture of three photodimers (17) [73CJC1267]. 3,3-Dimethylpyran-2,4-dione (18) produces a simple "cyclobutane" dimer (19) (Scheme 8) [73T1317].

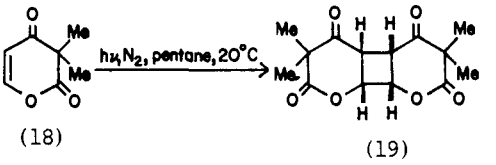
SCHEME 7



(16) 36% $R^1 = R^3 = H$, $R^2 = R^4 = Me$
60% $R^1 = R^4 = Me$, $R^2 = R^3 = H$
4% $R^1 = R^3 = Me$, $R^2 = R^4 = H$

(17)

SCHEME 8

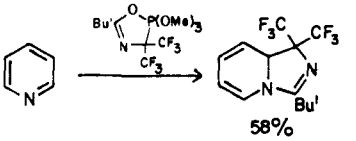


(18) (19)

2. In [2 + 4] Diels–Alder and 1,3-Dipolar Cycloadditions

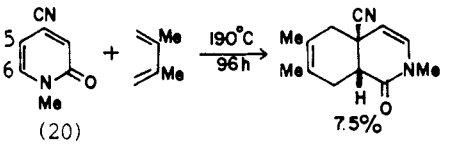
Pyridine undergoes 1,3-dipolar cycloaddition across the 1,2-position with bis(trifluoromethyl)oxazaphospholine [75S731] (Scheme 9); similar 1:1 thermal cycloadducts were obtained with quinolines and with pyrazine. At 190 °C, the 5,6-bond of 4-cyano-1-methylpyridin-2-one (20) acts as the 2π component in a Diels–Alder reaction with 2,3-dimethylbutadiene (Scheme 10) [79H(12)1].

SCHEME 9



58%

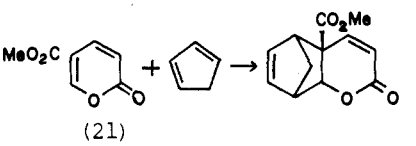
SCHEME 10



(20) 75%

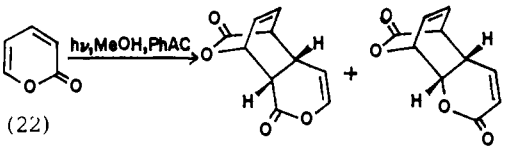
Methyl coumalate (21) reacts (Scheme 11) as a dienophile with cyclopentadiene [72CC388]. The irradiation of pyran-2-one (22) in methanol containing acetophenone as sensitizer yields a mixture of photostable dimers (Scheme 12). In this reaction the pyranone behaves as both diene and dienophile, and the dimers are believed to be formed via triplet excited states of the pyranone [68TL5279].

SCHEME 11



(21)

SCHEME 12



(22)

The retrodiene synthesis of 3-mono- and 2,3-disubstituted pyrimidin-4(3*H*)-ones via the facile thermolysis of 8,9,10-trinorbornene-fused pyrimidones has recently been described [87JCS(PI)237].

B. Heterocycle as 4π Component

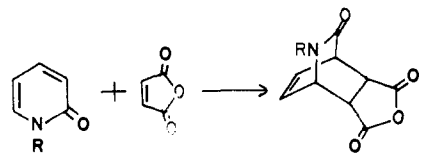
The usual reaction of this type is a Diels–Alder reaction in which the heterocycle acts as the diene. Some photochemical [4 + 4] cycloadditions are known, but

they are limited to dimerizations.

1. *In [4 + 2] Diels–Alder Cycloadditions*

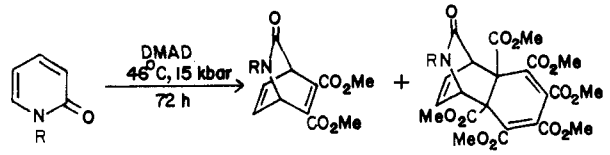
1-Benzylpyridin-2-one (**23**, R = CH_2Ph) cycloadds maleic anhydride (Scheme 13) to yield an adduct (**24**), which has been converted to 2-azabarrelenone [80AG(E)463]. N-Substituted pyridin-2-ones (**23**) react with dimethyl acetylenedicarboxylate under pressure (15 kbar) to yield 1:1 (**25**) and 1:3 (**26**) adducts (Scheme 14) [82H(19)499].

SCHEME 13



(23) (24)

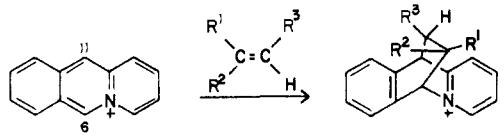
SCHEME 14



(23) (25) (26)

The acridizinium ion (**27**) adds across the 6 and 11 positions maleic anhydride, maleate and fumarate esters, acrylonitrile, and many other substituted ethylenes (Scheme 15) [58JA933, 68JOC390].

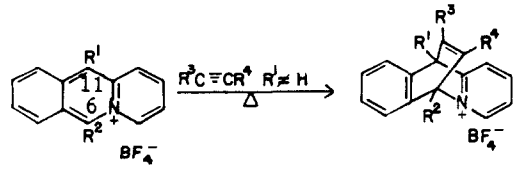
SCHEME 15



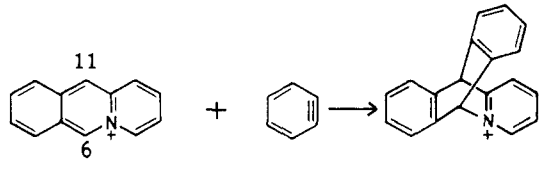
(27)

Alkynes will cycloadd to acridizinium ions (Scheme 16) provided that there is a substituent at position 11 [74AHC(16)289]. Benzyne undergoes polar cycloaddition with the acridizinium ion to yield azoniatryptycene (**28**) (Scheme 17) [71JOC3002, 75TL4639].

SCHEME 16



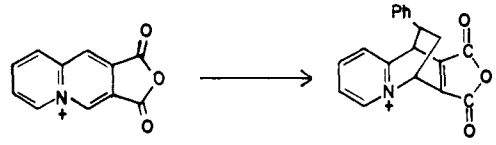
SCHEME 17



(28)

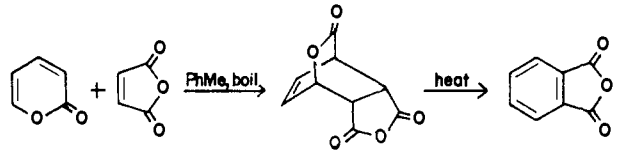
Quinolizinium 2,3-dicarboxylate (**29**) is the only quinolizinium derivative known to undergo polar cycloaddition (Scheme 18) [74AHC(16)289]. Pyran-2-one reacts with maleic anhydride to yield the expected endo cycloadduct (**30**) [31LA(490)257]. This adduct can be converted (Scheme 19) by prolonged heating and loss of carbon dioxide into the benzenoid compound (**31**) [75TL2389].

SCHEME 18



(29)

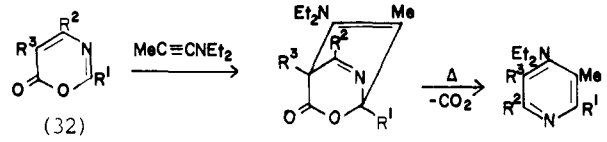
SCHEME 19



(30) (31)

1,3-Oxazin-6-ones (**32**) react with electron-rich dienophiles (Scheme 20) to give adducts (**33**), which lose carbon dioxide on heating [74AG(E)484].

SCHEME 20

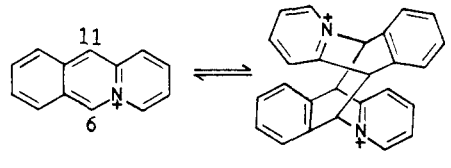


(32) (33)

2. *In [4 + 4] Photodimerizations*

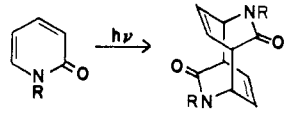
Acridizinium ion readily undergoes photodimerization to produce the [4 + 4] cycloadduct (**34**) (Scheme 21): the photodimer dissociates on heating in ethanol [57JOC1740]. N-Substituted pyridin-2-ones photodimerize (Scheme 22) to the trans,anti-1,4-dimer (**35**) [74HC(14-S1)1]. 2-Aminopyridines dimerize in aqueous acidic solution to produce "butterfly" dimers (**36**) (Scheme 23) [63JA776].

SCHEME 21



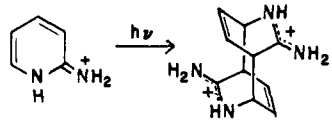
(34)

SCHEME 22



(35)

SCHEME 23



(36)

III. Cycloaddition Reactions of Six-Membered Heteroaromatic Betaines with Positive Charge on Nitrogen

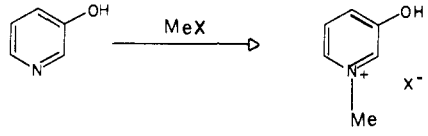
The β-oxidoaziniums react with a wide variety of π-electron-containing systems to give cycloadducts. We discuss in section A the various types of cyclic substrate that have been used and then in sections B–D the compounds that have been formed in the various types of cycloaddition reactions. Section E covers the rationalization of the reactivity type shown. Finally some of the more important further transformations of the adducts are described in section F.

A. Substrates

1. 3-Hydroxy- and 3-Aminopyridinium Salts

Known 3-hydroxypyridinium salts are gathered in Table 1. *N*-Methyl derivatives are known for a wide variety of 3-hydroxypyridines carrying various ring substituents. However, in the case of other N-substituents, the compounds are generally known only for 3-hydroxypyridine itself. Many of these compounds have been made by nucleophilic displacements involving 3-hydroxypyridine (**37**) or a substituted 3-hydroxypyridine as nucleophile and an appropriate halogen compound (Scheme 24). Thus the *N*-methyl derivatives (**38**) are generally being obtained by using methyl iodide, bromide, or tosylate (for references, see Table 1, entries 1, 2, and 3).

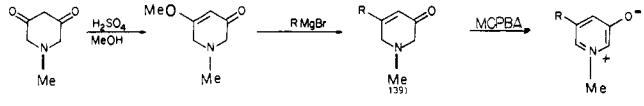
SCHEME 24



(37) (38)

However, *N*-methylpyridinium betaines have also been made by other methods. Thus, the oxidation of suitable 2,6-dihydro derivatives (**39**) has been used (Scheme 25) (for references, see Table 4, entries 20 and 21).

SCHEME 25

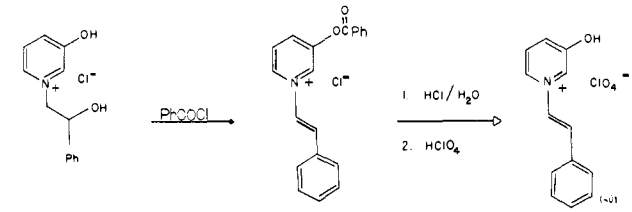


(39)

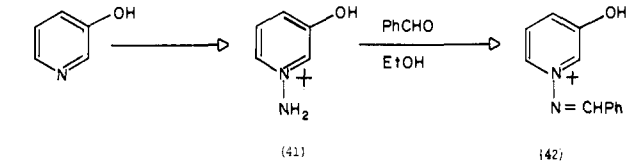
Styryl derivatives (**40**) have been made by the reaction of styrene oxide with 3-hydroxypyridine followed by dehydration in the presence of benzoyl chloride (Scheme 26) (for references, see Table 1, entries 31 and 32). The phenyl derivative (Table 1, entry 10) was made by the reaction of aniline and furfural. The (phenylsulfonyl)methyl derivatives (Table 1, entry 14) were made by S-oxidation of the corresponding sulfides.

The benzylideneamino derivative (**42**) (see Table 1, entry 16) was made from the amino derivative (**41**) and benzaldehyde (Scheme 27). The 1-(1-methylpyridin-4-yl) derivatives (Table 1, entries 43 and 44) were made by quaternization of the corresponding 1-(4-pyridyl) compounds. The 5-aryl-3-hydroxy-1-methylpyridinium bromides (**44**) (Table 1, entries 3, 4, and 8) were prepared by oxidation of the corresponding 5-aryl-1,2,3,6-tetrahydro-1,1-dimethyl-3-oxidopyridinium bromides (**43**) by pyridinium bromide perbromide (Scheme 28).

SCHEME 26

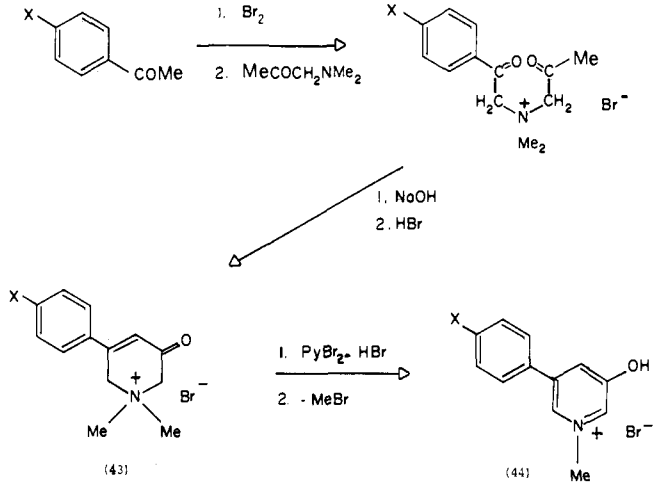


SCHEME 27



(41) (42)

SCHEME 28



(43) (44)

2-(Alkylthio)-3-hydroxy-1-methylpyridinium salts (Table 1, entries 51–55) were prepared by alkylation of the *N*-methylpyridinethione with alkyl halides. Oxidation of N-monosubstituted 2-(α-aminoalkyl)furans with chlorine in water gives quaternary 3-hydroxypyridinium chlorides (Table 1, entry 63).

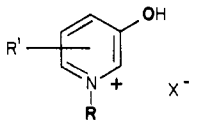
3-(Substituted amino)pyridinium salts are collected in Table 2.

2. Other β-Hydroxyazinium Salts

Examples are given in Table 3 of 4-hydroxyisoquinoliniums, 4-hydroxycinnoliniums, 4-hydroxyphthalaziniums, and β-hydroxy derivatives of pyridiniums containing fused thiazole or thiazine ring systems. These compounds were made in most cases by direct reaction of the corresponding hydroxy derivative with an appropriate chloro or bromo compound or tosylate as quaternizing agent.

Treatment of 3-hydroxypyridine-2-thione (**46**) with 1,2-dibromoethane or 1,3-chlorobromopropane yielded

TABLE 1. 3-Hydroxypyridinium Salts



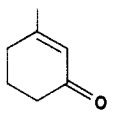
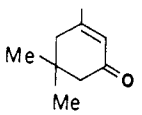
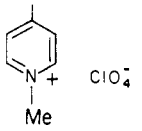
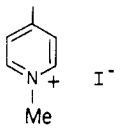
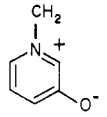
no.	R	R′	X	mp, °C	ref
1	Me	2-Br	OTs	183–185 177–178	80TH1 79JCS(PI)2528
2	Me	6-Me	I	202–203	76JCS(PI)2285
3	Me	5-(4-$MeOC_6H_4$)	Br	197–198	76JCS(PI)2329
4	Me	5-Ph	Br	222–224	76JCS(PI)2329
5	Me	2-Cl	OTs	149–150	79JCS(PI)2528
6	Me	2-CN	OTs		69ACS1785
7	Me	H	I	109–111	59JA5140
8	Me	5-(4-$NO_2C_6H_4$)	Br	266–268	76JCS(PI)2329
9	$(Me)_2NCO$	H	Cl	oil	79JCS(PI)399
10	Ph	H	Cl	222, 212–214	74TH1, 50JA2285
11	$PhCH_2$	H	Br	125–128	59JA5140
12	$PhCOCH_2$	H	Br	228–229	75CPB2904
13	$PhSCH_2$	H	Cl	171–172	79JCS(PI)399
14	$PhSO_2CH_2$	H	Cl	242–244	79JCS(PI)399
15	$PhCO_2CH_2$	H	ClO_4	222–224	79JCS(PI)399
16	PhCH=N	H	OTs	140–141	79JCS(PI)399
17	4,6-dimethoxy-*s*-triazin-2-yl	H	Cl	167–168	77JCS(PI)1930
18	4,6-dimethylpyrimidin-2-yl	H	Cl	224–225	76JCS(PI)2296
19	2,4-dinitrophenyl	H	Cl	205–206, 193–194	74JCS(PI)1883
20	4,6-diphenyl-*s*-triazin-2-yl	H	Cl	167–168	77JCS(PI)1930
21	5,6-diphenyl-1,2,4-triazin-3-yl	H	Cl	215–218	80JCS(PI)343
22	4-(2,3,5,6-F_4C_6)	H	F	171–172	79JCS(PI)399
23	H_2N	H	OTs	185–186	79JCS(PI)399
24	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	H	pic	254	81MI1351
25	5-nitro-2-pyridyl	H	Cl	205–206	74CC500, 76JCS(PI)2296
26	1-oxido-4-pyridyl	H	pic	90–91	80JCR(M)3337
27	5-phenyl-1,2,4-triazin-3-yl	H	Cl	234–236	80JCS(PI)343
28	2-pyridyl	H	Cl	180–181	80JCS(PI)343
29	2-pyridyl	H	ClO_4	155–157	80JCS(PI)343
30	4-pyridyl	H	Cl	226–227	80JCS(PI)343
31	styryl	H	ClO_4	168	79JCS(PI)2535
32	styryl	H	Br	208–209	79JCS(PI)2535
33	quinoxolin-2-yl	H	ClO_4	195–197	80JCS(PI)343
34	MeCOCH=CH	H	pic	175	79MI57
35	$(Me)_3CCOCH=CH$	H	Cl	202–203	79MI57
36	$PhCH=CH—COCH_2$	H	Br	167–169	79MI57
37	4-$ClC_6H_4COCH=CH$	H	Cl	212–213	80JCS(PI)362
38	4-$BrC_6H_4COCH=CH$	H	Cl	224–225	80JCS(PI)362
39	4-$BrC_6H_4COCH=CH$	6-Me	Cl	149–150	80JCS(PI)362
40	2-Cl-5-$NO_2C_6H_3COCH=CH$	H	pic	168–170	80JCS(PI)362
41		H	ClO_4	199–200	79MI57
42		H	Cl	200–205	79MI57
43		H	ClO_4	138–140	80JCS(PI)343
44		H	I	162–164	80JCS(PI)343
45	$PhCHOHCH_2$	H	Br	218–220	79JCS(PI)2535
46	$PhCHOHCH_2$	H	Cl	233–234	79JCS(PI)2535
47		H	I	211.5–212	78JCR(M)1182

TABLE 1 (Continued)

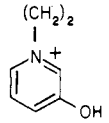
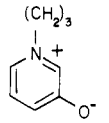
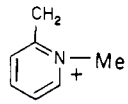
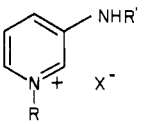
no.	R	R′	X	mp, °C	ref
48		H	2Br	289–290	78JCR(M)1182
49		H	Br	253–253.5	78JCR(M)1182
50	4-$NO_2C_6H_4CH_2$	H	Br	216–217	81MI1351
51	4-ClC_6H_4COCH=CH	2-SMe	Cl	196–197	80TH1, 81JCR(1S)208
52	Me	2-SCH_2CH=CH_2	Br	145–147	80TH1, 81JCR(S)208
53	Me	2-SCH_2Ph	Br	157–158	80TH1, 81JCR(S)208
54	Me	2-SMe	I	183–184.5	80TH1, 81JCR(S)208
55	H	2-SCH_2Ph	Br	171–173	80TH1
56	2-picolyl	H	Cl	140–142	80TH1, 81JCR(S)208
57		H	OTs	201–202.5	80TH1, 81JCR(S)208
58	Me	2-$SCHPhCO_2H$	Br	194–196	81JCR(S)208
59	$(CH_2)_3CH$=CH_2	H	Br		76CC367
60	6-phenyl-3-pyridazinyl	H	Cl	234–235	83JCR(S)37
61	6-(4-methoxyphenyl)-3-pyridazinyl	H	Cl	242–243	83JCR(S)37
62	4-methyl-6-phenyl-3-pyridazinyl	H	Cl	170–171	83JCR(S)37
63	Me	H	Cl	162–164	69ACS1785

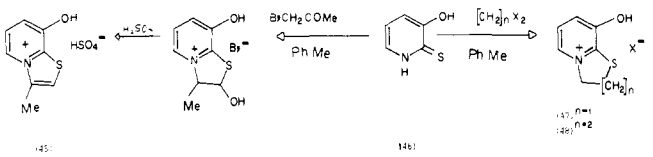
TABLE 2. 3-(Substituted amino)pyridinium Salts



no.	1-substituent	substituent on amino group	anion	mp, °C	ref
1	Me	SO_2Me	I	209–210	77JCS(PII)1304
2	Me	1-(2,4,6-$(NO_2)_3C_6H_2$)	I	200	77JCS(PII)1304
3	Me	1-(2-$NO_2C_6H_4$)	I	155–156	77JCS(PII)1304
4	1-(2,4-$(NO_2)_2C_6H_3$)	H	Cl	240	77JCS(PII)1304
				238–240	65JPR96
5	CH_2Ph	CONHPh	Cl	207	78ZN(B)84
6	$CH_2C_6H_3$(2,6-Cl_2)	$CONHCH_2OMe$	Cl	176–177	78ZN(B)84
7	CH_2Ph	$CONHCH_2OMe$	Cl	197	78ZN(B)84
8	$CH_2C_6H_3$(2,6-Cl_2)	CO_2Et	Cl	221–224	78ZN(B)84
9	$CH_2C_6H_3$(2,6-Cl_2)	$CONH_2$	Cl	216–219	78ZN(B)84

the expected dihydrothiazolo (**47**) and the dihydrothiazino (**48**) salts (Scheme 29). The thione **46** with α-bromoacetone gave a bicyclic salt that dehydrated exclusively to a thiazolo salt (**45**) [81JCR(S)208, 81JCR(M)2345].

SCHEME 29



3. 3-Oxidopyridiniums

Many of the 3-hydroxypyridinium salts (**49**) given in Table 1 have been converted to the corresponding 3-oxidopyridiniums (**50**) (Scheme 30; Table 4). Usually, the reaction proceeds quite readily with bases such as NaOH, Amberlite IRA-401 (OH^-) resin, or triethylamine. However, in certain cases, the entry in Table 4 is absent although the corresponding entry is given in Table 1, due to the fact that the 3-oxidopyridinium in question is so reactive that it spontaneously dimerizes (see Table 7).

SCHEME 30

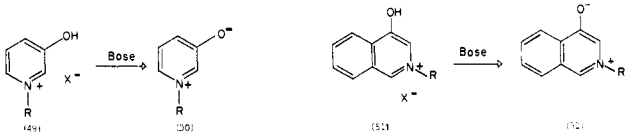
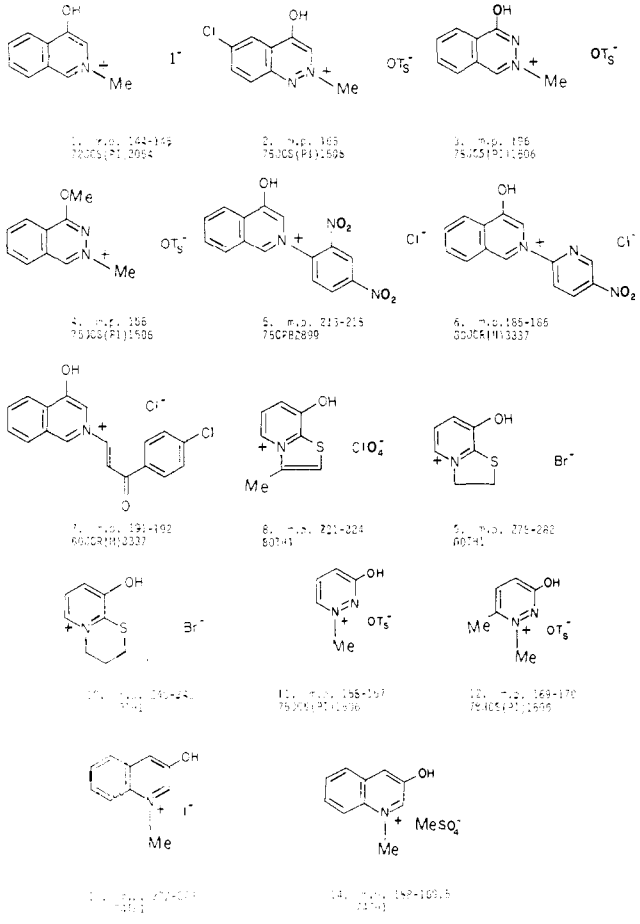


Table 5 lists pyridinium betaines with anionic N-linked 3-substituents. These were readily produced from the corresponding salts by using Amberlite IRA-401 (OH^-) or triethylamine. The betaines were recovered unchanged when heated with various olefinic dipolarophiles.

4. Other β-Oxidoaziniums

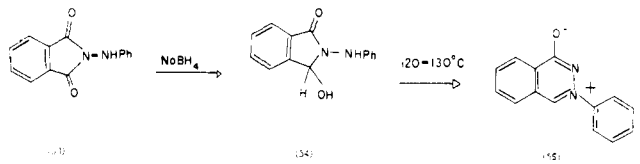
The β-oxidoaziniums (e.g., **52**) recorded in Table 6 correspond to the salts (e.g., **51**) given in Table 3. Again, they were generally prepared from the corresponding salts by using Amberlite IRA-401 (OH^-) resin or tri-

TABLE 3. Other β-Hydroxyazinium Salts



ethylamine (Scheme 30). 1-Oxido-3-phenylphthalazinium (**55**) was made by the reduction of *N*-anilinophthalimide (**53**) with sodium borohydride to *N*-anilino-3-hydroxyphthalimidine (**54**), which was thermally rearranged to the betaine (Scheme 31). Again, some very reactive β-oxidoaziniums could not be isolated before dimerization.

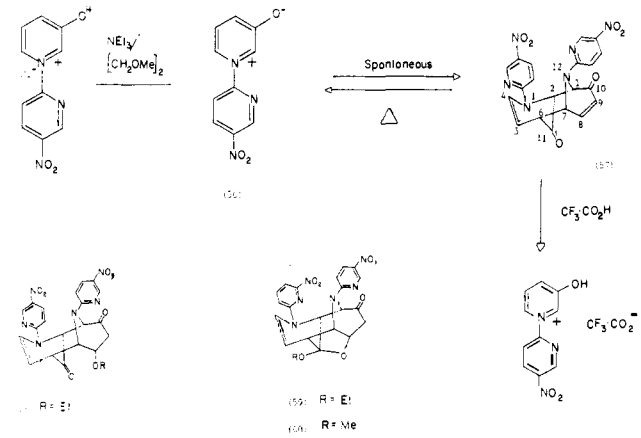
SCHEME 31



B. Dimerizations

Unsymmetrical dimers (Table 7) are generally formed spontaneously from 3-oxidopyridiniums when the N-substituent is a strongly electron-withdrawing one. In some cases, it is possible to isolate both the monomeric betaine and the dimer, as for example 1-(5-nitro-2-pyridyl)-3-oxidopyridinium (**56**) and 3,12-bis(5-nitro-2-pyridyl)-3,12-diazatricyclo[5.3.1.$1^{2,6}$]dodeca-4,8-diene-10,11-dione (**57**) [76JCS(PI)2296] (Scheme 32). However, in most cases, when a dimer is formed, the monomer is too unstable for isolation. The dimers are in thermal equilibrium with the corresponding monomers at elevated temperatures, and this dissociation is also induced by strong acids, e.g., trifluoroacetic acid, when protonation of the dimer carbonyl oxygen atoms initiates dissociation. The structure of the dimers has been confirmed by their spectral properties [76JCS(PI)2296]. The IR spectrum of the dimer (**57**) shows carbonyl stretching frequencies at 1735 (saturated) and 1680 cm^{-1} (conjugated α,β-unsaturated).

SCHEME 32



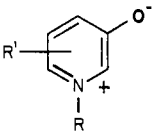
The NMR spectrum of **57** in $(CD_3)_2SO$ shows two clear AMX systems in the aromatic region assignable to the two nitropyridyl groups situated in different environments. In the olefinic region, the downfield quartet at δ 7.55 was assigned to H-8, and irradiation at this frequency simplified the absorptions of H-7 (δ 5.97) and H-9 (δ 6.29). Irradiation at the H-6 absorption frequency (δ 3.49) confirmed the coupling of H-6 to H-7 by 2.5 Hz and the coupling of H-6 to H-5 by 6.5 Hz, and as H-5 is in turn coupled to H-4 by 7.7 Hz, the positional sequence H-4 to H-9 was thus unambiguously established. The exo configuration of the dimer **57** is supported by the fact that H-6 is coupled to H-2 by 2.5 Hz. Molecular models demonstrate that only in the exo structure does the four-bond system connecting the two protons H-6 and H-2 assume a planar configuration necessary for W-type long-range coupling: the system deviates sharply from planarity in the endo structure.

The 1-(5-nitro-2-pyridyl)-3-oxidopyridinium dimer (**57**) on treatment with sodium ethoxide in ethanol at 30 °C produces a bright yellow solid, mp 202–203 °C. X-ray analysis of this compound has shown [85JCR(S)212] that the structure is not **58** as previously [76JCS(PI)2296] described, but **59**, having three six-membered rings and one saturated substituted tetrahydrofuran-type ring. A similar structure has been proposed [85JCR(M)2473] for the corresponding methoxy derivative (**60**) (Scheme 32).

Symmetrical dimers (Table 8) are formed photochemically from 3-oxidopyridiniums when irradiated above 3500 Å. The structures of the dimers were confirmed by their spectral properties [79JCS(PI)2535]. The IR spectrum of each dimer exhibited a carbonyl stretching frequency in the range 1740–1752 cm^{-1}, characteristic of a saturated ketone.

The NMR spectra clearly established the structure of the dimers. The pair of bridgehead protons 1- and 6-H give rise to an overlapping doublet of triplets (coupling with 2- and 7-H, and 10- and 5-H, and a long-range W-type coupling with 7- and 2-H). The second pair of bridgehead protons, 2- and 7-H, give a triplet (coupling with 1- and 6-H and long-range W-type coupling with 6- and 1-H). The vinylic pair 5- and 10-H give a double doublet (cis-vicinal coupling with 4- and 9-H and vicinal coupling with the bridgehead protons

TABLE 4. 3-Oxidopyridiniums



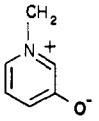
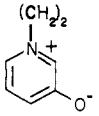
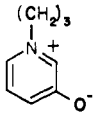
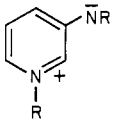
no.	1-substituent	other ring substituents	mp, °C	ref
1	Me	6-Me	134–136	76JCS(PI)2285
2	Me	5-(4-$MeOC_6H_4$)	182–184	76JCS(PI)2329
3	Me	5-Ph	39–40	76JCS(PI)2329
4	Me	2-CN	215–217	79JCS(PI)2528
5	Me	H	37–38	71JCS(C)874
6	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	H	270–272	81MI1351
7	1-oxido-4-pyridyl	H	224	80JCR(M)3337
8	4-pyridyl	H	105–106	80JCS(PI)343
9	styryl	H	138–142	79JCS(PI)2535
10	Ph	H	160	74JCS(PI)746
11	2,4-dinitrophenyl	H	112	74JCS(PI)1883
12	4-ClC_6H_4COCH=CH	H	124–125	80JCS(PI)362
13	4-ClC_6H_4COCH=CH	2-SMe	108–110	80TH1
14	4-BrC_6H_4COCH=CH	H	144–145	80JCS(PI)362
15	4-$NO_2C_6H_4CH_2$	H	120–121	81MI1351
16		H	97–99	78JCR(M)1182
17		H	184–185	78JCR(M)1182
18		H	142–143	78JCR(M)1182
19	$(CH_2)_3CH$=CH_2	H		76CC367
20	Me	5-OMe	55–57	77TL4075
21	Me	5-$CH(Me)_2$	oil	77TL4075

TABLE 5. Pyridinium Betaines with Anionic N-Linked 3-Substituent



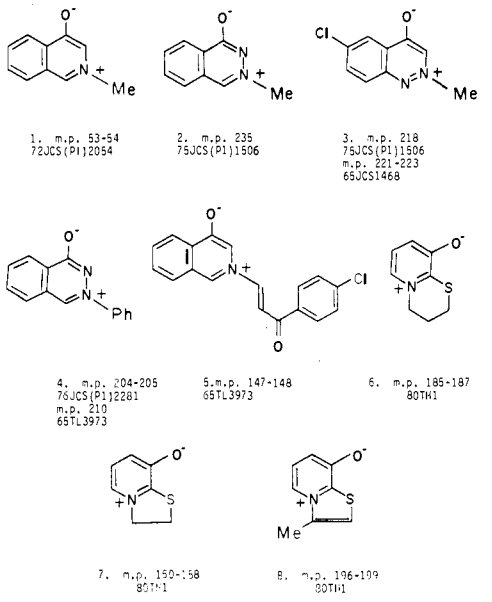
no.	1-substituent	3-substituent	mp, °C	ref
1	Me	NSO_2Me	209–210	77JCS(PII)1304
2	Me	N(2,4,6-$(NO_2)_3C_6H_2$)	258–259	77JCS(PII)1304
3	$PhCH_2$	NCONHPh	85	78ZN(B)84
4	1-(2,6-$Cl_2C_6H_3$)	$NCONHCH_2OMe$	120	78ZN(B)84

6- and 1-H). The olefinic pair 4- and 9-H give a doublet by cis coupling with 5- and 10-H. The exo stereochemistry is clearly defined by the small coupling constant (J = 2.0–3.3 Hz) between 1- and 2-H and 6- and 7-H (the dihedral angle of ca. 50° corresponds to a calculated J of ca. 3 Hz).

The dimers are presumably formed by a photochemically allowed [6 + 6]π 1,3-dipolar cycloaddition between two molecules of the betaine.

Irradiation of 3-oxido-1-phenylpyridinium yields two dimeric stereoisomers (Table 9, entries 1 and 2) formed by thermal addition of the bicyclic valence bond isomer (Table 9, entry 9) to a second molecule of the starting phenyl betaine. Structures were confirmed by NMR spectroscopy. Table 9 lists these and other related dimers together with substituted bicyclic valence bond isomers.

TABLE 6. Other β-Oxidoaziniums

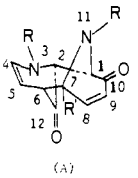


C. Cycloadditions with 2π Units

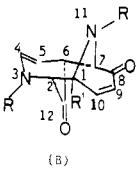
1. Cycloadducts with Olefinic Compounds

The ease of the cycloaddition reaction is dependent both on the structure of the olefin and on the structure of the N-substituent. 1-Methyl-3-oxidopyridinium reacts sucessfully only with olefins containing a strongly

TABLE 7. Unsymmetrical Betaine Dimers



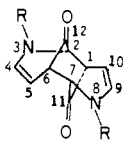
(A)



(B)

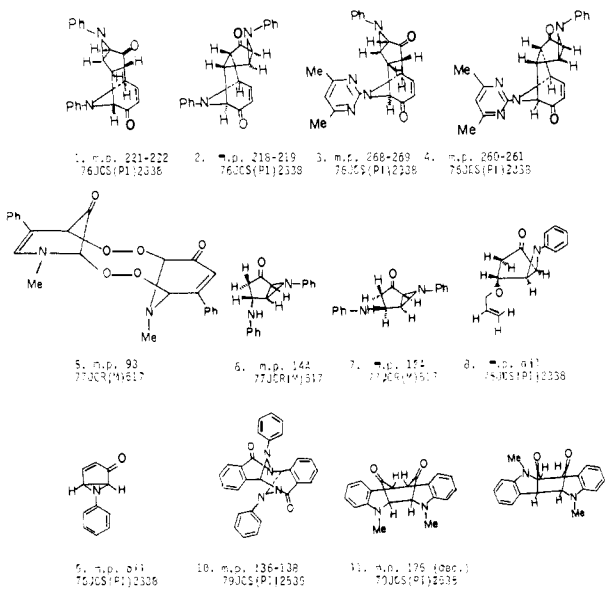
no.	N-substituent (R)	R′	regioisomer	mp, °C	ref
1	5-nitro-2-pyridyl	H	A	196 (dec)	74CC500, 76JCS(PI)2296
2	4,6-dimethylpyrimidin-2-yl	H	A ⇌ B	160–161 (dec)	75CC425, 76JCS(PI)2296
3	4,6-diphenyl-*s*-triazin-2-yl	H	A	>300	80JCS(PI)343
4	4,6-dimethoxy-*s*-triazin-2-yl	H	A	199–200	80JCS(PI)343
5	3-phenyl-1,2,4-thiadiazol-5-yl	H	A	210–212	79JCS(PI)399
6	5,6-diphenyl-1,2,4-triazin-3-yl	H	A	218–220	80JCS(PI)343
7	5-phenyl-1,2,4-triazin-3-yl	H	A	225 (dec)	80JCS(PI)343
8	4-$ClC_6H_4COCH{=}CH$	H	A	176–178	80JCS(PI)362
9	4-$BrC_6H_4COCH{=}CH$	H	A	159–160	80JCS(PI)362
10	4-$BrC_6H_4COCH{=}CH$	Me	A	135–137	80JCS(PI)362
11	2-Cl-5-$NO_2C_6H_3COCH{=}CH$	H	A	186–188	80JCS(PI)362

TABLE 8. Symmetrical Betaine Dimers



no.	N-substituent (R)	mp, °C	ref
1	Ph	175–176	79JCS(PI)2535
2	2-pyridyl	200	79JCS(PI)2535
3	4-pyridyl	220	79JCS(PI)2535
4	styryl	192–194	79JCS(PI)2535
5	4,6-dimethylpyrimidin-2-yl	256–257	79JCS(PI)2535

TABLE 9. Photoisomers and Their Adducts



electron-withdrawing group, e.g., acrylonitrile. Other olefins do not yield cycloadducts. The most reactive 5-nitro-2-pyridyl betaine reacts with the unreactive dipolarophile styrene. The 3-oxido-1-heteroarylpyridinium betaines have been shown to form a series that displays increasing reactivity in pericyclic reactions with olefinic dipolarophiles, viz., 5-phenyl-1,2,4-triazin-3-yl > 5,6-diphenyl-1,2,4-triazin-3-yl > quinoxolinyl > 3-pyridyl > 4-pyridyl > phenyl > methyl. 3-Oxidopyridiniums readily form cycloadducts with electron-deficient olefins, and a large number of such adducts are known. Details are given in Tables 10–18. The structure assignments depend largely on NMR evidence. A characteristic pattern is observed for H-3 and H-4 in the NMR spectra for all the N-substituted cycloadducts investigated: H-4 gives rise to a quartet with $J_{3,4}$ ca. 10.0 Hz and $J_{4,5}$ ca. 5.0 Hz, and H-3 gives a doublet of doublets with $J_{3,4}$ ca. 10.0 Hz and $J_{1,3}$ ca. 1.4 Hz. For the monosubstituted olefin (e.g., acrylonitrile, methyl acrylate), the H-1 signal appears as a doublet ($J_{1,7\text{-exo}}$ ca. 8.0 Hz), and that of the H-5 as a doublet ($J_{4,5}$ ca. 5.5 Hz) for the exo isomers and a quartet ($J_{4,5}$ ca. 5.5 Hz, $J_{5,6\text{-exo}}$ ca. 6.0 Hz) for the endo isomers. For the exo isomers, H-6-endo gives a quartet ($J_{6\text{-endo},7\text{-exo}}$ and $J_{6\text{-endo},7\text{-endo}}$), but for the endo isomers, H-6-exo gives a doublet of triplets because of significant additional coupling ($J_{5,6\text{-exo}}$ ca. 6.0 Hz). In the spectra of all four isomers, the H-7-exo gives an octet and the H-7-endo a quartet. Many assignments were confirmed by exhaustive NMR double-resonance experiments.

In general, the stereochemistry of the original olefin is preserved during the cycloaddition reaction. Diethyl fumarate reacts with 3-oxido-1-phenylpyridinium to yield a mixture of the expected trans cycloadducts. Diethyl maleate reacts with the isolated betaine to produce mainly the expected cis adducts together with small quantities of the isomeric trans adducts. The stereochemistry of the reactions of diethyl fumarate and maleate shows clearly [76JCS(PI)2289] that these reactions are concerted cycloadditions. In the 2-(2,4-dinitrophenyl)isoquinolinium series, reaction with dimethyl maleate did not proceed stereospecifically, a result that was attributed [75CPB2899] to subsequent epimerizations of the initially formed cis adducts in the presence of an excess of base.

Acenaphthylene adducts are detailed in Table 19. 3-Oxido-1-(2-pyridyl)pyridinium and 3-oxido-1-(5,6-diphenyl-1,2,4-triazin-3-yl)pyridinium both reacted with the strained olefin acenaphthylene to yield both exo and endo adducts. However, in the case of 1-(1-oxido-4-pyridyl)-3-oxidopyridinium and 3-oxido-1-(4-pyridyl)-pyridinium the exo adduct was produced exclusively.

Adducts from 3-oxidopyridiniums and *N*-phenylmaleimide are given in Tables 20 and 21. The evidence for their structure is mainly from NMR and is closely similar to that for the other olefinic derivatives already discussed. The splitting pattern of the two bridgehead

protons, H-1 and H-5, characterizes the stereochemistry of the cycloadducts, since $J_{5,6\text{-endo}}$ is negligibly small whereas $J_{5,6\text{-exo}}$ is relatively large (6–8 Hz). Thus the *exo-N*-phenylmaleimide adducts show the H-1 signal as a singlet and that of the H-5 as a doublet, whereas the spectrum of the endo isomer shows the H-1 signal as a doublet and that of H-5 as a quartet. The stereochemistry of the additions can be explained by MO considerations. Endo addition of conjugated olefins is favored by secondary orbital overlap but disfavored by steric factors and dipole–dipole interactions. The exclusive formation of the endo adducts from the reaction of *N*-phenylmaleimide with the dinitrophenyl, the nitropyridyl, the 4-pyridyl, and the 2-pyridyl betaines is predicted by MO calculations for $(2s + 4s)\pi$ processes, which should proceed preferentially via the endo transition state. The formation of the thermodynamically more stable exo products with the 5,6-diphenyl-1,2,4-triazin-3-yl and β-benzoylvinyl betaines is probably the result of thermal isomerism of the initially formed kinetic product, the endo isomer.

Adducts from other β-oxidoazinoniums and olefins are given in Tables 22 and 23. Once again, the structures depend heavily on NMR evidence. In the NMR spectra of the endo isomers, the signals for both of the bridgehead protons appear as doublets while in the exo isomers, the signals for one bridgehead proton appears as a doublet while that of the other bridgehead appears as a singlet. The 6- and 7-regioisomers were readily distinguished by the respective chemical shift differences between the bridgehead protons. Extensive spin–spin decoupling experiments confirmed these assignments.

N-Substituted isoquinolinium betaines react readily with a variety of olefinic dipolarophiles, including indene, the strained olefin acenaphthylene, and the diene cyclopentadiene acting as a monoene. Cycloadditions with acrylonitrile and methyl acrylate were not regiospecific, and all four possible isomers were produced in each case (Table 22A). The relatively unreactive dipolarophile styrene reacted with 2-(2,4-dinitrophenyl)-4-oxidoisoquinolinium to produce two regioisomers, the 6-endo adduct and the 7-endo cycloadduct. The NMR spectra confirmed the exo stereochemistry since H-6 and H-7 formed an AB quartet and the bridgehead protons, H-1 and H-5, exhibited a singlet and a doublet, respectively (endo stereochemistry would cause the bridgehead protons, H-1 and H-5, to exhibit a doublet and a triplet, respectively).

Indene adducts are listed in Table 22B. 3-Oxido-1-(5,6-diphenyl-1,2,4-triazin-3-yl)pyridinium, 3-oxido-1-(4,6-dimethylpyrimidin-2-yl)pyridinium, and 3-oxido-1-(6-phenylpyridazin-3-yl)pyridinium all reacted with indene to yield exclusively the endo adducts. The NMR spectra of these indene adducts exhibit double doublets for H-1, confirming the endo stereochemistry for the adducts. However, 3-oxido-1-(1-oxido-4-pyridyl)pyridinium yielded exclusively the exo isomer.

Adducts from 3-oxidopyridiniums and various activated olefins are given in Table 22C. 1,4-[(*tert*-Butyloxycarbonyl)amino]-1,4-dihydronaphthalene reacted [80JOC479] with 1-methyl-3-oxidopyridinium and 1-phenyl-3-oxidopyridinium under reflux in toluene to give 1:1 adducts in 70% and 40% yields, respectively. The NMR spectra confirmed the exo,exo stereochemistry in view of the absence of vicinal coupling between H-1 and H-2 and H-8 and H-9.

7-Isopropylidenebenzonorbornadiene and 1-methyl-3-oxidopyridinium in toluene under reflux yielded [81JA565] the 1:1 adduct in 10% yield. In the NMR spectrum, the absence of vicinal coupling between H-1 and H-2 (H-3 and H-4) indicated the exo,exo configuration. Norborn-2-ene and 1-(5-nitro-2-pyridyl)-3-oxidopyridinium furnished a mixture of endo adducts in 59% yield. Again, the NMR spectra confirmed the presence of endo isomers.

Thermolysis of 3-oxido-1-(pent-1-en-5-yl)pyridinium in acetonitrile at 140 °C yields a single cycloadduct (2,4-dinitrophenylhydrazine derivative, 225–227 °C) via intramolecular cycloaddition to an unactivated double bond (see Table 17).

1-Methyl-3-(3-phenyl-1,2,4-triazol-5-yl)pyridinium iodide when treated with triethylamine in the presence of acrylonitrile or methyl acrylate yields novel triazolonaphthyridine derivatives [86MI27]. Structures were confirmed by spectral data (see Table 22C).

2. Acetylene Cycloadducts

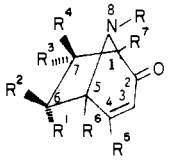
Adducts from 3-oxidopyridiniums and acetylenes are given in Table 24. A number of activated 3-oxidopyridinium betaines readily reacted with acetylenic dipolarophiles, including dimethyl acetylenedicarboxylate (DMAD), phenylacetylene, diphenylacetylene, and ethyl phenylpropiolate, to yield normal 2,6-adducts. The NMR spectra of 2,6-adducts substituted at both C-6 and C-7 exhibited a doublet (J ca. 5 Hz) for H-5 and a singlet for H-1. Adducts from other β-hydroxyazinoniums and acetylenes are given in Tables 25–27. The generally unreactive cinnolinium, phthalazinium, and isoquinolinium betaines readily reacted with acetylenic dipolarophiles at elevated temperatures. The structures of the corresponding cycloadducts were readily confirmed by their IR and NMR spectra. For instance, the single adduct, mp 149–150 °C (Table 26), isolated from 6-chloro-2-methyl-4-oxidocinnolinium and phenylacetylene was shown by NMR to be the regioisomer substituted at C-9, since H-3 and H-10 are coupled to each other as demonstrated by double resonance.

8-Methoxyberberine phenolbetaine readily reacts [79H(12)511] with various acetylenic compounds to afford 1,3-dipolar cycloadducts. For instance, treatment with dimethyl acetylenedicarboxylate in tetrahydrofuran yields a cycloadduct, mp 247–249 °C (see Table 24). These cycloadducts of berberine readily rearrange on warming.

Cycloaddition of dimethyl acetylenedicarboxylate with a variety of 1-substituted 3-oxidopyridinium betaines yields novel furan cycloadducts. For example, the *N*-phenyl betaine yields dimethyl 5-(3-(phenylimino)prop-1-enyl)furan-2,3-dicarboxylate (Table 24, entry 14) (83CC1216, 88JCS(PI)917). Cycloaddition occurs at the exocyclic oxygen atom and the ring carbon 2, with concomitant opening of the pyridine ring. The initially formed *cis*-1′-ene is thought to isomerize to the isolated trans isomer (see Table 24).

Cycloaddition of 1-oxido-3-phenylphthalazinium with dimethyl acetylenedicarboxylate gives the normal 2,6-adduct, mp 176–177 °C (Table 27, entry 5), by refluxing in xylene. However, the use of chloroform as solvent

TABLE 10. Cycloadducts from 3-Oxidopyridiniums with Acrylonitrile



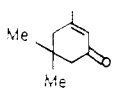
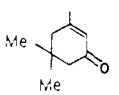
no.	R	R^1	R^2	R^3	R^4	R^5	R^6	R^7	mp, °C	ref
1	Me	CN	H	H	H	H	H	Br	oil	79JCS(PI)2528
2	Me	H	CN	H	H	H	H	Br	oil	79JCS(PI)2528
3	Me	CN	H	H	H	4-$MeOC_6H_4$	H	H	oil[a]	76JCS(PI)2329
4	Me	H	CN	H	H	4-$MeOC_6H_4$	H	H	103–105	76JCS(PI)2329
5	Me	CN	H	H	H	Ph	H	H	oil	76JCS(PI)2329
6	Me	H	CN	H	H	Ph	H	H	99–101	76JCS(PI)2329
7	Me	CN	H	H	H	H	H	Cl	125	79JCS(PI)2528
8	Me	H	CN	H	H	H	H	Cl	125	79JCS(PI)2528
9	Me	H	CN	H	H	H	H	H	94–95	71JCS(C)874
10	$NCCH_2CH_2$	CN	H	H	H	H	H	H	oil	79JCS(PI)2528
11	$NCCH_2CH_2$	H	CN	H	H	H	H	H	72–73[b]	79JCS(PI)2528
12	$(Me)_2NCO$	CN	H	H	H	H	H	H	oil	79JCS(PI)399
13	$(Me)_2NCO$	H	CN	H	H	H	H	H	oil	79JCS(PI)399
14	Ph	CN	H	H	H	H	H	H	170–171	74JCS(PI)746
15	Ph	H	CN	H	H	H	H	H	123–124	74JCS(PI)746
16	$PhCH_2$	CN	H	H	H	H	H	H	oil	76JCS(PI)2334
17	$PhCH_2$	H	CN	H	H	H	H	H	oil	76JCS(PI)2334
18	PhCH=N	CN	H	H	H	H	H	H	129–130	79JCS(PI)399
19	PhCH=N	H	H	CN	H	H	H	H	166–168	79JCS(PI)399
20	4,6-dimethoxy-*s*-triazin-2-yl	CN	H	H	H	H	H	H	185–187	77JCS(PI)1930
21	4,6-dimethoxy-*s*-triazin-2-yl	H	CN	H	H	H	H	H	169–170	77JCS(PI)1930
22	4,6-dimethylpyrimidin-2-yl	CN	H	H	H	H	H	H	216–217	79JCS(PI)1525
23	4,6-dimethylpyrimidin-2-yl	H	CN	H	H	H	H	H	206–207	79JCS(PI)1525
24	2,4-dinitrophenyl	H	CN	H	H	H	H	H	221–223	74JCS(PI)1883
25	2,4-dinitrophenyl	CN	H	H	H	H	H	H	193	74JCS(PI)1883
26	2,4-dinitrophenyl	H	H	CN	H	H	H	H	204–206	74JCS(PI)1883
27	4,6-diphenyl-*s*-triazin-2-yl	CN	H	H	H	H	H	H	236–237	77JCS(PI)1930
28	4,6-diphenyl-*s*-triazin-2-yl	H	CN	H	H	H	H	H	239–240	77JCS(PI)1930
29	5,6-diphenyl-1,2,4-triazin-3-yl	CN	H	H	H	H	H	H	225–226	80JCS(PI)343
30	5,6-diphenyl-1,2,4-triazin-3-yl	H	CN	H	H	H	H	H	175–177	80JCS(PI)343
31	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	CN	H	H	H	H	H	H	204–205	80JCS(PI)343
32	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	H	CN	H	H	H	H	H	226–228	81MI1351
33	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	H	H	CN	H	H	H	H	210–211	81MI1351
34	5-nitro-2-pyridyl	CN	H	H	H	H	H	H	208–209	76JCS(PI)2307
35	5-nitro-2-pyridyl	H	CN	H	H	H	H	H	163–165	76JCS(PI)2307
36	1-oxido-4-pyridyl	CN	H	H	H	H	H	H	213–215	80JCR(M)3337
37	1-oxido-4-pyridyl	H	CN	H	H	H	H	H	213–215	80JCR(M)3337
38	5-phenyl-1,2,4-triazin-3-yl	CN	H	H	H	H	H	H	209–210	80JCS(PI)343
39	5-phenyl-1,2,4-triazin-3-yl	H	CN	H	H	H	H	H	218–220	80JCS(PI)343
40	5-phenyl-1,2,4-triazin-3-yl	H	H	CN	H	H	H	H	198–200	80JCS(PI)343
41	2-pyridyl	CN	H	H	H	H	H	H	119–120	80JCS(PI)343
42	2-pyridyl	H	CN	H	H	H	H	H	136–137	80JCS(PI)343
43	2-pyridyl	H	H	CN	H	H	H	H	139–140	80JCS(PI)343
44	4-pyridyl	CN	H	H	H	H	H	H	253–255[c]	80JCS(PI)343
45	styryl	H	CN	H	H	H	H	H	gum	79JCS(PI)2535
46	quinoxolin-2-yl	CN	H	H	H	H	H	H	178–179	80JCS(PI)343
47	quinoxolin-2-yl	H	CN	H	H	H	H	H	218–220	80JCS(PI)343
48	$(Me)_3CCOCH{=}CH$	CN	H	H	H	H	H	H	197–200	79MI57
49	$(Me)_3CCOCH{=}CH$	H	CN	H	H	H	H	H	gum	79MI57
50	$(Me)_3CCOCH{=}CH$	H	H	CN	H	H	H	H	gum	79MI57
51	4-$ClC_6H_4COCH{=}CH$	CN	H	H	H	H	H	H	224–225	80JCS(PI)362
52	4-$ClC_6H_4COCH{=}CH$	H	CN	H	H	H	H	H	218–220	80JCS(PI)362
53	2-Cl-5-$NO_2C_6H_3COCH{=}CH$	CN	H	H	H	H	H	H	118–124	80JCS(PI)362
54	2-Cl-5-$NO_2C_6H_3COCH{=}CH$	H	CN	H	H	H	H	H	118–124	80JCS(PI)362
55		CN	H	H	H	H	H	H	192–194	79MI57
56		H	CN	H	H	H	H	H	192–194	79MI57
57	4-$ClC_6H_4COCH{=}CH$	H	H	CN	H	H	H	SMe	226–228	80TH1
58	Me	CN	H	H	H	H	H	$SCH_2CH{=}CH_2$	71–72.5	80TH1
59	Me	H	CN	H	H	H	H	$SCH_2CH{=}CH_2$	82.5–83.5	80TH1
60	Me	CN	H	H	H	H	H	SMe	102.5–104	80TH1
61	Me	H	CN	H	H	H	H	SMe	118–120	80TH1
62	2-picolyl	CN	H	H	H	H	H	H	107–110	80TH1
63	2-picolyl	H	CN	H	H	H	H	H	107–110	80TH1

TABLE 10 (Continued)

no.	R	R^1	R^2	R^3	R^4	R^5	R^6	R^7	mp, °C	ref
64	CH_2CH_2CN	CN	H	H	H	H	Me	H	128–129	79JCS(PI)2528
65	CH_2CH_2CN	H	CN	H	H	H	Me	H	128–129	79JCS(PI)2528
66	6-phenyl-3-pyridazinyl	CN	H	H	H	H	H	H	189–190	83JCR(S)37
67	6-(4-methoxyphenyl)-3-pyridazinyl	CN	H	H	H	H	H	H	198–200	83JCR(S)37
68	4-methyl-6-phenyl-3-pyridazinyl	CN	H	H	H	H	H	H	234–235	83JCR(S)37

[a] Picrate, 204–207 °C. [b] Methiodide, 150 °C. [c] Methyl perchlorate, 238–240 °C.

affords the ring-expanded diazocine, mp 150 °C (Table 28, entry 3). Both the 2,6-adduct and the diazocine are transformed into a third isomer, mp 190 °C (Table 28, entry 1), at 180 °C in the absence of solvent. Structures of adducts were confirmed by physical methods. Phenylacetylene reacted with 1-oxido-3-phenylphthalazinium to produce the related abnormal diazocine (Table 28, entry 4), which on sublimation yielded the second tricyclic derivative (Table 28, entry 2). The two abnormal phenylacetylene adducts were characterized by X-ray analysis. Hanoaka et al. have described a related ring expansion where the normal dimethyl acetylenedicarboxylate adduct (Table 24, entry 13) from 8-methoxyberberine phenolbetaine was heated in ethanol to form the azocine (Table 28, entry 8), mp 252–253 °C [79H(12)511].

3. Benzyne Cycloadducts

Benzyne behaves toward β-hydroxyazinoniums as a very reactive olefin, and many of the products formed (Table 29) can be explained in this way. Thus 3-oxido-1-phenylpyridinium readily reacted with benzyne to yield the corresponding cycloadduct. The structure was supported by IR and UV absorptions characteristic of an α,β-unsaturated carbonyl group, elemental analysis, and the mass spectrum, with a base peak at m/e 206 envisaged as being formed by loss of the fragment –CHCO, which was confirmed by the presence of a metastable peak at m/e 171.8.

3-Hydroxypyridine, 3-hydroxy-6-methylpyridine, phthalazin-1(2*H*)-one, and 6-chloro-4-cinnolone all react with benzyne via the corresponding initially formed *N*-phenyl betaine [76JCS(PI)2285]. Again, when 3-pyridinols were allowed to react with diazotized anthranilic acid itself, the major product was the tricyclic compound [2]benzopyrano[4,3-*b*]pyridin-6-one [74JCS(PI)750]. The IR and UV spectra were consistent with an α,β-unsaturated δ-lactone. The NMR assignments were supported by extensive double-irradiation experiments.

Also 1-methyl-3-oxidopyridinium reacted with benzyne to yield 6,13-dihydro-5-methyl-6,13-methano-5*H*-5-azadibenzo[*a*,*e*]cyclononen-14-one (Table 29, entry 5) in place of the expected cycloadduct. The IR spectrum showed the presence of a saturated ketone while the UV spectrum showed absorption at 247.5 nm from an n → π transition characteristic of *N*,*N*-dimethylaniline.

4. Ketene Cycloadducts

Cycloadducts formed with ketenes are listed in Tables 30 and 31. The evidence for these structures is mainly spectroscopic. The IR spectra for the isomeric 3,4-disubstituted-2-oxo-4*H*-furo[3,2-*b*]pyridines show corresponding ν(C=O) and ν(C=C) stretching frequencies. The ν(C=O) stretching frequencies of the furo[3,2-*b*]-pyridines are usually at higher wavelengths than those for the ν(C=O) for the isomeric furo[2,3-*c*]pyridines. The 3-chloro-2-oxo-6-substituted-2,6-dihydrofuro[2,3-*c*]pyridines exhibit consistently higher ν(C=O) stretching frequencies (1730–1740 cm^{-1}) characteristic of α-chloro-α,β-unsaturated γ-lactones.

The 2-oxo-2,6-dihydrofuro[2,3-*c*]pyridines and the 2-oxo-2,4-dihydrofuro[3,2-*b*]pyridines exhibit strong UV absorption due to π → π* transitions but, in general, the latter absorb at shorter wavelengths than the former.

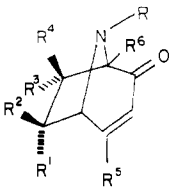
The NMR spectra exhibit consistent and characteristic patterns for H-4, H-5, H-6, and H-7. In the spectra of the furo[2,3-*c*]pyridines, the signal for H-7 appears as a fine doublet; H-5 appears as a finely split doublet coupled by 7–8 Hz, with H-4 as a doublet or double doublet. By contrast, H-5, H-6, and H-7 for the furo-[3,2-*b*]pyridines form an ABC system of which H-5 is clearly seen as either a doublet (J = 7–8 Hz) or as a double doublet, whereas H-6 and H-7 are obscured by the benzene ring protons. The formation is possible of two types of ketene cycloadduct by reaction at the oxygen and 4-position or the oxygen and 2-position. The ratio of the two products formed varies considerably. Cycloadditions of N-substituted 3-oxidopyridiniums with electron-deficient dipolarophiles are the result of the interaction of the highest occupied molecular orbital (HOMO) of the former with the lowest unoccupied molecular orbital (LUMO) of the latter. In the present case, the interaction presumably involves the low-lying LUMO of the ketene. The observed periselectivity can be rationalized by the frontier molecular orbital (FMO) approach (CNDO/2) method. Since the addition is governed by betaine HOMO–ketene LUMO interaction and the ketene LUMO has a high coefficient on the carbonyl carbon atom, this carbon would be expected to interact with the oxygen atom of the betaine, which possesses the highest betaine HOMO coefficient. The other bond is formed to either the 4-position or the 2-position. The FMO calculations indicate that the "covalent term" favors the O,2-orientation, while the "steric term" favors the O,4-orientation: thus the betaine with the slender aroylvinyl substituent group yields only the O,2-isomers. The addition of dichloroketene to betaines with bulky N-substituent groups yields exclusively O,4-adducts. The aroyl(bromo)-ketenes react at both the O,2- and O,4-positions of all betaines investigated.

D. Cycloadditions with Polyenes

1. Cycloadducts with Dienes

Cycloadducts formed with acyclic dienes are given in Tables 32 and 33. 1,3-Dienes readily react either as 2π-electron components across the betaine 2- and 6-positions or as 4π-electron components across the 2- and 4-positions. The different types of adduct are clearly

TABLE 11. Adducts from 3-Oxidopyridiniums and Acrylate Esters

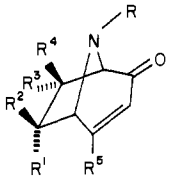


no.	R	R^1	R^2	R^3	R^4	R^5	R^6	mp, °C	ref
1	Me	H	CO_2Me	H	H	H	Br	oil	79JCS(PI)2528
2	Me	H	H	H	CO_2Me	H	Br	106–108	79JCS(PI)2528
3	Me	H	CO_2Me	H	H	Ph	H	63–67	76JCS(PI)2329
4	Me	CO_2Me	H	H	H	Ph	H	128–129	76JCS(PI)2329
5	Me	H	CO_2Me	H	H	H	Cl	85–86	79JCS(PI)2528
6	Me	CO_2Me	H	H	H	H	Cl	85–86	79JCS(PI)2528
7	Me	H	CO_2Me	H	H	H	CN	102–104	79JCS(PI)2528
8	Me	CO_2Me	H	H	H	H	CN	102–104	79JCS(PI)2528
9	Me	H	CO_2Me	H	H	H	H	151–153	71JCS(C)874
10	Me	CO_2Me	H	H	H	H	H	151–153	71JCS(C)874
11	$CH_2CH_2CO_2Me$	H	CO_2Me	H	H	H	H	oil	79JCS(PI)2528
12	$CH_2CH_2CO_2Me$	CO_2Me	H	H	H	H	H	oil	79JCS(PI)2528
13	Ph	H	CO_2Me	H	H	H	H	80–90	74JCS(PI)746
14	Ph	CO_2Me	H	H	H	H	H	97–98[a]	74JCS(PI)746
15	$PhSCH_2$	H	CO_2Me	H	H	H	H	104–106	79JCS(PI)399
16	PhCH=N	CO_2Me	H	H	H	H	H	120–121	79JCS(PI)399
17	Me	H	CO_2Me	H	H	$CHMe_2$	H	oil[b]	77TL4075
18	4,6-dimethoxy-*s*-triazin-2-yl	CO_2Me	H	H	H	H	H	149–150	77JCS(PI)1930
19	4,6-dimethoxy-*s*-triazin-2-yl	H	CO_2Me	H	H	H	H	160–162	77JCS(PI)1930
20	4,6-dimethylpyridimidin-2-yl	H	CO_2Me	H	H	H	H	87–88	79JCS(PI)1525
21	4,6-dimethylpyrimidin-2-yl	CO_2Me	H	H	H	H	H	110–111	79JCS(PI)1525
22	4,6-dimethylpyrimidin-2-yl	CO_2Et	H	H	Ph	H	H	oil	81JHC1461
23	2,4-dinitrophenyl	H	CO_2Me	H	H	H	H	170–172	74JCS(PI)1883
24	2,4-dinitrophenyl	CO_2Me	H	H	H	H	H	171	74JCS(PI)1883
25	4,6-diphenyl-*s*-triazin-2-yl	CO_2Me	H	H	H	H	H	209–210	77JCS(PI)1930
26	4,6-diphenyl-*s*-triazin-2-yl	H	CO_2Me	H	H	H	H	195–196	77JCS(PI)1930
27	5,6-diphenyl-1,2,4-triazin-3-yl	CO_2Me	H	H	H	H	H	184–185	80JCS(PI)343
28	5,6-diphenyl-1,2,4-triazin-3-yl	H	CO_2Me	H	H	H	H	129–130	80JCS(PI)343
29	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	CO_2Me	H	H	H	H	H	195–196	81MI1351
30	5-nitro-2-pyridyl	CO_2Me	H	H	H	H	H	170	76JCS(PI)2307
31	5-nitro-2-pyridyl	H	CO_2Me	H	H	H	H	158	76JCS(PI)2307
32	1-oxido-4-pyridyl	CO_2Me	H	H	H	H	H	210	80JCR(M)3337
33	1-oxido-4-pyridyl	H	CO_2Me	H	H	H	H	106	80JCR(M)3337
34	5-phenyl-1,2,4-triazin-3-yl	H	CO_2Me	H	H	H	H	50–52	80JCS(PI)343
35	5-phenyl-1,2,4-triazin-3-yl	CO_2Me	H	H	H	H	H	129–130	80JCS(PI)343
36	2-pyridyl	CO_2Me	H	H	H	H	H	96–97	80JCS(PI)343
37	2-pyridyl	H	CO_2Me	H	H	H	H	68–70	80JCS(PI)343
38	4-pyridyl	CO_2Me	H	H	H	H	H	143–145[c]	80JCS(PI)343
39	styryl	H	CO_2Et	H	H	H	H	gum	79JCS(PI)2535
40	3-phenyl-1,2,4-thiadiazol-5-yl	CO_2Me	H	H	H	H	H	170–171	79JCS(PI)399
41	3-phenyl-1,2,4-thiadiazol-5-yl	H	CO_2Me	H	H	H	H	95–96	79JCS(PI)399
42	quinoxolin-2-yl	CO_2Me	H	H	H	H	H	169–170[d]	80JCS(PI)343
43	quinoxolin-2-yl	H	CO_2Me	H	H	H	H	135–137	80JCS(PI)343
44	$(Me)_3CCOCH=CH$	CO_2Me	H	H	H	H	H	168–170	79MI57
45	$4\text{-}ClC_6H_4COCH=CH$	H	CO_2Me	H	H	H	H	132	80JCS(PI)362
46	$4\text{-}ClC_6H_4COCH=CH$	CO_2Me	H	H	H	H	H	168–170	80JCS(PI)362
47	$2\text{-Cl-}5\text{-}NO_2C_6H_3COCH=CH$	CO_2Et	H	H	H	H	H	182–184	80JCS(PI)362
48	$2\text{-Cl-}5\text{-}NO_2C_6H_3COCH=CH$	H	CO_2Et	H	H	H	H	148–150	80JCS(PI)362
49	$4\text{-}ClC_6H_4COCH=CH$	CO_2Me	H	H	H	H	H	75–77	80TH1, 81JCR(S)208
50	$4\text{-}ClC_6H_4COCH=CH$	H	CO_2Me	H	H	H	H	75–77	80TH1, 81JCR(S)208
51	Me	CO_2Me	H	H	H	H	thioallyl	47–49	80TH1, 81JCR(S)208
52	Me	H	CO_2Me	H	H	H	thioallyl	47–49	80TH1, 86JCR(S)208
53	Me	CO_2Me	H	H	H	H	SMe	53–54	80TH1, 86JCR(S)208
54	Me	H	CO_2Me	H	H	H	SMe	53–54	80TH1
55	Me	CO_2Et	H	H	H	H	SMe	86–88	80TH1, 81JCR(S)208
56	Me	H	CO_2Et	H	H	H	SMe	86–88	80TH1, 81JCR(S)208
57	2-picolyl	CO_2Me	H	H	H	H	H	oil	86TH1
58	2-picolyl	H	CO_2Me	H	H	H	H	oil	80TH1, 81JCR(S)208
59	6-phenyl-3-pyridazinyl	CO_2Me	H	H	H	H	H	250–251	83JCR(S)37
60	6-phenyl-3-pyridazinyl	H	CO_2Me	H	H	H	H	171–172	83JCR(S)37
61	6-(4-methoxyphenyl)-3-pyridazinyl	CO_2Me	H	H	H	H	H	197–198	83JCR(S)37

[a] Methyl fluorosulfonate, 191–193 °C. [b] Methiodide, 165–167 °C. [c] Methiodide, 179–181 °C. [d] Methiodide, 193–195 °C.

distinguished spectroscopically. For instance, 2,3-dimethylbuta-1,3-diene reacted with the pyridyl betaine dimer at 50–60 °C in chlorobenzene to yield a stable 2,4-adduct. The IR spectrum showed strong ν(C=O) bands at 1720 cm^{-1} for the saturated cyclic ketone, and medium ν(C=C) at ca. 1640 cm^{-1} for the enamine double bond. The ^1H NMR spectrum was consistent only with a 2,4-adduct. The downfield doublet at δ 7.19

TABLE 12. Adducts from 3-Oxidopyridiniums



no.	R	R^1	R^2	R^3	R^4	R^5	mp, °C	ref
1	Me	Ph	H	H	H	Ph	oil	76JCS(PI)2329
2	Me	H	Ph	H	H	Ph	oil	76JCS(PI)2329
3	Ph	Ph	H	H	H	H	105–106[a]	76JCS(PI)2289
4	Ph	4-BrC_6H_4	H	H	H	H	180–181[b]	76JCS(PI)2289
5	Ph	4-ClC_6H_4	H	H	H	H	171–172[c]	76JCS(PI)2289
6	Ph	4-pyridyl	H	H	H	H	165–166[d]	76JCS(PI)2289
7	PhCH=N	Ph	H	H	H	H	133–134	79JCS(PI)399
8	4,6-dimethoxy-*s*-triazin-2-yl	Ph	H	H	H	H	129–130	77JCS(PI)1930
9	4,6-dimethylpyrimidin-2-yl	H	2-pyridyl	H	H	H	105–106	77JCS(PI)1930
10	4,6-dimethylpyrimidin-2-yl	2-pyridyl	H	H	H	H	157–158[e]	79JCS(PI)1525
11	4,6-dimethylpyrimidin-2-yl	4-pyridyl	H	H	H	H	150	79JCS(PI)1525
12	2,4-dinitropyridyl	Ph	H	H	H	H	188–189	74JCS(PI)1883
13	4,6-diphenyl-*s*-triazin-2-yl	Ph	H	H	H	H	219–220	77JCS(PI)1930
14	4,6-diphenyl-*s*-triazin-2-yl	H	Ph	H	H	H	240–242	77JCS(PI)1930
15	5,6-diphenyl-1,2,4-triazin-3-yl	Ph	H	H	H	H	203–205	80JCS(PI)343
16	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	Ph	H	H	H	H	214–215	81MI1351
17	5-nitro-2-pyridyl	Ph	H	H	H	H	176–177	76JCS(PI)2307
18	5-nitro-2-pyridyl	H	Ph	H	H	H	160–165	76JCS(PI)2307
19	1-oxido-4-pyridyl	Ph	H	H	H	H	233	80JCR(M)3337
20	5-phenyl-1,2,4-triazin-3-yl	Ph	H	H	H	H	160–162	80JCS(PI)343
21	2-pyridyl	Ph	H	H	H	H	125–126[f]	80JCS(PI)343
22	2-pyridyl	3-ClC_6H_4	H	H	H	H	84–86	80JCS(PI)343
23	4-pyridyl	Ph	H	H	H	H	195–197[g]	80JCS(PI)343
24	styryl	Ph	H	H	H	H	gum	79JCS(PI)2535
25	quinoxolin-2-yl	Ph	H	H	H	H	191–192[h]	80JCS(PI)343
26	$(CH_3)_3CCOCH=CH$	Ph	H	H	H	H	248–250	79MI57
27	4-$ClC_6H_4COCH=CH$	Ph	H	H	H	H	206–208	80JCS(PI)362
28	2-Cl-5-$NO_2C_6H_3COCH=CH$	Ph	H	H	H	H	118–120	80JCS(PI)362
29	5-nitro-2-pyridyl	4-$MeOC_6H_4$	H	H	H	H	216–217	76JCS(PI)2307
30	5-nitro-2-pyridyl	4-BrC_6H_4	H	H	H	H	206	76JCS(PI)2307
31	5-nitro-2-pyridyl	4-pyridyl	H	H	H	H	215–216	76JCS(PI)2307
32	CH_2Ph	Ph	H	H	H	H	50	76JCS(PI)2334
33	CH_2Ph	H	Ph	H	H	H	104–106	76JCS(PI)2334
34	Me	Ph	H	H	H	OMe	oil[i]	78TL1751
35	6-phenyl-3-pyridazinyl	Ph	H	H	H	H	220–221	83JCR(S)37
36	6-(4-methoxyphenyl)-3-pyridazinyl	Ph	H	H	H	H	194–195	83JCR(S)37

[a] Methyl fluorosulfonate, 189–191 °C. [b] Methyl trifluoromethanesulfonate, 209–235 °C. [c] Methyl trifluoromethanesulfonate, 234–235 °C. [d] Dimethyl bis(trifluoromethanesulfonate), 191–192 °C. [e] Methiodide, 172–173 °C. [f] Methiodide, 185–186 °C. [g] Methiodide, 295–297 °C. [h] Methiodide, 218–220 °C. [i] Picrate, 165–166 °C.

was assigned to the vinylic H-8, and the double doublet at δ 4.95 was assigned to H-9. The vinylic methyl groups absorbed at δ 1.5 and 1.7. The spectrum was further analyzed by using $Eu(fod)_3$ in conjunction with double-resonance experiments. Protons at position 1 as well as 6 were greatly affected by the shift reagent owing to their proximity to the complexation site. The endo structure of the adduct was demonstrated by the LIS technique. The LIS was greater at H-2n and at H-5n than at H-2x and H-5x. The former protons point toward the carbonyl group (the complexation site) and the latter away from it. In the alternative exo structure all four protons are equidistant from the carbonyl group.

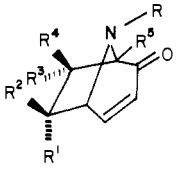
The reaction of the pyridyl betaine dimer with *trans*-penta-1,3-diene at 40 °C gave a mixture of 2,4- and 2,6-cycloadducts. For convenience, cycloadducts with cyclopentadiene are shown separately in Tables 34, 35, and 36; however, the principle of their formation is similar to that of the acyclic dienes. Cyclopentadiene readily reacted with the nitropyridyl betaine at 20 °C to give both the 2,4- and the 2,6-adducts. The IR spectrum of the 2,4-adduct showed a ν(C=O) band at 1740 cm^{-1} and an enamine ν(C=C) at 1640 cm^{-1}. The ^1H NMR spectrum of the 2,4-adducts showed the characteristic signals of the enamine protons: H-8, a doublet at δ 7.46; and H-9, a double doublet at δ 5.17 ($J_{8,9}$ = 8.0 Hz). The vinylic protons H-3 and H-4 appeared as double doublets at δ 6.26 and 6.00, respectively. Evidence of the exo structure for the 2,4-adduct was provided by the spectral features. The δ(C=O) value (1750 cm^{-1}) is high compared to those of the endo adducts (1710–1720 cm^{-1}), indicating a strained system in the exo structure. The adduct failed to complex with either $Eu(fod)_3$ or $Pr(fod)_3$, indicating considerable crowding about the carbonyl groups. The value of $J_{5\text{-exo},6}$ (4.0 Hz) is small and is consistent with an exo model.

2,4-Cycloadducts formed from dienes and 3-oxidopyridiniums were readily reduced catalytically at the double bonds and at the ketone group to form the fully saturated adducts (Table 37).

2. Adducts with Fulvenes

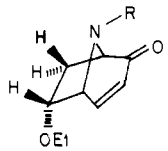
Adducts from fulvenes are formed only when a very strongly electron-attracting substituent is attached to

TABLE 13. Adducts for 3-Oxidopyridiniums and Maleate or Fumarate Esters



no.	R	R^1	R^2	R^3	R^4	R^5	mp, °C	ref
1	Me	H	CO_2Me	H	CO_2Me	Br	oil	79JCS(PI)2528
2	Ph	H	CO_2Et	H	CO_2Et	H	120–121	76JCS(PI)2289
3	Ph	H	CO_2Et	CO_2Et	H	H	79.5–80.5	76JCS(PI)2289
4	Ph	CO_2Et	H	CO_2Et	H	H	69–71	76JCS(PI)2289
5	Ph	CO_2Et	H	H	CO_2Et	H	105–106	76JCS(PI)2289
6	4,6-dimethylpyrimidin-2-yl	CO_2Et	H	H	CO_2Et	H	100–101	79JCS(PI)1525
7	4,6-dimethylpyrimidin-2-yl	H	CO_2Et	CO_2Et	H	H	90–91	79JCS(PI)1525
8	2,4-dinitrophenyl	CO_2Me	H	H	CO_2Me	H	174	74JCS(PI)1883
9	2,4-dinitrophenyl	H	CO_2Me	CO_2Me	H	H	141–142	74JCS(PI)1883
10	2,4-dinitrophenyl	H	CO_2Me	H	CO_2Me	H	129–130	74JCS(PI)1883
11	5,6-diphenyl-1,2,4-triazin-3-yl	H	CO_2Et	CO_2Et	H	H	129–131	80JCS(PI)343
12	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	H	CO_2Et	CO_2Et	H	H	210–211	80MI1351
13	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	CO_2Et	H	H	CO_2Et	H	210–211	80MI1351
14	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	CO_2Me	H	H	CO_2Me	H	195–198	81MI1351
15	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	H	CO_2Me	CO_2Me	H	H	195–198	81MI1351
16	5-nitro-2-pyridyl	CO_2Me	H	H	CO_2Me	H	174	76JCS(PI)2307
17	5-nitro-2-pyridyl	H	CO_2Me	CO_2Me	H	H	141–142	76JCS(PI)2307
18	5-nitro-2-pyridyl	H	CO_2Me	H	CO_2Me	H	129–130	76JCS(PI)2307
19	2-picolyl	CO_2Me	H	H	H	H	oil	80TH1
20	2-picolyl	H	CO_2Me	H	H	H	oil	80TH1
21	$(CH_2)_2CO_2Bu^t$	CO_2Bu^t	H	H	H	H	gum	79JCS(PI)2528
22	$(CH_2)_2CO_2Bu^t$	H	CO_2Bu^t	H	H	H	gum	79JCS(PI)2528
23	4,6-dimethoxy-*s*-triazin-2-yl	CO_2Bu^t	H	H	H	H	110–112	79JCS(PI)2528
24	4,6-dimethoxy-*s*-triazin-2-yl	H	CO_2Bu^t	H	H	H	120–121	79JCS(PI)2528
25	$4\text{-}BrC_6H_4COCH{=}CH$	CO_2Bu^t	H	H	H	H	190–191	79JCS(PI)1525, 79JCS(PI)2528
26	$4\text{-}BrC_6H_4COCH{=}CH$	H	CO_2Bu^t	H	H	H	165–166	79JCS(PI)1525, 79JCS(PI)2528
27	1-oxido-4-pyridyl	H	CO_2Et	CO_2Et	H	H	186–187	80JCR(M)3337
28	2-pyridyl	CO_2Et	H	H	CO_2Et	H	95–96	80JCS(PI)343
29	styryl	H	CO_2Et	CO_2Et	H	H	180–181	79JCS(PI)2535
30	$4\text{-}ClC_6H_4COCH{=}CH$	H	CO_2Et	CO_2Et	H	H	143–144	80JCS(PI)362
31	$2\text{-Cl-5-}NO_2C_6H_3COCH{=}CH$	H	CO_2Et	CO_2Et	H	H	gum	80JCS(PI)362

TABLE 14. Adducts from 3-Oxidopyridiniums and Ethyl Vinyl Ether



no.	R	mp, °C	ref
1	5-nitro-2-pyridyl	108–109	76JCS(PI)2307
2	4,6-dimethylpyrimidin-2-yl	126–127	79JCS(PI)1525
3	4-pyridyl	164–165[a]	80JCS(PI)343
4	2-pyridyl	51–53	80JCS(PI)343
5	$4\text{-}ClC_6H_4COCH{=}CH$	146–148	80JCS(PI)362

[a] Methiodide, 233–235 °C.

the 3-oxidopyridinium nitrogen atom. The adducts are listed in Table 38. Their structure is based mainly on spectral evidence. For instance, 6,6-dimethylfulvene reacted with the nitropyridyl betaine to yield a single 1:1 adduct. The strong conjugated ketone ν(C=O) band at 1690 cm^{-1} was indicative of addition across the 2- and 6-positions of the betaine. The ^1H NMR patterns of H-1, -3, -4, and -5 were similar to those for other 2,6-adducts. The protons of the cyclopentadiene moiety exhibited characteristic coupling constants. The allylic methyl groups (δ 1.28 and 1.32) confirmed the general structure. The regiostructure shown was supported by the H-1 signal being downfield of that of the H-5 signal, indicating that it is H-1 that is allylic. This was further confirmed by LIS values induced by $Eu(fod)_3$.

An exothermic reaction of the pyrimidinyl betaine dimer with (*p*-methoxyphenyl)fulvene yielded the expected 1:1 dimer together with two 2:1 adducts (betaine:fulvene) produced by the addition of an additional betaine molecule to the initially formed 2,6-adduct.

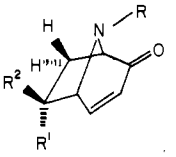
E. Rationalization of Regioselectivity, Site Selectivity, and Stereoselectivity

1. Cycloaddition Reactions Possible

As discussed above, it is seen that olefins and acetylenes react across the 2,6-positions, dienes across the 2,4-positions, ketenes across the O,2- or O,4-positions, and fulvenes across the 2,6-positions. Thermal dimers are formed by the reaction of one molecule at the 2,6- and one at the 2,4-positions, whereas photochemical dimers are formed by both molecules reacting at the 2,4-positions. The site selectivity, regioselectivity, and stereoselectivity in these reactions can be rationalized by molecular orbital considerations.

Regioselectivity is well correlated by using eq 1 [79JCS(PI)408]. This equation is derived from the general PMO equation [68JA223, 68JA543,553] for the energy of interaction between two molecules considering only those interactions due to overlap of the HOMO and LUMO orbitals at atoms that are becoming directly bonded to each other. However, reactivity is much better rationalized by the simple equation (2)

TABLE 15. Adducts from 3-Oxidopyridiniums and α-Chloroacrylonitrile



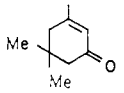
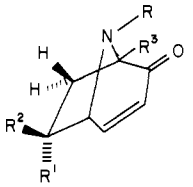
no.	R	R^1	R^2	mp, °C	ref
1	4,6-dimethylpyrimidin-2-yl	Cl, CN	CN, Cl	151–152	79JCS(PI)1525
2	5,6-diphenyl-1,2,4-triazin-3-yl	Cl, CN	CN, Cl	169–170	80JCS(PI)343
3	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	Cl, CN	CN, Cl	198–199	81MI1351
4	1-oxido-4-pyridyl	Cl, CN	CN, Cl	>300	80JCR(M)3337
5	2-pyridyl	Cl, CN	CN, Cl	98–99	80JCS(PI)343
6	quinoxolin-2-yl	Cl, CN	CN, Cl	170–172	80JCS(PI)343
7	styryl	Cl, CN	CN, Cl	124	79JCS(PI)2535
8		Cl, CN	CN, Cl	156–158	79MI57

TABLE 16. Adducts from 3-Oxidopyridiniums and Methyl Vinyl Ketone



no.	R	R^1	R^2	R^3	mp, °C	ref
1	4,6-dimethylpyrimidin-2-yl	H	COMe	H	130–131	79JCS(PI)1525
2	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	COMe	H	H	200–202	81MI1351
3	5-nitro-2-pyridyl	COMe	H	H	146–147	76JCS(PI)2307
4	5-nitro-2-pyridyl	H	COMe	H	151–152	76JCS(PI)2307
5	1-oxido-4-pyridyl	COMe	H	H	oil[a]	80JCR(M)3337
6	1-oxido-4-pyridyl	H	COMe	H	oil[a]	80JCR(M)3337
7	Me	COMe	H	SMe	oil	80TH1
8	Me	H	COMe	SMe	oil	80TH1

[a] Picrate, 202–203 °C.

[74PAC569], which derives from eq 1 if the numerators are constant.

SCHEME 33

$$\Delta E = \frac{[(C_{HO^1}C_{LU^{1'}} + C_{HO^2}C_{LU^{2'}})\beta_{rs}]^2}{E_{HO^A} - E_{LU^B}} + \frac{[(C_{HO^{1'}}C_{LU^1} + C_{HO^{2'}}C_{LU^2})\beta_{rs}]^2}{E_{HO^B} - E_{LU^A}} \quad (1)$$

$$\Delta E = K\left[\frac{1}{E_{HO^A} - E_{LU^B}} + \frac{1}{E_{HO^B} - E_{LU^A}}\right] \quad (2)$$

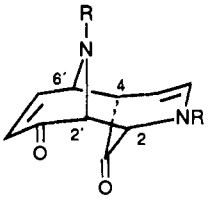
$$\Delta E_{steric} = \sum_k^A \sum_l^B (e^2/r_{kl} - \gamma_{kl})Z_kZ_l \quad (3)$$

If the second-order perturbational treatment is limited to the principal frontier orbital interactions (eq 1 and 2), it is not possible to differentiate between exo and endo isomers. However, eq 3 can be used to estimate first-order repulsion terms for species not bearing high charges. This is essentially a steric interaction, and Sustmann [71MI9] has shown that the orientation of addition of cyclopropene to cyclopentadiene could be correlated by using this approach.

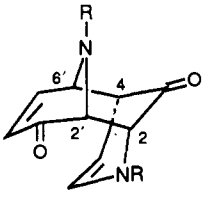
2. Dimerization

Application of eq 1 indicated that regioisomers of type 2,2′–4,6′ (**61**/**62**) should be formed more easily than those of type 4,2′–2,6′ (**63**/**64**), in complete agreement with experimental observation (Scheme 34). The relative ease of dimerization can be explained by eq 2, which leads to the order *N*-methyl < *N*-phenyl < *N*-4-pyridyl < *N*-2-pyridyl < *N*-pyrimidin-2-yl < *N*-triazin-2-yl, in complete agreement with experiment.

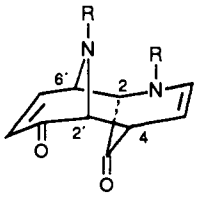
SCHEME 34



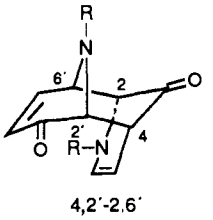
2,2′-4,6′
(61)



2,2′-4,6′
(62)



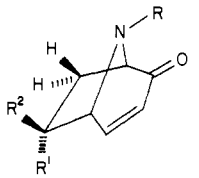
4,2′-2,6′
(63)

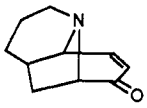


4,2′-2,6′
(64)

Attempts to rationalize the stereochemistry of addition proved unsuccessful. The steric term (eq 3) should favor endo addition in place of the exo process

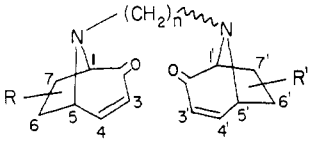
TABLE 17. Adducts from 3-Oxidopyridinium Betaines and Other 1,1-Disubstituted Olefins



no.	R	R^1	R^2	mp, °C	ref
1	4,6-dimethylpyrimidin-2-yl	OCOMe	H	150–151	79JCS(PI)152
2	4,6-dimethylpyrimidin-2-yl	Me, CN	CN, Me	186–187	79JCS(PI)152
3	4,6-dimethylpyrimidin-2-yl	Me, OCOMe	OCOMe, Me	92–93	79JCS(PI)152
4	4,6-dimethylpyrimidin-2-yl	2-oxopyrrolidin-2-yl	H	180–181	79JCS(PI)152
5	4,6-dimethylpyrimidin-2-yl	H	CH_2OH	gum	79JCS(PI)152
6	4,6-dimethylpyrimidin-2-yl	*trans*-MeCH=CH	H	128–130	79JCS(PI)152
7	5-nitro-2-pyridyl	CH_2OCOMe	H	145–147	79JCS(PI)152
8	5-nitro-2-pyridyl	CHO	Me	168–169	76JCS(PI)230
9	5-nitro-2-pyridyl	*trans*-MeCH=CH	H	95–97	76JCS(PI)230
10	5-nitro-2-pyridyl	Me	Ph	187–188	76JCS(PI)230
11	5-nitro-2-pyridyl	Ph	Me	192–193	76JCS(PI)230
12	5-nitro-2-pyridyl	CH_2NHSO_2Ph	H	207–208	79JCS(PI)152
13	Me	Me, CO_2Me	CO_2Me, Me	93–94	71JCS(C)874
14				oil[a]	76CC367

[a] 2,4-Dinitrophenylhydrazine derivative, 225–227 °C.

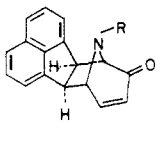
TABLE 18. Adducts from Bis(3-oxidopyridiniums) and Acrylonitrile



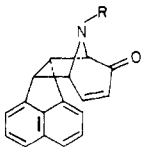
R = R' = CN

no.	R	R^1	n	mp, °C	mp of methyl perchlorate, °C	ref
1	6-endo	6′-endo	3	142–143		78JCR(M)1182
2	6-endo	6′-endo	1	gum	125	78JCR(M)1182
3	6-exo	6′-exo	3	gum	125–126	78JCR(M)1182
4	6-exo	6′-exo	2	181–182		78JCR(M)1182
5	6-exo	6′-endo	3	gum	116–118	78JCR(M)1182
6	6-exo	7′-endo	3	gum		78JCR(M)1182
7	6-endo/exo	7′-exo	3	gum		78JCR(M)1182
8	6-endo	7′-endo	3	124.5–125.5	118–122	78JCR(M)1182
9	6-exo	6′-endo	1	gum	125	78JCR(M)1182
10	6-endo	6′-endo	2	gum	120–121	78JCR(M)1182

TABLE 19. Adducts from Acenaphthylene and 3-Oxidopyridiniums



(exo)



(endo)

no.	N-substituent (R)	stereoisomer	mp, °C	ref
1	5,6-diphenyl-1,2,4-triazin-3-yl	exo	131–132	80JCS(PI)343
2	5,6-diphenyl-1,2,4-triazin-3-yl	endo	231–233	80JCS(PI)343
3	1-oxido-4-pyridyl	exo	181–182	80JCR(M)3337
4	2-pyridyl	exo	228–229	80JCS(PI)343
5	2-pyridyl	endo	174–175	80JCS(PI)343
6	4-pyridyl	exo	264–266[a]	80JCS(PI)343
7	6-phenyl-3-pyridazinyl	exo	275–276	83JCR(S)37

[a] Methyl perchlorate, 275–278 °C.

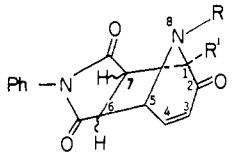
exclusively found. It is thought that steric hindrance between remote parts of the molecules intervenes to disfavor endo attack.

3. Additions to 2π Addends

The preferred regioselectivity of the betaines toward the (4π + 2π) addition of monosubstituted ethylenes, CH_2=CHR, across the 2,6-positions can be accounted for by using eq 1. Similarly, the relative rates of addition are rationalized by treatment using eq 2. Again, the use of eq 3 explains the generally preferred formation of endo stereoisomers [79JCS(PI)408].

For acrylonitrile, the covalent term (eq 1) favors addition across the O,2-positions, while the steric term (eq 3) favors O,4-addition. The observed 2,6-addition arrives from the fact that O,2- and O,4-addition do not lead to a stable product. For difluoroketene, a similar pattern emerges, but now both O,2- and O,4-addition can lead to stable products by elimination of HF. Thus, experimentally dichloroketene does add across the

TABLE 20. Adducts from 3-Oxidopyridiniums and *N*-Phenylmaleimide



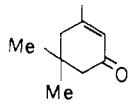
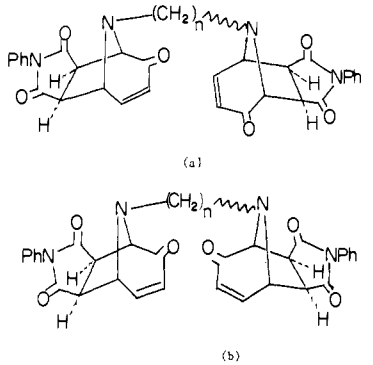
no.	R	R^1	exo/endo	mp, °C	ref
1	Me	Br	exo	173.5–174.5	79JCS(PI)2528
2	Me	Cl	exo	99–100	79JCS(PI)2528
3	Ph	H	exo	219–220.5	74JCS(PI)746
4	Ph	H	endo	209–210	74JCS(PI)746
5	$PhCH_2$	H	exo	134	76JCS(PI)2334
6	PhCH=N	H	exo	171–172	79JCS(PI)399
7	PhCH=N	H	endo	204–206	79JCS(PI)399
8	4,6-dimethoxy-*s*-triazin-2-yl	H	exo	234–235	77JCS(PI)1930
9	2,4-dinitrophenyl	H	endo	247	74JCS(PI)1883
10	4,6-diphenyl-*s*-triazin-2-yl	H	exo	264–265	77JCS(PI)1930
11	5,6-diphenyl-1,2,4-triazin-3-yl	H	exo	150–151	80JCS(PI)343
12	5,6-diphenyl-1,2,4-triazin-3-yl	H	endo	253–255	80JCS(PI)343
13	α-(4-nitrophenyl)-β-(3-nitrophenyl)vinyl	H	endo	241–242	81MI1351
14	1-oxido-4-pyridyl	H	endo	270	80JCR(M)3337
15	2-pyridyl	H	endo	225–227	80JCS(PI)343
16	4-pyridyl	H	endo	247–249	80JCS(PI)343
17	styryl	H	exo	gum	79JCS(PI)2535
18	$4\text{-}ClC_6H_4COCH{=}CH$	H	exo	282–284	80JCS(PI)362
19	$2\text{-}Cl\text{-}5\text{-}NO_2C_6H_3COCH{=}CH$	H	exo	274–275	80JCS(PI)362
20		H	endo	254–256	79MI57
21		H	endo	260–262	79MI57
22	$4\text{-}ClC_6H_4COCH{=}CH$	SMe	exo	255–257	80TH1, 81JCR(S)208
23	Me	SMe	exo	149–150	80TH1, 81JCR(S)208
24	Me	SMe	endo	149–150	80TH1, 81JCR(S)208
25	Me	H	exo	164–165	71JCS(C)874
26	2-picolyl	H	exo	72–74	81JCR(S)208
27	$(CH_2)_3CH{=}CH_2$	H	exo		76CC367

TABLE 21. Adducts from Bis(3-oxidopyridiniums) and *N*-Phenylmaleimide



no.	*n*	isomer	mp, °C	ref
1	2	a or b	149–150	78JCR(M)1182
2	2	b or a	248–249	78JCR(M)1182
3	3	a or b	131–132	78JCR(M)1182
4	3	b or a	228–229	78JCR(M)1182

O,4-positions while aryl(chloro)ketenes react at both the O,2- and O,4-positions.

4. Additions to 4π Addends

Dienes undergo permitted cycloaddition at either the 2,6-positions (acting as conjugated monoenes) or the 2,4-positions (acting as dienes). The covalent term (eq 1) indicated that the addition of *trans*-penta-1,3-diene to 1-(pyrimidin-2-yl)-3-oxidopyridinium should occur more favorably at the 2,4-positions rather than at the 2,6-positions. Equation 3 indicated rather similar steric terms for both modes of addition. 2,4-Addition is predicted to be exo; although the endo 2,4-product is found experimentally, this is believed to be the result of ring inversion of the initially formed exo adducts.

Equations 1 and 3 indicate that for cyclopentadiene the exo 2,4-addition is favored, followed by endo 2,6-addition. The predicted exo 2,4-cycloadduct is isolated since ring inversion to the more stable endo adduct is not possible.

5. Additions to 6π Addends

The FMO theory does not presently explain experimental results for fulvene addition to 1-(pyrimidin-2-yl)-3-oxidopyridinium. The products actually observed can be explained by 2,2′–6,6′ addition [79JCS(PI)408] followed by a 1,5-hydrogen shift.

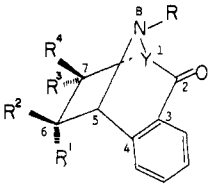
F. Transformations of Cycloadducts

1. Tricyclic Adducts

The tricyclic adducts in Tables 39–42 are formed by cyclization of the initially formed 8-azabicyclo[3.2.1]-oct-3-en-2-ones. The IR spectra clearly show the loss of unsaturation of the α,β-unsaturated carbonyl group (e.g. ν(C=O) ca. 1715 cm^{-1} compared with ν(C=O) ca. 1680 cm^{-1}). In the NMR spectra, the characteristic pattern of H-3 and H-4 of the parent cycloadducts disappeared.

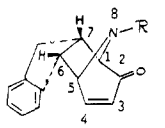
TABLE 22

A. Adducts from 4-Oxidoisoquinoliniums and 1-Oxido-3-substituted-phthalaziniums[a]

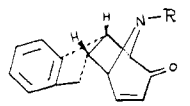


no.	R	R^1	R^2	R^3	R^4	Y	mp, °C	ref
1	2,4-dinitrophenyl	CN	H	H	H	CH	94–95	75CPB2899
2	2,4-dinitrophenyl	Ph	H	H	H	CH	245–246	75CPB2899
3	2,4-dinitrophenyl	H	H	Ph	H	CH	250–251	75CPB2899
4	2,4-dinitrophenyl	H	CO_2Me	CO_2Me	H	CH	185–186	75CPB2899
5	2,4-dinitrophenyl	CO_2Me	H	H	CO_2Me	CH	183–184	75CPB2899
6	5-nitro-2-pyridyl	Ph	H	H	H	CH	225–227	80JCR(M)3337
7	5-nitro-2-pyridyl	H	Ph	H	H	CH	198–200	80JCR(M)3337
8	Me	CN	H	H	H	CH	127–128[b]	72JCS(PI)2054
9	Me	CO_2Me	H	H	H	CH	oil[c]	72JCS(PI)2054
10	Me	H	CO_2Me	H	H	CH	101–102[d]	72JCS(PI)2054
11	4-ClC_6H_4COCH=CH	CN	H	H	H	CH	238–239	80JCR(M)3337
12	4-ClC_6H_4COCH=CH	H	CN	H	H	CH	265–266	80JCR(M)3337
13	4-ClC_6H_4COCH=CH	H	H	CN	H	CH	252–253	80JCR(M)3337
14	4-ClC_6H_4COCH=CH	H	H	H	CN	CH	283–284	80JCR(M)3337
15	Ph	H	H	Ph	H	N	154	76JCS(PI)2281
16	4,6-dimethylpyrimidin-2-yl	H	CN	H	H	CH	203 (dec)	80JCS(PI)331
17	4,6-dimethylpyrimidin-2-yl	H	H	H	CN	CH	203 (dec)	80JCS(PI)331
18	4,6-dimethylpyrimidin-2-yl	CN, Cl	Cl, CN	H	H	CH	189–191	80JCS(PI)331

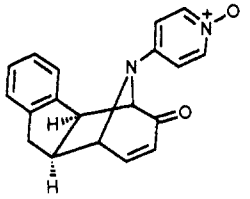
B. Adducts from 3-Oxidopyridinium Betaines and Indene



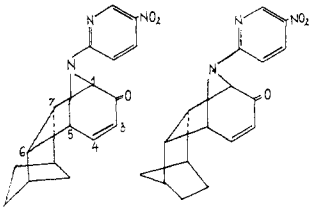
(A)



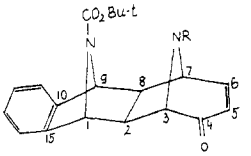
(B)

no.	R	product structure	mp, °C	ref
1	5,6-diphenyl-1,2,4-triazin-3-yl	A	218–220	80JCS(PI)343
2	5,6-diphenyl-1,2,4-triazin-3-yl	B	221–223	80JCS(PI)343
3	4,6-dimethylpyrimidin-2-yl	A	160–160.5	81JHC1461
4	6-phenylpyridazin-3-yl	A	201–202	83JCR(S)37
5			gum[e]	80JCR(S)249

C. Various Cycloadducts

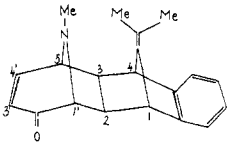


1. m.p. 140 (one isomer 164-166) 76JCS(P1)2307

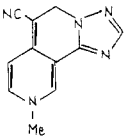


2. m.p. 228-230, R = Me 80J0C479

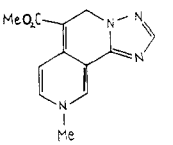
3. m.p. 205-207, R = Ph 80J0C479



4. m.p. 168-170 81JA565



5. m.p. 210 86M127



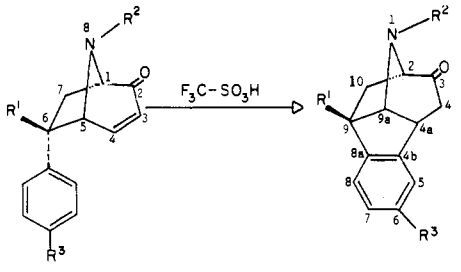
6. m.p. 250 86M127

[a] Structure numbering is nonsystematic. [b] Methiodide, 163–164 °C. [c] Methiodide, 167–170 °C. [d] Methiodide, 185 °C. [e] Picrate, 202–204 °C.

The readily available 6-aryl-8-(4-nitro-2-pyridyl)-8-azabicyclo[3.2.1]oct-3-en-2-ones (**65a–e**) are cyclized smoothly to 1,2,4,4a,9,9a-hexahydro-1-aryl-2,9-methanoindeno[2,1-*b*]pyridin-3-ones (**66a–e**) by trifluoromethanesulfonic acid in yields of 33–100%. The reaction has been extended to *N*-phenyl (**65g**) and *N*-(2,4-dinitrophenyl) (**65f**) analogues and also to the 6-methyl compound (**65b**) (Table 39) (Scheme 35).

The reactions of betaines **50** (R = 5-nitro-2-pyridyl, R = 4,6-dimethylpyrimidin-2-yl, and R = 4,6-dimethoxy-1,3,5-triazin-2-yl) with allyl alcohol each gave the corresponding product **69** (in 48%, 85%, and 10% yield,

SCHEME 35

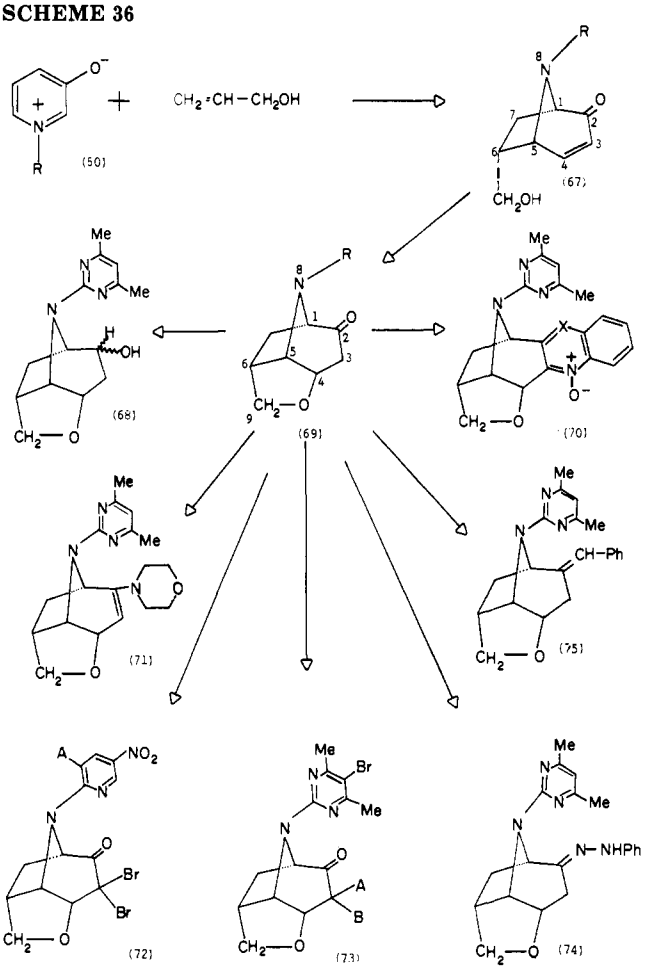


(65) (66)

	R^1	R^2	R^3
(a)	H	5-nitro-2-pyridyl	H
(b)	Me	5-nitro-2-pyridyl	H
(c)	H	5-nitro-2-pyridyl	Cl
(d)	H	5-nitro-2-pyridyl	Br
(e)	H	5-nitro-2-pyridyl	OMe
(f)	H	2,4-dinitrophenyl	H
(g)	H	phenyl	H

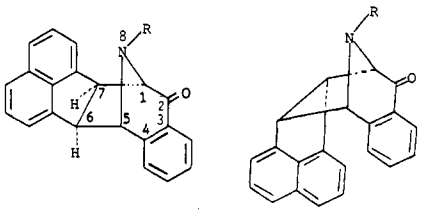
respectively) in which cyclization of the expected intermediates **67** (R = 5-nitro-2-pyridyl, R = 4,6-dimethylpyrimidin-2-yl, and R = 4,6-dimethoxy-1,3,5-triazin-2-yl) had taken place (Table 40) (Scheme 36).

SCHEME 36



The pyrimidinyl derivative **69** reacted with phenylhydrazine to give the corresponding phenylhydrazone **74**. The cycloadduct **69** condensed with benzaldehyde to form the styryl derivative **75** and with morpholine to form the enamine **71**, which did not condense smoothly with methyl vinyl ketone. Borohydride reduction of **69** gave the corresponding alcohol **68** (Scheme 36).

TABLE 23. Adducts from Acenaphthylene and 4-Oxidoisoquinoliniums[a]



exo endo

no.	R	stereoisomer	mp, °C	ref
1	4-ClC_6H_4COCH=CH	exo	257–258	80JCR(M)3337
2	4-ClC_6H_4COCH=CH	endo	273–274	80JCR(M)3337

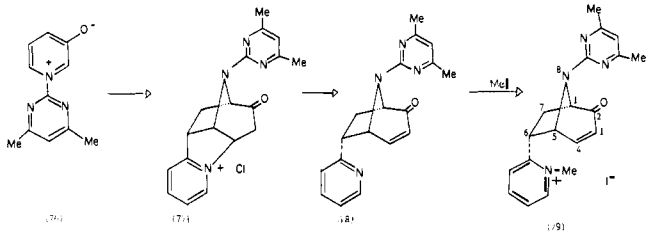
[a] Structure numbering is nonsystematic.

Benzofuroxan reacted with **69** to form the quinoxaline 1,4-dioxide (**70**, X = N^+–O^-) in an example of the Beirut reaction. The dioxide was stereospecifically reduced with KBH_4 to the monoxide (**70**, X = N) (Scheme 36).

Under acidic conditions, bromination of **69** occurred exclusively in the pyrimidine ring to give the *N*-(5-bromo-4,6-dimethylpyrimidin-2-yl) derivative (**73**, A = B = H). In pyridine solution, **69** yielded the tribrominated compound (**73**, A = B = Br), whereas the 2-pyridyl tricyclic adduct **69** gave a mixture of the dibromo (**72**, A = H) and the tribromo (**72**, A = Br) compounds (Table 40) (Scheme 36). The value of ν(C=O) was raised by the α-halogenation to 1750–1740 cm^{-1}.

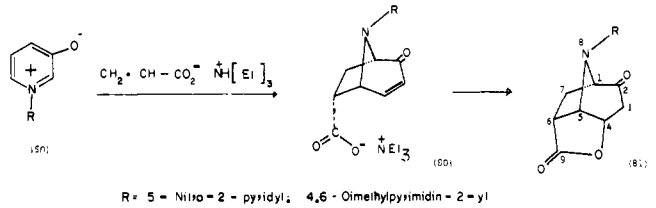
The adduct **78** from the pyrimidinyl betaine **76** and 2-vinylpyridine formed a cation that cyclized spontaneously to give the tricyclic compound **77**. Reaction of **77** with aqueous base regenerated the intermediate **78**. Quaternization of adduct **78** with methyl iodide gave a quaternary salt **79** (N^+–Me at δ 4.49) (Scheme 37).

SCHEME 37



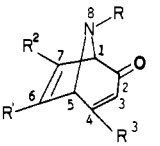
Triethylammonium acrylate reacted with the pyridyl (**50**, R = 5-nitro-2-pyridyl) and pyrimidinyl (**50**, R = 4,6-dimethylpyrimidin-2-yl) betaines, forming the tricyclic products **81** (R = 5-nitro-2-pyridyl) and **81** (R = 4,6-dimethylpyrimidin-2-yl) in 44% and 52% yield, respectively (Scheme 38). Presumably the endo adducts **80** cyclize spontaneously. The IR spectra of both products showed the lactone ν(C=O) at 1770–1780 cm^{-1} and the ketone ν(C=O) at 1720 cm^{-1}.

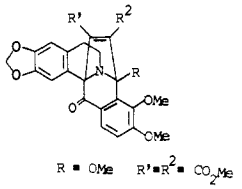
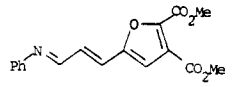
SCHEME 38



R = 5 - Nitro - 2 - pyridyl; 4,6 - Dimethylpyrimidin - 2 - yl

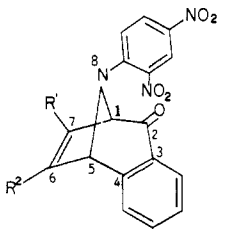
TABLE 24. Adducts from 3-Oxidopyridiniums and Acetylenes



no.	R	R^1	R^2	R^3	mp, °C	ref
1	$EtO_2CC{=}CHCO_2Et$	CO_2Et	CO_2Et	H	287–288	79JCS(PI)399
2	Ph	Ph	H	H	182–183	76JCS(PI)2289
3	4,6-dimethoxy-*s*-triazin-2-yl	CO_2Et	CO_2Et	H	207–208	77JCS(PI)1930
4	2,4-dinitrophenyl	CO_2Et	Ph	H	155–156	79JCS(PI)1525
5	2,4-dinitrophenyl	Ph	CO_2Et	H	162–163	79JCS(PI)1525
6	4,6-diphenyl-*s*-triazin-2-yl	CO_2Me	CO_2Me	H	207–208	77JCS(PI)1930
7	5,6-diphenyl-1,2,4-triazin-3-yl	CO_2Me	CO_2Me	H	80–82	80JCS(PI)343
8	5,6-diphenyl-1,2,4-triazin-3-yl	CO_2Me	H	H	160–162	80JCS(PI)343
9	$4\text{-}ClC_6H_4COCH{=}CH$	CO_2Me	CO_2Me	H	143–144	80JCS(PI)362
10	$2\text{-Cl-5-}NO_2C_6H_3COCH{=}CH$	CO_2Me	CO_2Me	H	90–92	80JCS(PI)362
11	Me	Ph	H	OMe	oil[a]	78TL1751
12	Me	CO_2Et	H	OMe	oil[b]	77TL4075
13					247–249	79H(12)511
14					112–113	83CC1216

[a] Picrate, 229–230 °C. [b] Methiodide, 140–141 °C.

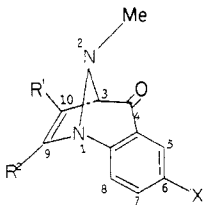
TABLE 25. Adducts from 2-(2,4-Dinitrophenyl)-4-oxidoisoquinolinium and Acetylenes[a]



no.	R^1	R^2	mp, °C	ref
1	Ph	H	178–179	75CPB2899
2	H	Ph	166–167	75CPB2899
3	Ph	Ph	140–142	75CPB2899
4	CO_2Me	CO_2Me	188–189	75CPB2899

[a] Structure numbering is nonsystematic.

TABLE 26. Adducts from 2-Methyl-4-oxidocinnoliniums and Acetylenes

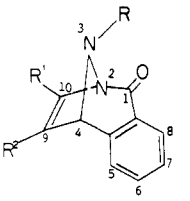


no.	R^1	R^2	X	mp, °C	ref
1	Ph	Ph	Cl	64–68	75JCS(PI)1506
2	H	Ph	Cl	149–150	75JCS(PI)1506
3	H	Ph	H	118–119	75JCS(PI)1506, 64CI(L)1805
4	CO_2Me	CO_2Me	Cl	89	75JCS(PI)1506
5	CO_2Me	CO_2Me	H	71–72	75JCS(PI)1506, 69JCS(C)2355

2. *Preparation of Tropones and Tropolones*

One of the first synthetic applications of the cycloaddition reactions lay in the preparation of tropones and tropolones (Table 43) (Scheme 39). The initial cycloaddition to 1-methyl-3-oxidopyridinium (**82**, R = CH_3, R′ = H) yielded the bicyclic intermediate (**83**, R = Me, R′ = H), which was quaternized to **84** (R = Me,

TABLE 27. Adducts from 4-Oxidophthalaziniums and Acetylenes



no.	R	R^1	R^2	mp, °C	ref
1	Me	Ph	Ph	170	75JCS(PI)1506
2	Ph	Ph	Ph	214	76JCS(PI)2281
3	Ph	H	Ph	195–196	76JCS(PI)2281
4	Ph	Ph	H	220	76JCS(PI)2281
5	Ph	CO_2Me	CO_2Me	176–177	76JCS(PI)2281
6	$MeO_2C\text{-}C{=}CHCO_2Me$	CO_2Me	CO_2Me	140–141	75JCS(PI)1506

TABLE 28. Rearranged Cycloadducts

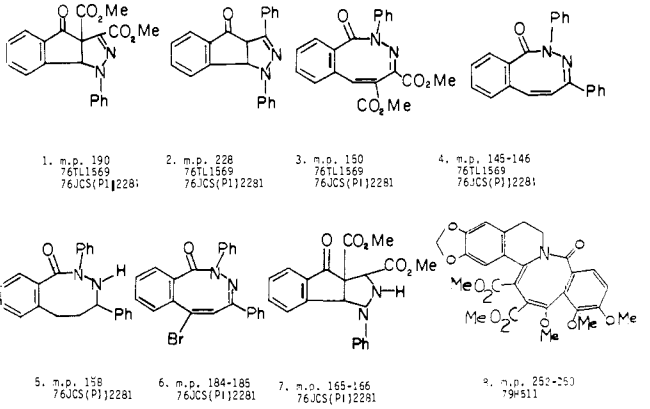
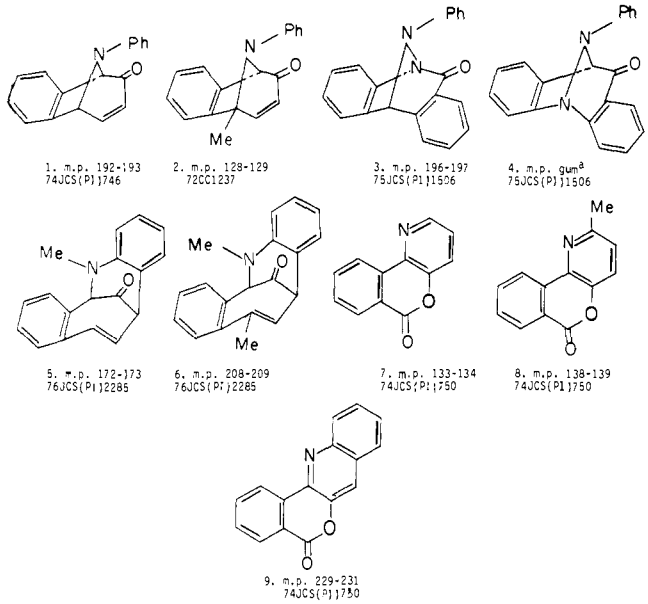


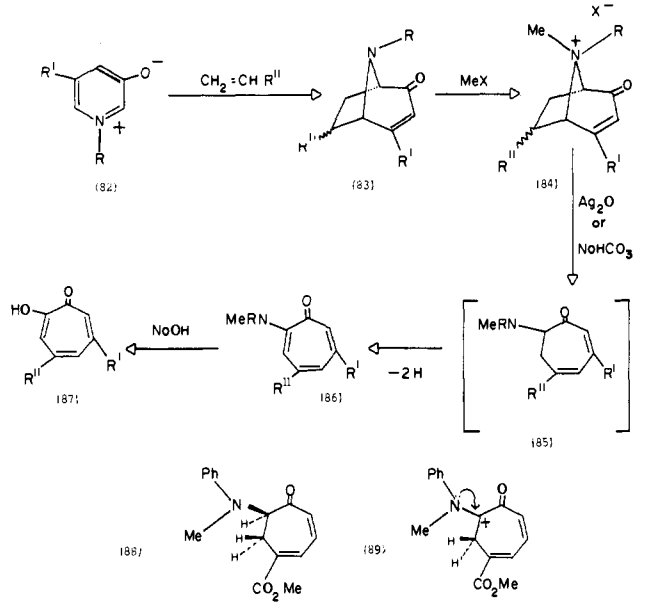
TABLE 29. Benzyne Cycloadducts



[a] 2,4-Dinitrophenylhydrazone, 219 °C (dec).

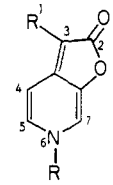
R′ = H). Often, degradation of this salt with silver oxide or sodium hydrogen carbonate led without isolation of the intermediate (**85**, R = Me, R′ = H) to the (dimethylamino)tropone **86** (R = Me, R′ = H), which was easily hydrolyzed to the tropolone **87** (R′ = H).

SCHEME 39



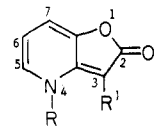
Conversion of the adducts (**83**, R′ = H, R = Ph) of 3-oxido-1-phenylpyridinium (**82**, R = Ph, R′ = H) into tropones was more difficult because of the low tendency of the adducts to form quaternary salts. However, with methyl fluorosulfonate, quaternary salts of the type **84** (R″ = CO_2Me, R′ = H) could be prepared in high yield (75%). Here sodium hydrogen carbonate caused Hofmann degradation to the deep red cycloheptadienone **88**, which was stable to light and air. Assignment of structure **88** was based on spectral and analytical evidence. Oxidation of the compound **88** with silver oxide, which can also be used as a strong base in Hofmann degradations, gave 4-(methoxycarbonyl)tropolone (**87**, R″ = CO_2CH_3, R′ = H). This oxidation probably involves hydride ion loss to the silver oxide, with **89** as

TABLE 30. Ketene Cycloadducts



no.	R	R^1	mp, °C	ref
1	Ph	Cl	222–223	76TL2959
2	$PhCH_2$	Cl	279–280	76TL2959
3	4,6-dimethoxy-*s*-triazin-2-yl	Cl	245–246	76TL2959
4	4,6-dimethyl-pyrimidin-2-yl	Cl	275–276	76TL2959
5	Ph	Ph	206	80JCS(PI)1176
6	Ph	4-BrC_6H_4	201	80JCS(PI)1176
7	Ph	4-$NO_2C_6H_4$	267–268	80JCS(PI)1176
8	Ph	4-$MeOC_6H_4$	249–250	80JCS(PI)1176
9	$PhCH_2$	Ph	188–189	80JCS(PI)1176
10	$PhCH_2$	4-BrC_6H_4	171–172	80JCS(PI)1176
11	$PhCH_2$	4-$NO_2C_6H_4$	225–227	80JCS(PI)1176
12	$PhCH_2$	4-$MeOC_6H_4$	219–220	80JCS(PI)1176
13	PhCH=CH	Ph	238–240	80JCS(PI)1176
14	1-oxido-4-pyridyl	Ph	258–262	80JCS(PI)1176
15	4,6-dimethyl-pyrimidin-2-yl	Ph	256	80JCS(PI)1176

TABLE 31. Products from Reaction of Haloketenes across the 2,O-Positions of 3-Oxidopyridiniums



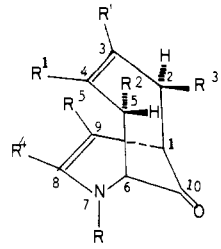
no.	R	R^1	mp, °C	ref
1	Ph	Ph	232	80JCS(PI)1176
2	Ph	4-BrC_6H_4	240–241	80JCS(PI)1176
3	Ph	4-$NO_2C_6H_4$	impure	80JCS(PI)1176
4	Ph	4-$MeOC_6H_4$	219–220	80JCS(PI)1176
5	$PhCH_2$	Ph	237	80JCS(PI)1176
6	$PhCH_2$	4-BrC_6H_4	135–136	80JCS(PI)1176
7	$PhCH_2$	4-$NO_2C_6H_4$	225–227	80JCS(PI)1176
8	$PhCH_2$	4-$MeOC_6H_4$	190–191	80JCS(PI)1176
9	PhCH=CH	Ph	157–177	80JCS(PI)1176
10	1-oxido-4-pyridyl	Ph	268	80JCS(PI)1176
11	4,6-dimethyl-pyrimidin-2-yl	Ph	226–227	80JCS(PI)1176
12	4-ClC_6H_4COCH=CH	Ph	224–226	80JCS(PI)1176
13	4-ClC_6H_4COCH=CH	4-$NO_2C_6H_4$	258–260	80JCS(PI)1176
14	4-ClC_6H_4COCH=CH	4-$MeOC_6H_4$	186–188	80JCS(PI)1176

intermediate.

1-Methyl-5-phenyl-3-oxidopyridiniums (**82**, R = Me, R′ = Ph) readily form cycloadducts (**83**, R = Me, R′ = Ph), which can be converted into quaternary salts (**84**, R = Me, R′ = Ph) and then into the tropones 2-(dimethylamino)-4-(methoxycarbonyl)-6-phenyltropone (**86**, R = Me, R′ = Ph, R″ = CO_2Me) and 4-cyano-2-(dimethylamino)-6-phenyltropone (**86**, R = Me, R′ = Ph, R″ = CN) and the tropolone 4-cyano-6-phenyltropolone (**87**, R′ = Ph, R″ = CN).

Adducts formed from 3-hydroxypyridine and 2 mol of the dipolarophiles, acrylonitrile and methyl acrylate, are converted by quaternization and Hofmann elimination to 4-cyanotropolone (**87**, R′ = H, R″ = CN) via 2-[methyl(2-cyanoethyl)amino]-4-cyanotropone (**86**, R = $(CH_2)_2CN$, R′ = H, R″ = CN) and 4-(methoxycarbonyl)tropolone (**87**, R′ = H, R″ = CO_2Me) via 4-(methoxycarbonyl)-2-[methyl(2-(methoxycarbonyl)-ethyl)amino]tropone (**86**, R′ = H, R″ = CO_2Me, R = $(CH_2)_2CO_2Me$). Overall yields for tropolones of ca. 25%

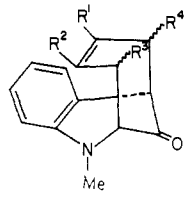
TABLE 32. Acyclic Diene Adducts from 3-Oxidopyridiniums



no.	R	R^1	R^2	R^3	R^4	R^5	mp, °C	ref
1	3-phenyl-1,2,4-thiadiazol-5-yl	Me	H	H	H	H	139–140	79JCS(PI)399
2	4,6-dimethoxy-*s*-triazin-2-yl	Me	H	H	H	H	125–127	77JCS(PI)1930
3	4,6-dimethoxy-*s*-triazin-2-yl	H	H	H	H	H	132	77JCS(PI)1930
4	3,4-dihydro-6-methoxy-4-oxo-*s*-triazin-2-yl	H	H	H	H	H	205	77JCS(PI)1930
5	4,6-dimethylpyrimidin-2-yl	Me	H	H	H	H	102–103	76JCS(PI)2307
6	4,6-dimethylpyrimidin-2-yl	H	H	H	H	H	101–102[a]	79JCS(PI)1525
7	4,6-dimethylpyrimidin-2-yl	H	H	H	H	Br	150–151	79JCS(PI)1525
8	4,6-dimethylpyrimidin-2-yl	H	H	Me	H	H	gum	76JCS(PI)2307
9	4,6-dimethylpyrimidin-2-yl	H	Me	H	H	H	gum	76JCS(PI)2307
10	4,6-diphenyl-*s*-triazin-2-yl	Me	H	H	H	H	165–167	77JCS(PI)1930
11	5,6-diphenyl-1,2,4-triazin-3-yl	Me	H	H	H	H	88–89	80JCS(PI)343
12	5,6-diphenyl-1,2,4-triazin-3-yl	H	H	H	H	H	178–180	80JCS(PI)343
13	5-nitro-2-pyridyl	Me	H	H	H	H	123–124	76JCS(PI)2307
14	5-nitro-2-pyridyl	H	H	H	H	H	139–140[b]	79JCS(PI)1525
15	4-BrC_6H_4COCH=CH	Me	H	H	H	H	210–211	79MI57
16	5-nitro-2-pyridyl	H	H	Me	H	H	140–150	76JCS(PI)2307
17	5-nitro-2-pyridyl	H	Me	H	H	H	140–150	76JCS(PI)2307
18	5-nitro-2-pyridyl	H	H	H	H	Br	143–144	79JCS(PI)1525
19	5-phenyl-1,2,4-triazin-3-yl	H	H	H	H	H	148–150	80JCS(PI)343
20	styryl	Me	H	H	H	H	gum	79JCS(PI)2535
21	4-BrC_6H_4COCH=CH	Me	H	H	Me	H	210–211	80JCS(PI)362
22	4-ClC_6H_4COCH=CH	Me	H	H	H	H	196–198	80JCS(PI)362
23	2-Cl-5-$NO_2C_6H_3COCH$=CH	Me	H	H	H	H	110–112	80JCS(PI)362
24	1-oxido-4-pyridyl	H	OCOMe	H	H	H	90–91	80JCR(M)3337
25	Me	Me	H	H	H	Ph	130–132	76JCS(PI)2329

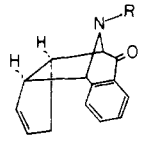
[a] Oxime, 170–171 °C. [b] Phenyl oxime, 197–198 °C.

TABLE 33. Adducts Formed by the Addition of Dienes across the 2,4-Positions of 3-Oxidoquinoliniums



no.	R^1	R^2	R^3	R^4	mp, °C	ref
1	H	H	H	H	gum	74TH1, 74CC608
2	Me	Me	H	H	70–73	74TH1, 74CC608
3	H	H	Me	H	78–80	74TH1, 74CC608
4	H	H	H	Me	78–80	74TH1
5	Me	H	H	H	syrup	74TH1, 74CC608
6	H	Me	H	H	syrup	74TH1
7	H	H	OMe	H	gum	74TH1, 74CC608
8	H	H	H	OMe	gum	74TH1

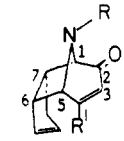
TABLE 34. Adducts of Cyclopentadiene and 4-Oxidoisoquinoliniums



no.	R	mp, °C	ref
1	H	oil	80JCR(M)3337
2	Me	oil[a]	80JCR(M)3337
3	4-ClC_6H_4COCH=CH	209–210	80JCR(M)3337

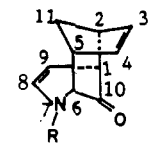
[a] Methiodide, 213–214 °C; *N*-oxide, oil; picrate of *N*-oxide, 180–181 °C.

TABLE 35. Adducts Formed by Addition of Cyclopentadiene across the 2,6-Positions of 3-Oxidopyridiniums



no.	R	R′	mp, °C	ref
1	4,6-dimethylpyrimidin-2-yl	H	167–169	75CC425, 76JCS(PI)2307
2	5,6-diphenyl-1,2,4-triazin-3-yl	H	150–152	80JCS(PI)343
3	4-ClC_6H_4COCH=CH	H	164–166	80JCS(PI)362
4	5-nitro-2-pyridyl	H	194	75CC425, 76JCS(PI)2307
5	Me	OMe	72–73.5	78TL1751

TABLE 36. Cyclopentadiene Adducts Formed by Addition across the 2,4-Positions of 3-Oxidopyridiniums



no.	R	mp, °C	ref
1	4,6-dimethylpyrimidin-2-yl	146–147	75CC425, 76JCS(PI)2307
2	4-ClC_6H_4COCH=CH	156–158	80JCS(PI)362
3	5-nitro-2-pyridyl	137	75CC425, 76JCS(PI)2307

TABLE 37. Reduced Adducts

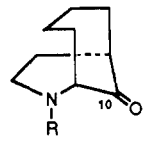
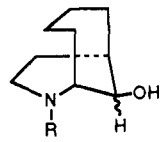
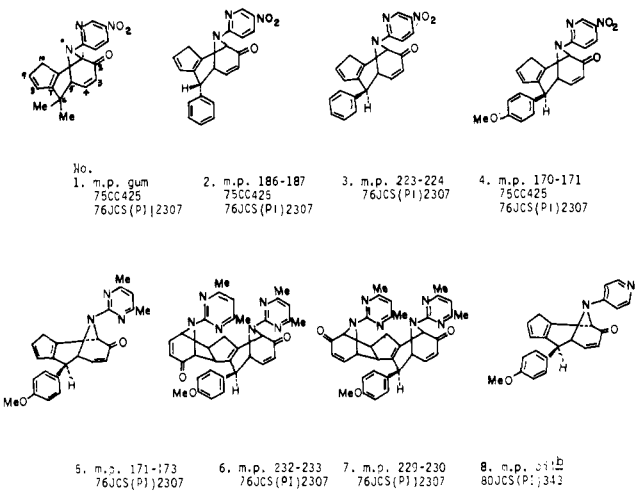
no.	compd	R	mp, °C	ref
1		4,6-dimethoxy-*s*-triazin-2-yl	95	77JCS(PI)1930
2		6-ethoxy-3,4-dihydro-4-oxo-*s*-triazin-2-yl	185	77JCS(PI)1930
3		4,6-dimethylpyrimidin-2-yl	89–90	79JCS(PI)1525
4		4,6-dimethoxy-1,3,5-triazin-2-yl	153	77JCS(PI)1930
5		4,6-dimethylpyrimidin-2-yl	139–140	79JCS(PI)1525

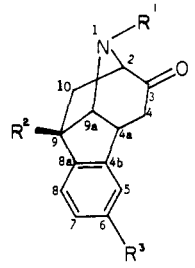
TABLE 38. Adducts from Fulvenes and 3-Oxidopyridiniums[a]



No.
1. m.p. gum 75CC425 76JCS(PI)2307
2. m.p. 186-187 75CC425 76JCS(PI)2307
3. m.p. 223-224 76JCS(PI)2307
4. m.p. 170-171 75CC425 76JCS(PI)2307
5. m.p. 171-173 76JCS(PI)2307
6. m.p. 232-233 76JCS(PI)2307
7. m.p. 229-230 76JCS(PI)2307
8. m.p. [illegible][b] 80JCS(P1)342

[a] Structure numbering is nonsystematic. [b] Methiodide, 220 °C (dec).

TABLE 39. Tricyclic Adducts



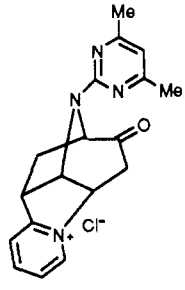
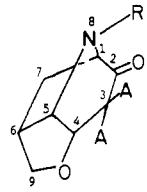
no.	R^1	R^2	R^3	mp, °C	ref
1	2,4-dinitrophenyl	H	H	220–221	76S105
2	5-nitro-2-pyridyl	H	H	231–233	76S105
3	5-nitro-2-pyridyl	H	Cl	273–274	76S105
4	5-nitro-2-pyridyl	H	Br	259–260	76S105
5	5-nitro-2-pyridyl	H	OMe	275	76S105
6	5-nitro-2-pyridyl	Me	H	233–234	76S105
7	Ph	H	H	165–166	76S105
8				235–236	79JCS(PI)1525

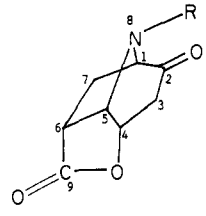
TABLE 40. Adducts from Allyl Alcohol and 3-Oxidopyridiniums



no.	N-substituent (R)	A, A	mp, °C	ref
1	4,6-dimethoxy-*s*-triazin-2-yl	H, H	120–121	79JCS(PI)1525
2	4,6-dimethylpyrimidin-2-yl	H, H	120–121[a]	79JCS(PI)1525
3	4,6-dimethylpyrimidin-2-yl	=CHPh	135–136	79JCS(PI)1525
4	5-bromo-4,6-dimethyl-pyrimidin-2-yl	H, H	95–96	79JCS(PI)1525
5	5-bromo-4,6-dimethyl-pyrimidin-2-yl	Br, Br	206–207	79JCS(PI)1525
6	5-nitro-2-pyridyl	H, H	217–218	79JCS(PI)1525
7	5-nitro-2-pyridyl	Br, Br	225–226	79JCS(PI)1525
8	3-bromo-5-nitro-2-pyridyl	Br, Br	215–216	79JCS(PI)1525
9	6-phenyl-3-pyridazinyl	H, H	194–195	83JCR(S)37
10	6-(4-methoxyphenyl)-3-pyridazinyl	H, H	201–202	83JCR(S)37

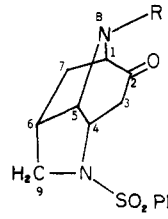
[a] Phenylhydrazone, 227–228 °C.

TABLE 41. Adducts from Acrylic Acid and 3-Oxidopyridiniums



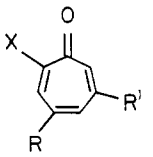
no.	R	mp, °C	ref
1	5-nitro-2-pyridyl	265–266	79JCS(PI)1525
2	4,6-dimethylpyrimidin-2-yl	136–137	79JCS(PI)1525

TABLE 42. Adducts from *N*-Allylbenzenesulfonamide and 3-Oxidopyridiniums



no.	R	mp, °C	ref
1	4,6-dimethylpyrimidin-2-yl	212–213	79JCS(PI)1525
2	5-nitro-2-pyridyl	198–199	79JCS(PI)1525

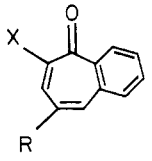
TABLE 43. Tropones and Tropolones



no.	X	R	R^1	mp, °C	ref
1	NMe_2	CN	H	72–73	71JCS(C)878
2	NMe_2	CO_2Me	H	66–67	71JCS(C)878
3	NMe_2	CN	Ph	95–96	71JCS(C)878
4	NMe_2	CO_2Me	Ph	138–139	71JCS(C)878
5	NMe_2	CO_2Et	OMe	80–81	51JCS2352
6	NMe_2	CO_2Me	$CHMe_2$	—[a]	51JCS2352
7	$MeN(CH_2)_2CN$	CN	H	110–112	79JCS(PI)2528
8	$MeN(CH_2)_2CO_2Me$	CO_2Me	H	50–51	79JCS(PI)2528
9	$NHC_5H_4N^+MeClO_4^-$	C_6H_5	H	250 (dec)	80JCS(PI)343
10	OH	CN	H	194–195	71JCS(C)878, 61BCJ504
11	OH	CO_2Me	H	117–118	71JCS(C)878
12	OH	CN	Ph	158–159	76JCS(PI)2329
13	OH	CO_2Et	OMe	153–155	51JCS2352
14	OH	CO_2H	OH	280 (dec)	51JCS2352
15	OH	CO_2Me	$CHMe_2$	82–83	51JCS2352
16	OH	CO_2H	OMe	257–260	51JCS2352
17	OH	H	$CHMe_2$	49–50	51JCS2352
18	OH	CO_2H	$CHMe_2$	180–182	51JCS2352

[a] Boiling point 170–180 °C/0.3 mm.

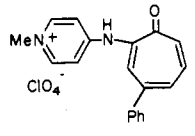
TABLE 44. Benzotropones



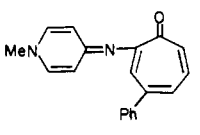
no.	X	R	mp, °C	ref
1	NMe_2	CN	126–127	72JCS(PI)2054
2	NMe_2	CO_2Me	98–100	72JCS(PI)2054

have been obtained in one-pot reactions from 3-hydroxypyridine.

Hofmann degradation of the methiodide (**84**, R′ = H, R″ = Ph, R = $C_5H_4N^+MeI^-$) with silver oxide produced the corresponding tropone perchlorate (**90**), mp 250 °C. Further hydrolysis of this perchlorate to the corresponding 4-phenyltropolone (**87**, R′ = H, R″ = C_6H_5) proved unsuccessful, presumably owing to the intervention of species **91** under basic conditions.



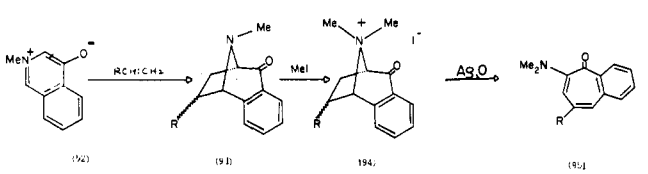
(90)



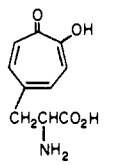
(91)

The synthesis of tropones can be extended to the benzotropones listed in Table 44. Cycloadducts **93** derived from 2-methyl-4-oxidoisoquinolinium (**92**) were readily quaternized with methyl iodide to the salts **94**. Hofmann elimination readily led to 2-(dimethylamino)-4-cyano-6,7-benzotropone (**95**, R = CN) (Scheme 40).

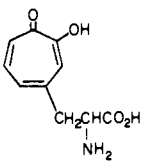
SCHEME 40



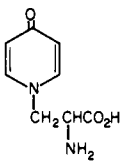
Teitei and Harris [79AJC1329] recently described attempts to synthesize the tropolone analogues **96** and **97** of the wool-growth-inhibiting amino acid mimosine (**98**) via the cycloaddition process from 1-methyl-3-oxidopyridinium.



(96)



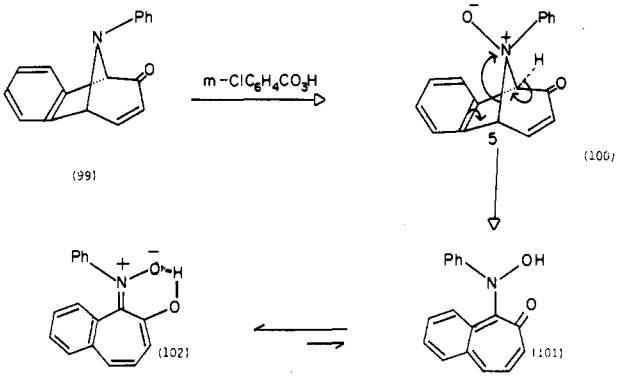
(97)



(98)

The cycloadduct **99** with *m*-chloroperbenzoic acid yields the orange compound **101** ⇌ **102**, mp 137–138 °C, for which IR and NMR spectral data indicate the nitrone tautomeric structure **102**. This reaction presumably proceeds via the intermediate *N*-oxide **100**, which suffers cleavage of the C(5)–N bond (Scheme 41) (76JCS(PI)2334).

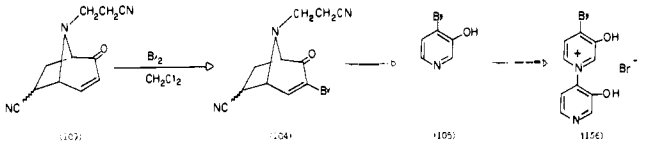
SCHEME 41



The thermal instability of adducts of the type **103** has been successfully utilized to introduce substituents into 3-hydroxypyridine. As an example (Scheme 42) of the substitution of a 3-hydroxypyridine, the bromination–dehydrobromination of the acrylonitrile adduct **103** gave the bromo adduct **104**, which was readily ther-

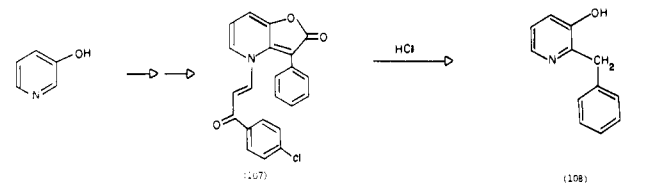
molyzed at 180 °C at 1 mmHg to 4-bromo-3-hydroxypyridine (**105**) as the quaternary salt (**106**) via a thermally induced retro-1,3-dipolar cycloaddition (76JCS(PI)2334).

SCHEME 42



Treatment of 4-[*trans*-3-(4-chlorophenyl)-3-oxoprop-1-enyl]-2-oxo-3-phenyl-2,4-dihydrofuro[3,2-*b*]pyridine (**107**) (Scheme 43) with dilute HCl afforded 2-benzyl-3-hydroxypyridine (**108**), mp 188 °C, in 50% yield. 2-Benzyl-3-hydroxypyridine was previously prepared by Leditschke [53CB123] from benzyl 2-furyl ketone in low yields (26%). This last conversion represents a useful method for the regiospecific substitution of 3-hydroxypyridine in 30% overall yield.

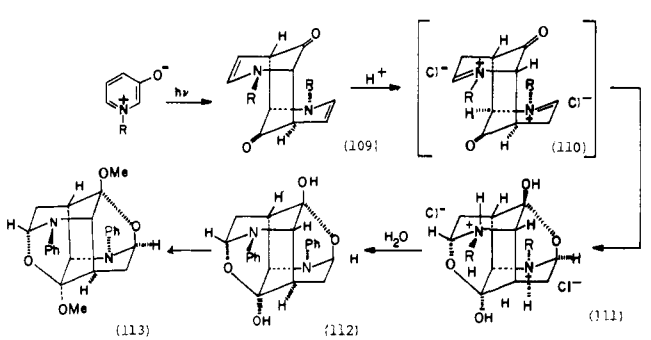
SCHEME 43



3. Transformations of Photodimers (Table 45) and Thermal Dimers (Table 46)

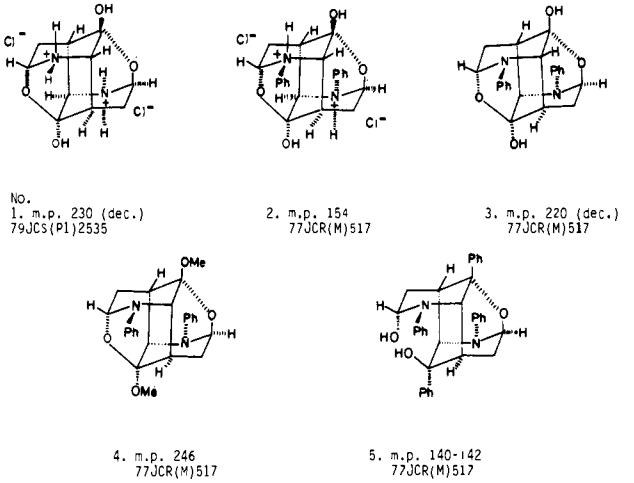
The photodimers **109** (R = CH=CHPh, Ph) were readily converted to the bis(hemiketal) salts **111** (R = CH=CHPh, Ph) with aqueous HCl. The formation of these salts probably involves the intermediacy of the immonium salt **110** (R = CH=CHPh, Ph). The bis(hemiketal) salt **111** (R = Ph) was transformed to the free base, the hemiketal **112**, by treatment with water. With boiling methanol, the salt **111** (R = Ph) yielded the bisketal **113**. Attempts to convert the bis(hemiketal) salt **111** (R = CH=CHPh) to the free base proved unsuccessful. Presumably the α-amino alcohol of the free base is subject to further hydrolysis (Scheme 44).

SCHEME 44



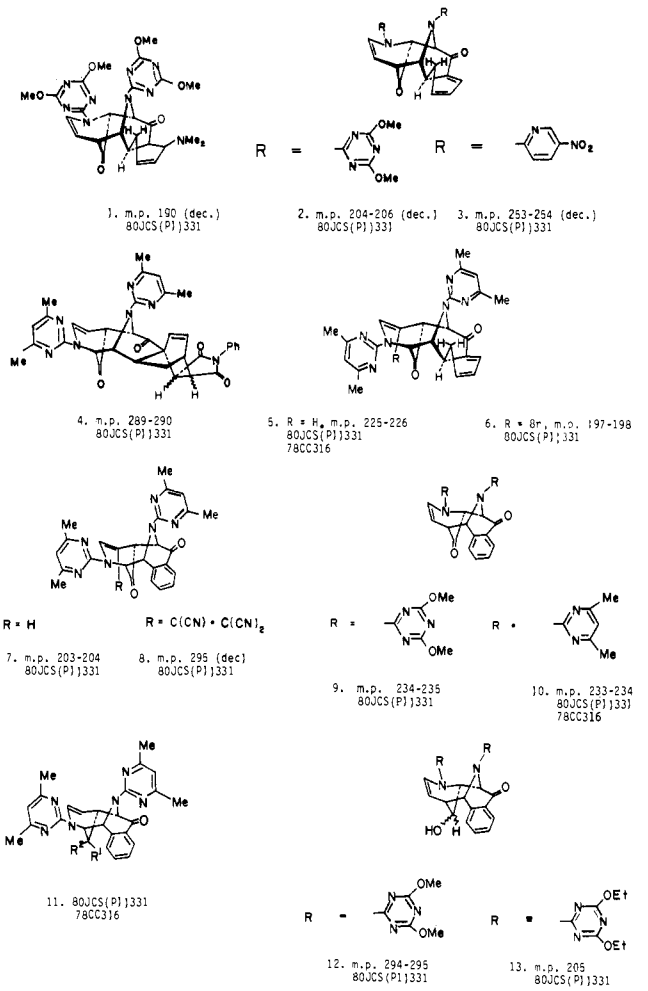
Phenylmagnesium bromide readily converted the photodimer **114** to a mixture of at least four components from which the diol **117** was isolated in 32% yield. The initial product of the Grignard reaction is thought to be the bismagnesium salt **115**. During workup, the initially formed diol **116** undergoes hydration at one enamine moiety and intramolecular ring closure at the remaining enamine moiety to yield the diol **117** (Scheme 45).

TABLE 45. 3,10-Dioxa-5,13-diazadiadamantanes and Related Compounds



1. m.p. 230 (dec.) 79JCS(P1)2535
2. m.p. 154 77JCR(M)517
3. m.p. 220 (dec.) 77JCR(M)517
4. m.p. 246 77JCR(M)517
5. m.p. 140-142 77JCR(M)517

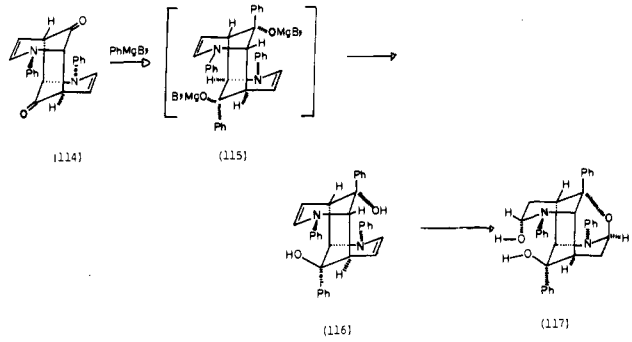
TABLE 46. Dimers Produced by Diels–Alder Annelation to 3-Oxidopyridinium Dimers



1. m.p. 190 (dec.) 80JCS(P1)331
2. m.p. 204-206 (dec.) 80JCS(P1)331
3. m.p. 253-254 (dec.) 80JCS(P1)331
4. m.p. 289-290 80JCS(P1)331
5. R = H, m.p. 225-226 80JCS(P1)331 78CC316
6. R = Br, m.p. 197-198 80JCS(P1)331
7. m.p. 203-204 80JCS(P1)331
8. m.p. 295 (dec) 80JCS(P1)331
9. m.p. 234-235 80JCS(P1)331
10. m.p. 233-234 80JCS(P1)331 78CC316
11. 80JCS(P1)331 78CC316
12. m.p. 294-295 80JCS(P1)331
13. m.p. 205 80JCS(P1)331

1-Heteroaryl-3-oxidopyridinium dimers with dienamines produced cycloadducts (e.g., Table 46, entries 1–3) that were dehydrated to "mixed dimers" (e.g., Table 46, entry 7) of the corresponding 2-heteroaryl-4-oxidoisoquinolinium with the starting 1-heteroaryl-3-oxidopyridinium. The mixed dimers undergo reversible thermal dissociation to produce the corresponding monomer, which could be trapped by various dipola-

SCHEME 45



rophiles [80JCS(PI)311]. Table 46 lists dimers produced by Diels–Alder annelation to 3-oxidopyridinium dimers.

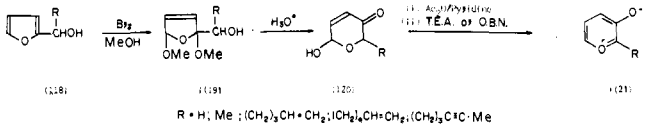
IV. Cycloaddition Reactions of Six-Membered Heteroaromatic Betaines with Positive Charge on Oxygen or Sulfur

A. Substrates

1. 3-Oxidopyryliums

Transient 3-oxidopyryliums (**121**) are readily prepared from the corresponding pyranulose acetates. Treatment of furfuryl alcohol **118** with bromine in methanol yielded [80JOC3359] the acetal **119** as a mixture of epimers. Acid hydrolysis produced the alcohol **120**, which was readily acylated with acetic anhydride in pyridine. The 3-oxidopyrylium ylides **121** can be generated [82CC1056] from the pyranulose acetate with base, e.g., triethylamine or diazabicyclo-[4.3.0]non-5-ene, or thermally in acetonitrile in a sealed tube at 150 °C (Scheme 46).

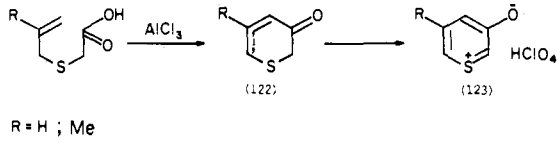
SCHEME 46



R = H; Me; $(CH_2)_3CH=CH_2$; $(CH_2)_4CH=CH_2$; $(CH_2)_3C\equiv C\text{-}Me$

3-Oxidothiopyrylium perchlorate (**123**) is prepared [75JCS(PI)2099] by cyclization of allylthioglycoloyl chloride with aluminum chloride followed by oxidation of the intermediate isomeric thiopyranones (**122**) with triphenylmethyl perchlorate (Scheme 47). The 5-methyl homologue was prepared in an analogous manner.

SCHEME 47

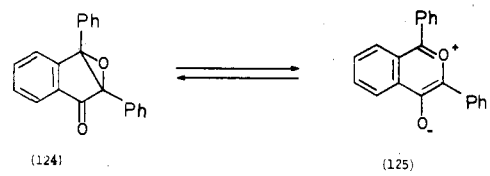


R = H ; Me

2. 4-Oxido-2-benzopyrylium and Related Derivatives

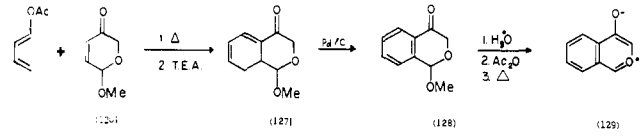
Heating or irradiating 2,3-diphenyl-2,3-epoxyindenone (**124**) readily yields [64JA3814] the relatively stable ylide, 1,3-diphenyl-4-oxido-2-benzopyrylium (**125**) (Scheme 48).

SCHEME 48



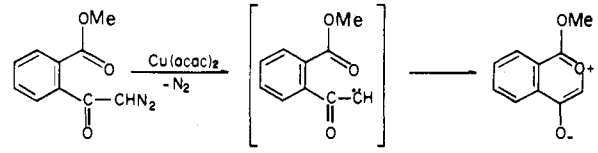
The parent 4-oxido-2-benzopyrylium (**129**) can be conveniently prepared [84CC702] from the corresponding benzoannelated pyranoside. Cycloaddition of 1-acetoxybutadiene with 6-methoxypyran-3(6*H*)-one (**126**), followed by treatment with triethylamine, affords the cyclohexadiene **127**. Dehydrogenation with palladium on charcoal yielded the benzopyranose **128**, which could be hydrolyzed with acid and then acylated to yield the required acetate. Treatment of the acetate with either base or heat generated the reactive 4-oxido-2-benzopyrylium (**129**) (Scheme 49).

SCHEME 49



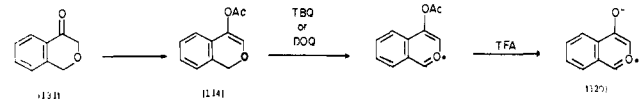
The related 1-methoxy-4-oxido-2-benzopyrylium (**132**) has been prepared by [83CL1453] copper chelate catalyzed decomposition of *o*-(methoxycarbonyl)-α-diazoacetophenone (**130**) (Scheme 50). The transient carbonyl ylide is formed by the intramolecular carbene–carbonyl reaction of the intermediate ketocarbene (**131**).

SCHEME 50



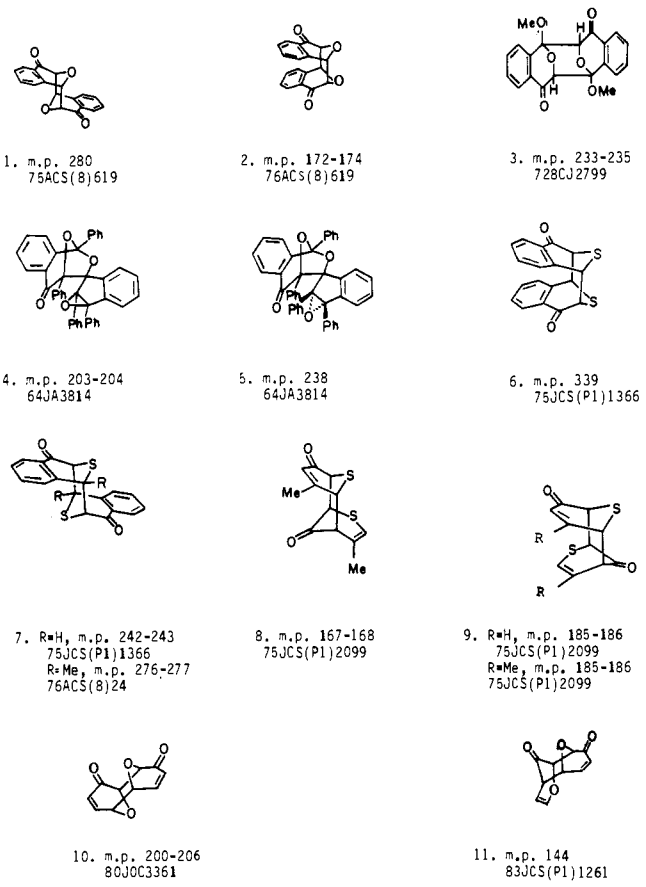
Nilsen and Undheim [76ACS(B)619] have claimed an alternative route to 4-oxido-2-benzopyrylium (**129**), involving the oxidation of 4-acetoxyisochromene (**134**) with either 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or tetrachloro-1,2-benzoquinone (TBQ) followed by reaction with acid (Scheme 51). The isochroman-4-one (**133**) was prepared by cyclization of ((*o*-carboxybenzyl)oxy)acetic acid. However, Sammes and Whitby [87JCS(PI)195] were unable to trap the supposed zwitterion **129** produced by this route using dipolarophiles.

SCHEME 51



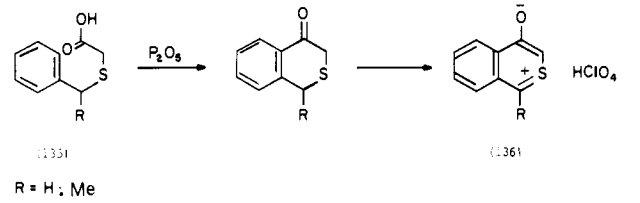
4-Oxido-2-benzothiopyrylium (**136**, R = H) is obtained [75JCS(PI)1366] as its perchlorate by cyclization of (benzylthio)acetic acid (**135**, R = H) using phosphorus pentoxide followed by oxidation of the inter-

TABLE 47. Betaine Dimers



mediate with triphenylmethyl perchlorate (Scheme 52). The 1-methyl homologue (**136**, R = Me) was prepared in a similar manner.

SCHEME 52



B. Dimerizations

4-Oxido-2-benzopyrylium has been reported [76ACS(B)619] to dimerize in TFA to yield both the syn and the anti dimers (Table 47, entries 2 and 1). In the NMR spectra, the coupling constants between the vicinal methine protons of the anti isomer are small (broad singlets at δ 4.4 and 5.3) whereas in the case of the syn isomer the coupling was 11 Hz (δ 4.9 and 5.5). However, Sammes et al. reported [87JCS(PI)195] no formation of dimers (Table 47, entries 1 and 2) from their 4-oxido-2-benzopyrylium.

The closely related 1-methoxy-4-oxido-2-benzopyrylium yielded [72BCJ2779] the corresponding dimer, (Table 47, entry 3) mp 233–235 °C, for which no stereochemistry was assigned. The IR spectrum of this dimer showed a stretching vibration band for a carbonyl group at 1712 cm^{-1}.

Ullman and Milks [64JA3814] have obtained a second type of dimer formed by the pyrolysis of 2,3-diphenylindenone oxide. The two dimers, (Table 47, entry 4, mp 203–204 °C, and Table 47, entry 5, mp 238 °C) were formed by a 1,3-dipolar cycloaddition between the benzopyrylium oxide and the carbonyl group of the indenone oxide.

Undheim et al. have reported the dimerization at 4-oxido-2-benzothiopyrylium to produce syn and anti dimers (Table 47, entries 6 and 7) [75JCS(PI)1366] [84ACS(B)617].

3-Oxidothiopyryliums readily dimerize in trifluoroacetic acid to yield [75JCS(PI)2099] both the syn and anti dimers (Table 47, entries 9 and 8), with the syn dimer as the major product. The IR spectra for both dimers show unsaturated and saturated carbonyl absorption. In the NMR spectra, the coupling constants between the vicinal methine protons were ca. 10 Hz for the syn form and ca. 4 Hz for the anti form. Secondary coupling of ca. 2 Hz occurs over the sulfur bridge between H-1 and H-7.

C. Cycloadditions with 2π Units

1. Cycloaddition with Olefinic Compounds

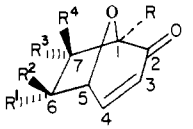
Cycloadducts from 3-oxidopyrylium betaines and simple olefins are listed in Tables 48 and 49. The stereochemistry of the adducts was again determined by NMR; the exo adducts have a dihedral angle of ca. 90° between H-5 and H-6 so that the H-5 absorption is only a doublet and becomes a singlet on irradiation of H-4. For endo adducts, the coupling $J_{5,6}$ is of the range 5–7 Hz. A W-coupling between H-1 and H-3 of 1.5–2.0 Hz is also observed.

Hendrickson and Farina [80JOC3359] reported that 3-oxidopyrylium only reacted sluggishly with electron-deficient dipolarophiles, giving reasonable yields of cycloadducts with only the most reactive of these, such as acrolein. 2-Methyl-3-oxidopyrylium and 3-oxido-2-phenylpyrylium betaines show a tendency to form the reverse (i.e., C-7) regioisomer from that observed with the unsubstituted betaine. This is in agreement with studies on 2-methyl-3-oxido-1-phenylpyridinium and 3-oxido-2-phenyl-1-phenylpyridinium betaines [82CC262], which also have a tendency to form C-7 regioisomers.

Strained olefins also react with 3-oxidopyrylium. Both norbornene [83JCS(PI)2729] and norbornadiene [83JCS(PI)1261] react to produce cycloadducts. With norbornadiene, a single "exo-syn" isomer, mp 110 °C, was produced in 50% yield. The stereochemistry was assigned by NMR, in which the coupling constants across positions 1,2 and 7,8 (see Table 48) are both less than 0.2 Hz, attributable to a dihedral angle of ca. 90°, as expected for the exo adduct. The syn configuration is substantiated by the shielding influence observed on one of the protons at position 13 by the oxygen bridge.

Table 49 lists cycloadducts of 3-oxidopyrylium betaines bearing unsubstituted side chains. Thus thermolysis of the pyranulose 6-acetoxy-2-(pent-4-enyl)-2*H*-pyran-3(6*H*)-one at 150 °C for 16 h in acetonitrile afforded a bicyclic adduct (n = 1) as the major product (61%) (Table 49). The reaction is presumed to proceed via the intermediate generation of the 3-oxidopyrylium betaine, which undergoes spontaneous intramolecular 1,3-dipolar cycloaddition across the olefinic bond. Studies on model compounds have shown that the intramolecular cycloaddition of 2- and 6-(alk-4-enyl)-3-

TABLE 48. Cycloadducts from 3-Oxidopyryliums with Substituted Olefins



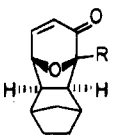
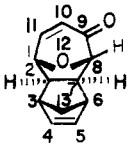
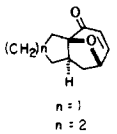
no.	R	R^1	R^2	R^3	R^4	mp, °C	ref
1	H	OEt	H	H	H	oil	83JCS(PI)1261
2	H	Ph	H	H	H	42	83JCS(PI)1261
3	Me	OEt	H	H	H	oil	83JCS(PI)1261
4	H	OCH_2Ph	H	H	H	oil	83JCS(PI)2729
5	H	Me	CHO	H	H	oil	80JOC3359
6	H	CHO	Me	H	H	oil	80JOC3359
7	H	$C_4F_9SO_2$	H	H	H	175–181	80JOC3359
8	H	CN	H	H	H	122	84JCR(S)196
9	Me	H	CN	H	H	oil	84JCR(S)196
10	Me	H	H	CN	H	oil	84JCR(S)196
11	Ph	H	H	Ph	H	oil	84JCR(S)196
12	Ph	H	H	H	Ph	oil	84JCR(S)196
13	Ph	H	H	OEt	H	oil	84JCR(S)196
14	Me	H	H	H	CN	oil	84JCR(S)196
15	H	CHO	H	H	H	oil	80JOC3359
16	H	H	CHO	H	H	oil	80JOC3359
17	H	$MeC{=}CH_2$	H	H	H	oil	83JCS(PI)1261
18	H	$MeC{=}CH_2$	Me	H	H	oil	83JCS(PI)1261
19			R = H			82	83JCS(PI)2729
20			R = Me			oil	83JCS(PI)2729
21						110	83JCS(PI)1261

TABLE 49. Cycloadducts from 3-Oxidopyryliums by Intramolecular Cycloaddition



n = 1
n = 2

1. m.p. oil
83JCS(P1J)2729
82CC1056

2. m.p. -
82CC1056

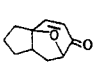
3. m.p. oil
85JCS(P1)1725

4. m.p. oil
85JCS(P1)1725

5. m.p. oil
85JCS(P1)1725

6. m.p. oil
85JCS(P1)1725

7. m.p. -
82CC1056



8. m.p. -
82CC1056

oxidopyrylium betaines occurs stereochemically in an exo manner [82CC1056].

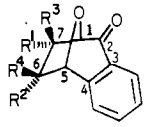
Adducts from 4-oxido-2-benzopyryliums and olefins are given in Tables 50–52. The reaction of unsubstituted 4-oxido-2-benzopyrylium and the relatively unreactive dipolarophile styrene yields two regioisomeric endo adducts. This contrasts with the reaction of styrene with 3-oxidopyrylium, where a single 6-endo isomer is produced. The reaction of 4-oxido-2-benzopyrylium with the electron-rich ethyl vinyl ether gives the single 7-endo adduct, again in the reverse regiochemistry to that observed in the 3-oxidopyrylium series [83JCS(PI)1261]. Similarly, the substituted 4-oxido-2-benzopyrylium produced thermally from 2,3-diphenylindenone oxide reacts with the electron-deficient acrylonitrile to yield a single 7-endo adduct.

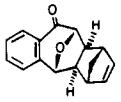
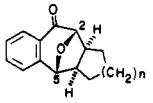
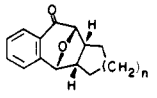
Substituted 4-oxido-2-benzopyryliums produce [71CJC3443] 1,3-dipolar cycloadducts with a variety of symmetrical ethylenic dipolarophiles such as dimethyl fumarate, dimethyl maleate, maleic anhydride, *trans*-1,2-dibenzoylethylene, N-substituted maleimides, acenaphthylene, and tetracyanoethylene [84KGS167]. As in the case of adducts produced from N-substituted isoquinolinium betaines, the configuration of the adducts was confirmed by NMR coupling patterns of the methine protons of the adducts. The stereospecificity of the cycloadditions was confirmed in the reactions of dimethyl maleate, dimethyl fumarate, and *trans*-1,2-dibenzoylethylene and indicated that the cycloadditions proceed in a (2s + 4s)π-type concerted mechanism.

2. Cycloaddition with Carbonyl Compounds

Cycloadducts from 4-oxido-2-benzopyrylium and carbonyl compounds are listed in Tables 53 and 54. The photolysis of 2,3-diphenylindenone oxide in the presence of cyclohexanone yielded a single cycloadduct (Table 54, entry 4), mp 196–197 °C [64JA3814]. The activated 1-methoxy-4-oxido-2-benzopyrylium reacts with a wide variety of aldehydes and ketones. Aromatic aldehydes react with this betaine to produce two ad-

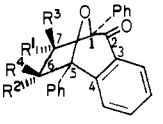
TABLE 50. Cycloadducts from 4-Oxido-2-benzopyrylium with Substituted Olefins[a]



no.	R^1	R^2	R^3	R^4	mp, °C	ref
1	OAc	H	H	H	gum	87JCS(PI)195
2	H	OAc	H	H	gum	87JCS(PI)195
3	H	H	OAc	H	gum	87JCS(PI)195
4	H	H	H	OAc	gum	87JCS(PI)195
5	Ph	H	H	H	gum	84CC702, 87JCS(PI)195
6	H	Ph	H	H	gum	84CC702, 87JCS(PI)195
7	H	H	Ph	H	gum	87JCS(PI)195
8	H	H	H	Ph	gum	87JCS(PI)195
9	OEt	H	H	H	gum	84CC702, 87JCS(PI)195
10	H	OEt	H	H	gum	87JCS(PI)195
11	H	H	OEt	H	gum	87JCS(PI)195
12	H	H	H	OEt	gum	87JCS(PI)195
13	H	CHO	H	H	gum	87JCS(PI)195
14	H	H	CHO	H	gum	87JCS(PI)195
15	H	H	H	CHO	gum	87JCS(PI)195
16					96–97	87JCS(PI)195
17		$n = 1$			gum	87JCS(PI)195
18		$n = 2$			amorphous solid	87JCS(PI)195
19		$n = 1$			gum	84CC702, 87JCS(PI)195
20		$n = 2$			gum	87JCS(PI)195

[a] Structure numbering is nonsystematic.

TABLE 51. Cycloadducts from 4-Oxido-1,3-diphenyl-2-benzopyrylium with Substituted Olefins[a]

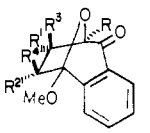


no.	R^1	R^2	R^3	R^4	mp, °C	ref
1	Cl	Cl	H	H	129–131	71CJC3443
2	H	Cl	Cl	H	132	71CJC3443
3	Cl	H	H	Cl	132	71CJC3443
4	1,8-naphthyl	1,8-naphthyl	H	H	219	71CJC3443
5	H	H	1,8-naphthyl	1,8-naphthyl	219	71CJC3443
6	-OCOO-		H	H	218	71CJC3443
7	H	H	-OCOO-		218	71CJC3443
8	-COOCO-		H	H	227	71CJC3443
9	-CONPhCO-		H	H	261	71CJC3443
10	CO_2Me	H	H	CO_2Me	188	71CJC3443
11	H	CO_2Me	CO_2Me	H	188	71CJC3443
12	H	H	CO_2Me	CO_2Me	157	71CJC3443
13	CO_2Me	CO_2Me	H	H	157	71CJC3443
14	Ph	H	H	Ph	193	71CJC3443
15	H	Ph	Ph	H	193	71CJC3443
16	CN	H	H	CN	203	71CJC3443
17	H	CN	CN	H	203	71CJC3443
18	COPh	H	H	COPh	216	71CJC3443
19	Ph	Ph	H	H	68	71CJC3443
20	H	H	Ph	Ph	68	71CJC3443
21	CN	Me	H	H	191	71CJC3443
22	CN	H	H	H	179	71CJC3443
23	-CONHCO-		H	H	275	71CJC3443
24	CO_2H	CO_2H	H	H	150	71CJC3443

[a] Structure numbering is nonsystematic.

ducts, the 7-endo and the 7-exo regioisomers [83CL1453]. In the NMR spectra of the endo isomers, the signals for the methine protons appear as doublets (J = 6.0 Hz), while in the exo isomers, the methine

TABLE 52. Cycloadducts from 4-Oxido-1-methoxy-2-benzopyrylium with Substituted Olefins



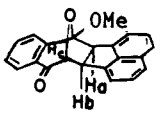
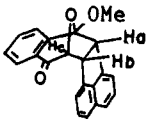
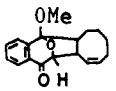
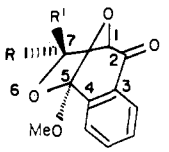
no.	R	R^1	R^2	R^3	R^4	mp, °C	ref
1	H	H	CO_2Me	CO_2Me	H	111–112	81BCJ240
2	H	H	H	CO_2Me	CO_2Me	145–147	81BCJ240
3	H	CO_2Me	H	H	CO_2Me	115–117	81BCJ240
4	H	H	COPh	COPh	H	151–152	81BCJ240
5	H	COPh	H	H	COPh	236–239	81BCJ240
6	H	H	H	CO_2H	CO_2H	215–216	81BCJ240
7	H	H	H	-OCNPhCO-		238–239	81BCJ240
8	H	-OCNPhCO-		H	H	206–207	81BCJ240
9	H	H	H	-OCNEtCO-		195–197	81BCJ240
10	H	H	H	-OCNMeCO-		293–295	81BCJ240
11	H	-OCNMeCO-		H	H	208–210	81BCJ240
12	H	Me	H	$CH=CH_2$	H	oil	72BCJ2779
13	H	$CH=CH_2$	H	Me	H	oil	72BCJ2779
14	Me	-OCNPhCO-		H	H	204–206	81BCJ240
15	Me	H	H	-OCNPhCO-		215–217	81BCJ240
16	Me	-OCNEtCO-		H	H	162–163	81BCJ240
17	Me	H	H	-OCNEtCO-		184–186	81BCJ240
18	Me	-OCNMeCO-		H	H	191–192	81BCJ240
19	Me	H	H	-OCNMeCO-		229–230	81BCJ240
20						210–212	81BCJ240
21						178–179	81BCJ240
22						oil	72BCJ2779

TABLE 53. Cycloadducts from 4-Oxido-1-methoxy-2-benzopyrylium and Carbonyl Compounds



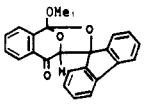
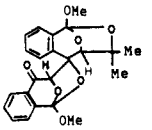
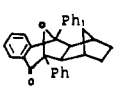
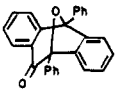
no.	R	R^1	mp, °C	ref
1	$4\text{-}ClC_6H_4$	H	135–137	83CL1453
2	H	$4\text{-}ClC_6H_4$	126.5–127.5	83CL1453
3	$2,4\text{-}Cl_2C_6H_3$	H	136.5–138.0	83CL1453
4	H	$2,4\text{-}Cl_2C_6H_3$		83CL1453
5	$2,6\text{-}Cl_2C_6H_3$	H	148–150	83CL1453
6	H	$2,6\text{-}Cl_2C_6H_3$	156–161	83CL1453
7	$4\text{-}NO_2C_6H_4$	H	152–154	83CL1453
8	H	$4\text{-}NO_2C_6H_4$	147.5–148.8	83CL1453
9	$3\text{-}NO_2C_6H_4$	H	115–117	83CL1453
10	H	$3\text{-}NO_2C_6H_4$		83CL1453
11	$4\text{-}MeOC_6H_4$	H		83CL1453
12	H	$4\text{-}MeOC_6H_4$	116–118.5	83CL1453
13	Et	H		83CL1453
14	H	Et		83CL1453
15	Me	Me	112	83CL1453
16			218–219	83CL1453
17				83CL1453

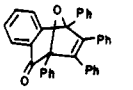
TABLE 54. Cycloadducts from 2-Benzopyryliums



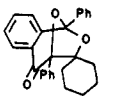
1. m.p. 203-207
64JA3814



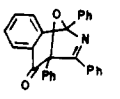
2. m.p. 78-80
71CJC3443



3. m.p. -
71CJC3443



4. m.p. 196-197
64JA3814



5. m.p. 148-151.5
64JA3814

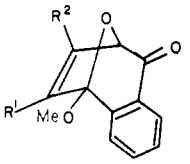
protons appear as doublets with small couplings (J = 1.3 Hz) [85BCJ1787].

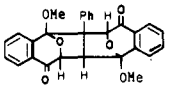
Ketones such as fluorenone and acetone yield single 1:1 cycloadducts [83CL1453]. The ^{13}C NMR spectrum of the fluorenone adduct exhibits a singlet at 119.1 ppm, which was assigned to the bridgehead C-1, thus confirming the direction of cycloaddition. In the case of acetone addition, further reaction of the betaine across the carbonyl group of the initially formed 1:1 adduct produced 12% of the 2:1 adduct [85BCJ1787].

3. Acetylene Cycloadducts

3-Oxidopyrylium reacts with DMAD to produce a single adduct, mp 115–119 °C [80JOC3359]. Adducts from 4-oxido-2-benzopyrylium and acetylenes are given in Table 55.

TABLE 55. Cycloadducts from 4-Oxido-2-benzopyrylium and Acetylenes



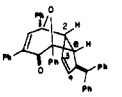
no.	R^1	R^2	mp, °C	ref
1	PhCO	PhCO	146–148	79BCJ3582
2	CO_2Me	CO_2Me	79–80	79BCJ3582
3	CO_2Me	H	87–88	79BCJ3582
4	Ph	H	oil	79BCJ3582
5	H	Ph	oil	79BCJ3582
6	CO_2Me	Ph	112–113	79BCJ3582
7	Ph	CO_2Me	124–127	79BCJ3582
8	CO_2H	Ph	260–262	79BCJ3582
9			244–246	79BCJ3582

D. Cycloadditions with Polyenes

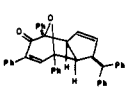
1. Adducts with Fulvenes

6,6-Diphenylfulvene reacts with 3-oxido-2,4,6-triphenylpyrylium to yield three (2 + 4)π cycloadducts [83JHC1621]. The adducts are listed in Table 56. The structures are based mainly on spectral evidence. The strong conjugated ketone ν(C=O) band at 1680–1690 cm^{-1} supports addition across the 2- and 6-positions of the ketone. The intense UV absorption at 285–290 nm (ϵ = 12 000–17 000) was assigned to π,π^* absorption characteristic of the 1,1-diphenylbutadiene chromophore.

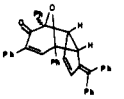
TABLE 56. Various Cycloadducts of 3-Oxidopyryllums with Fulvenes and Dienes



1. m.p. 158
83JHC1621



2. m.p. 203-204
83JHC1621



3. m.p. 205
83JHC1621

4. R^1=R^2=Me, oil
5. R^1=H or Me, R^2=Me or H, respectively, oil
83JCS(PI)1261

2. Cycloadducts with Dienes

3-Oxidopyrylium reacts [83JCS(PI)1261] with 2,3-dimethylbutadiene to yield the expected 2,4-adduct as the principal product (44%) together with a small quantity of the 2,6-adduct assigned as the endo isomer. In the presence of isoprene, reaction across the 2,4-positions of the betaine produced a mixture of regioisomers, ratio 3:2, in a yield of 30%. A single 2,6-cycloadduct was formed in 26% yield and was assigned the endo configuration on the basis of the NMR spectrum ($J_{5,6}$ = 7 Hz) (Table 48, entry 18).

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