CYCLOADDITION REACTIONS OF PYRIDINES

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Abstract - Examples of cycloaddition reactions of pyridines and related compounds, as well as pyridinium N-methylides and pyridinium N-imino-ylides are reported.

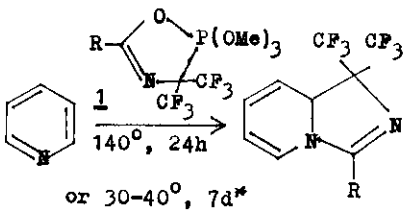
Among enormous number of cycloaddition reactions - a powerful synthetic method in chemistry - those performed on azaaromatic compounds are of special interest, providing route to new classes of heterocycles. This topic is included into reviews [1-9]; the present paper is dealing with cycloaddition reactions of pyridine and related compounds.

Cycloaddition reactions of pyridines are classified into 3 groups:

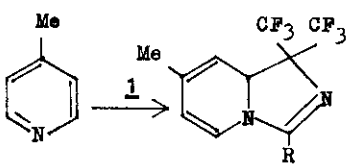
1. Cycloadditions of pyridines
2. Cycloadditions and intramolecular cyclizations of pyridinium N-methylides
3. Cycloadditions and intramolecular cyclizations of pyridinium N-imino-ylides

1. Cycloadditions of pyridines

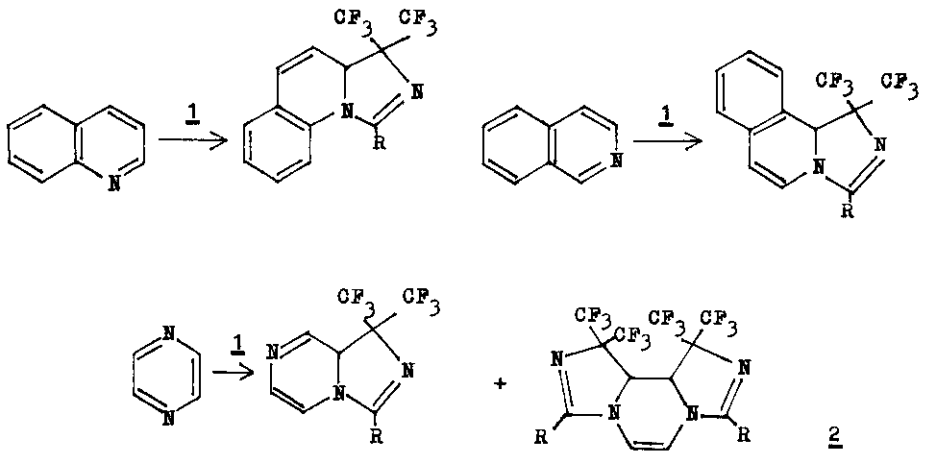
Burger et al. in the series of investigations of bis-trifluoromethyloxazaphospholine 1 as the 1,3-dipole precursor[10], examined the direct imidazoannelation of heterocycles[11]. When the thermal decomposition of 1 was carried out in N-heterocycles such as pyridines or quinolines, the 1:1 adducts were obtained. In the reaction of pyrazine with 1, also the 1:2 adduct 2 was isolated.



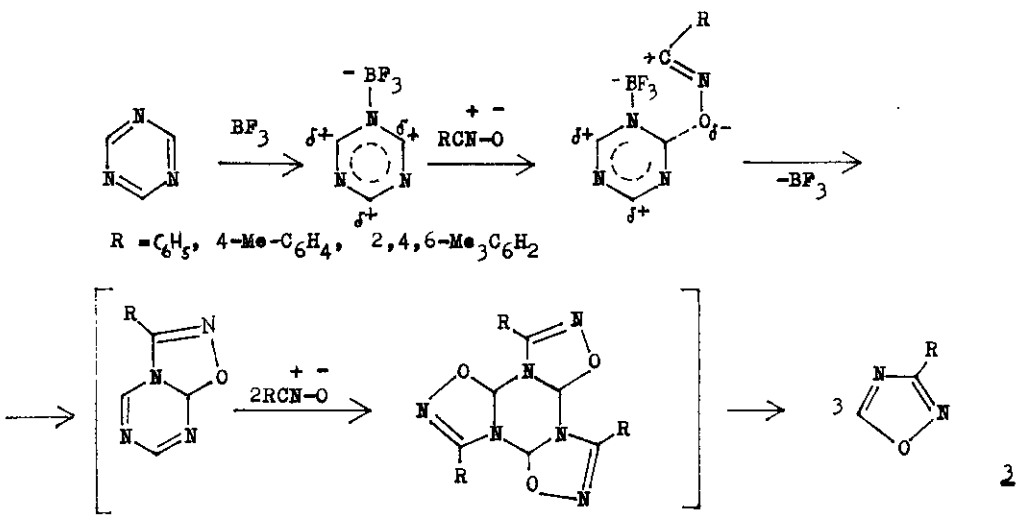
R = ^{t}Bu, C_6H_5, p-Me-C_6H_4, p-Cl-C_6H_4 etc.



*d = days

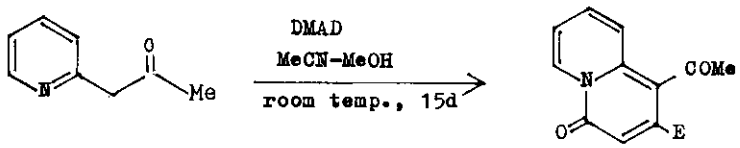


The reaction of 1,3,5-triazine with aromatic nitrile oxides was reported by Kurabayashi and Grundmann[12]. The resulting 3-substituted 1,2,4-oxadiazoles 3 are obtained in fair yields only when BF_3 is added.



Cycloaddition reactions of 2-substituted pyridines and quinolines were studied by Acheson[13]. 2-Pyridylacetone with DMAD* in MeCN-MeOH gives 4; 2-quinolylacetone however, under similar conditions yields the 1:2 molar cycloadduct 5:[13,14]

*DMAD = dimethyl acetylenedicarboxylate ; E=COOMe



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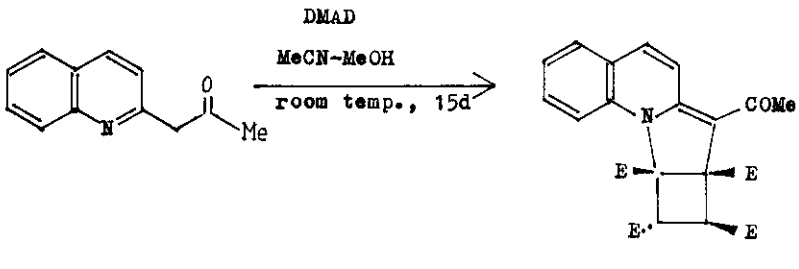
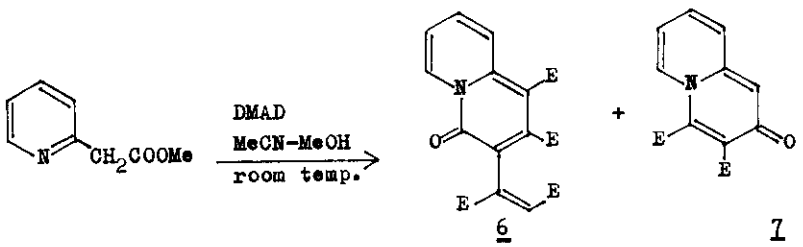
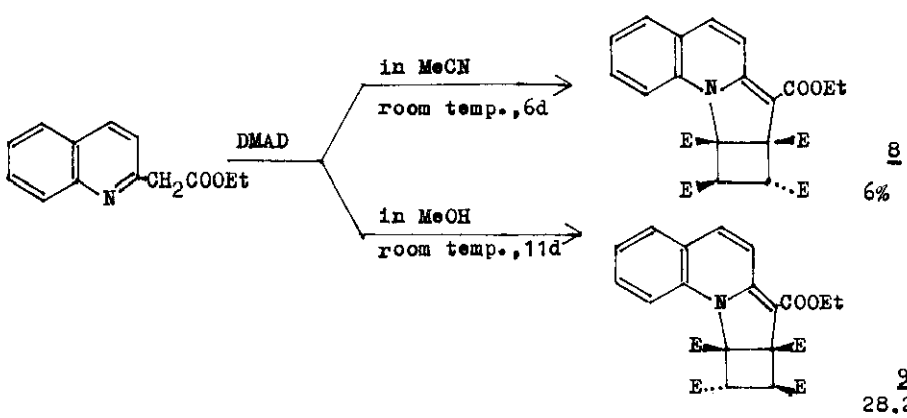


5
3.7%

The reaction of methyl pyridyl-2-acetate with DMAD in MeCN-MeOH affords 6 and 7, while in the case of ethyl quinoline-2-acetate the 1:2 molar adducts, cyclobutapyrroles 8 and 9 were obtained:



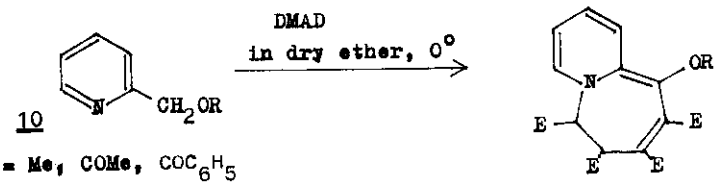
6 + 7



8 6%

9 28.2%

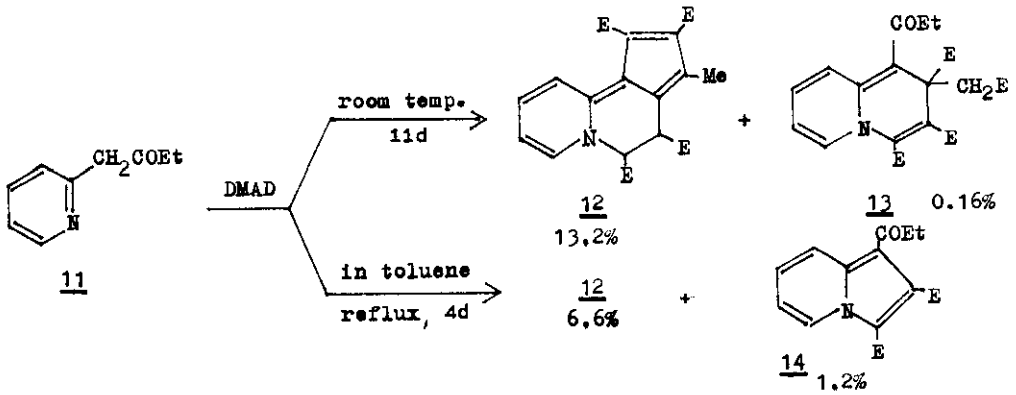
10 upon treatment with DMAD yielded pyridoazepines:[14]



10

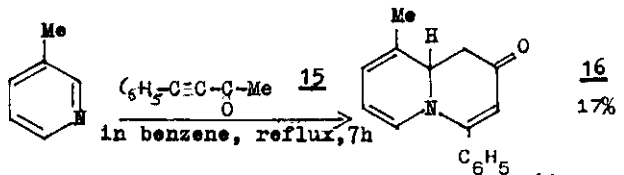
R = Me, COMe, COC_6H_5

11 with DMAD at room temperature gave the quinolizines 12 and 13, while at higher temperature 12 and the indolizine 14 were formed.[14]

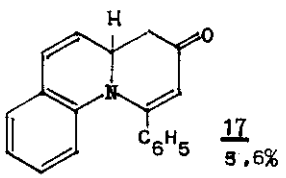


11

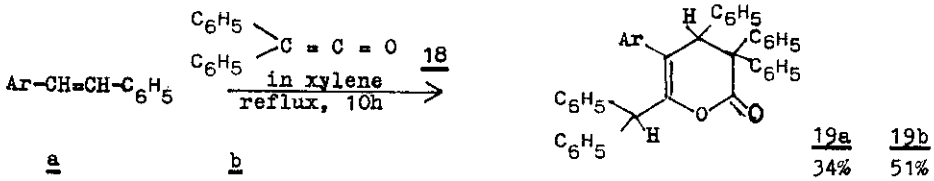
3-Methylpyridine with acetylenic ketone 15 produced the adduct of the novel type 16, which could be formed as follows:



Quinoline in a similar reaction afforded 17[14].



Sakamoto et al.[16] examined the reaction of 2-styrylpyridine and 2-styrylquinoline with diphenylketene 18 yielding 1:2 molar cycloadducts 19a and 19b:

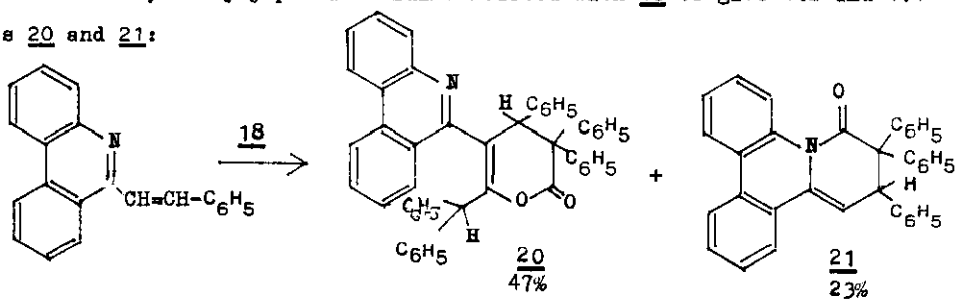


a b

Ar = 2-pyridyl , 2-quinolyl

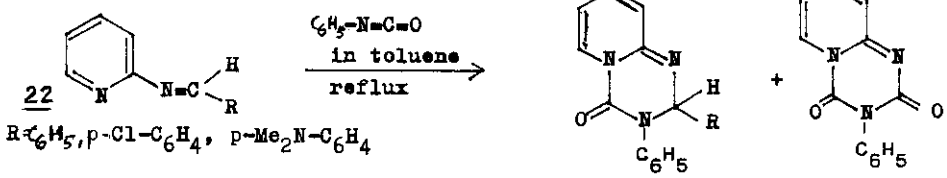
19a 34% 19b 51%

On the other hand, 6-styrylphenanthridine reacted with 18 to give 1:2 and 1:1 adducts 20 and 21:



20 47% 21 23%

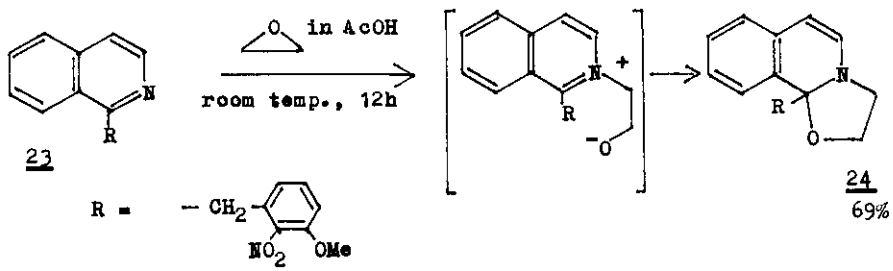
The cycloaddition of substituted pyridines 22 with phenyl isocyanate and diphenyl ketene was described by Bödeker et al.[17,18] In the reaction of 22 with phenyl isocyanate the following cycloadducts were formed:



22

R = C_6H_5, p-Cl-C_6H_4, p-Me_2N-C_6H_4

Treatment of 1-(3-methoxy-2-nitrobenzyl) isoquinoline 23 with ethylene oxide in acetic acid yielded stable 10b-substituted oxazoloisoquinoline 24 :[19]

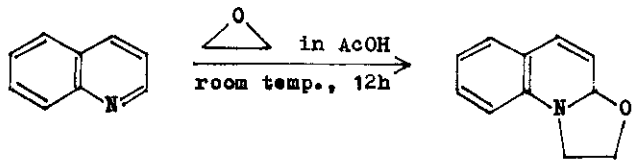


23

24 69%

R = $-CH_2$ (2-nitro-3-methoxyphenyl)

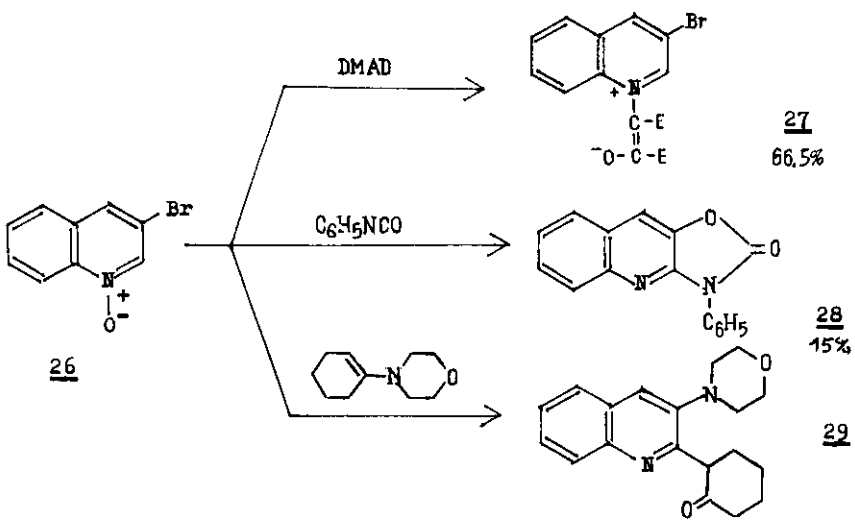
When quinoline was treated with ethylene oxide in AcOH, the novel labile oxazoloquinoline 25 was obtained.



25
100%

1,3-Dipolar cycloaddition reactions of 3-substituted and 3,4-disubstituted quinoline N-oxides were studied by Hamana et al.[20] in order to investigate the effect of substituents on the reactivity of their N-O groups. It was shown that the reactivity was enhanced as compared with that of quinoline N-oxide itself.

Among the examined reactions were following: 3-bromoquinoline N-oxide 26, on treatment with DMAD, phenyl isocyanate or 1-morpholinocyclohexene, gives N-ylide 27, oxazoloquinoline 28 and 2,3-disubstituted quinoline 29, respectively.



26

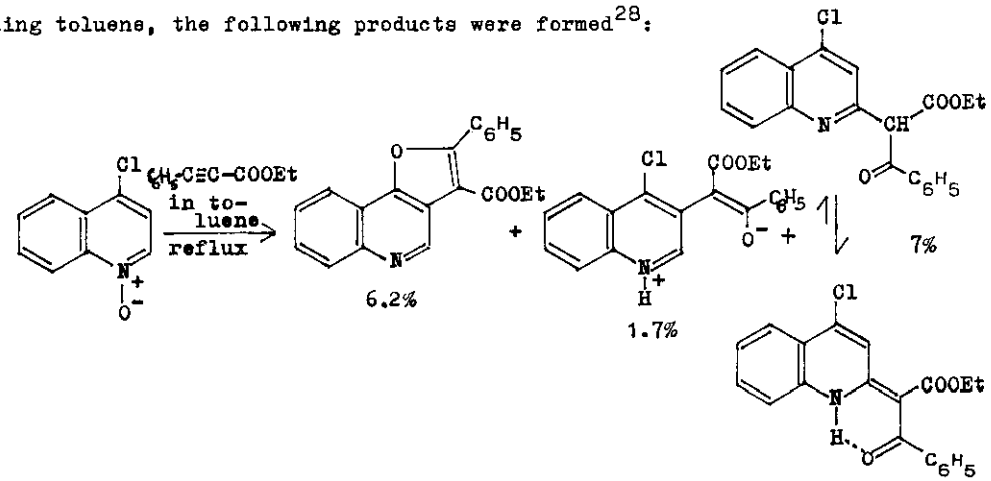
27
66.5%

28
15%

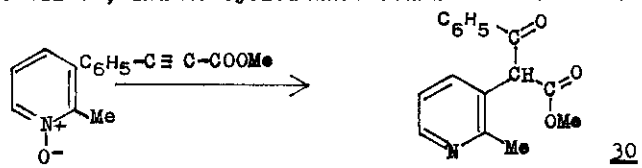
29

Abramovitch investigated reactions of quinoline N-oxides with activated acetylenes and compared the results with those for pyridine N-oxides[21-27].

When 4-chloroquinoline N-oxide was heated with ethyl phenylpropiolate in boiling toluene, the following products were formed[28]:

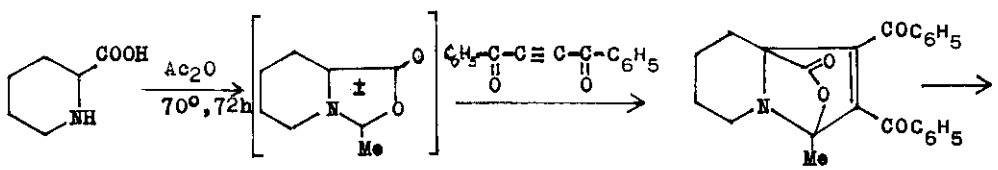


However, when α-picoline N-oxide reacted with methyl phenylpropiolate, only 30 was obtained, and no cycloadduct could be detected in the reaction mixture[29].



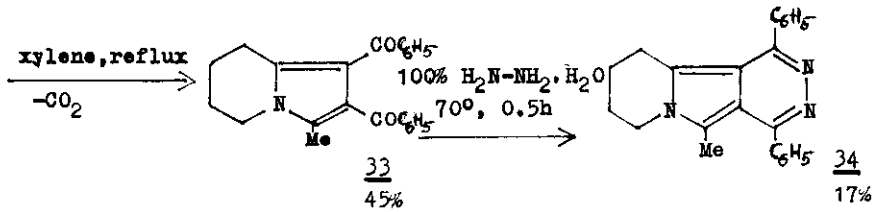
30

Uchida reported the reaction of 2-piperidinecarboxylic acid and dibenzoylacetylene in the presence of Ac_2O, producing via the 1,3-dipolar intermediate 31 the N-bridged lactone 32, and 33. The thermal decomposition of 32 yielded 33, which upon treatment with hydrazine hydrate gave tetrahydropyridazinoindolizine 34. In a similar way reacted other dipolarophiles such as DMAD, p-benzoquinone, 1,4-naphthoquinone etc. The above reaction provides a useful route to indolizines[30].



31

32
10%

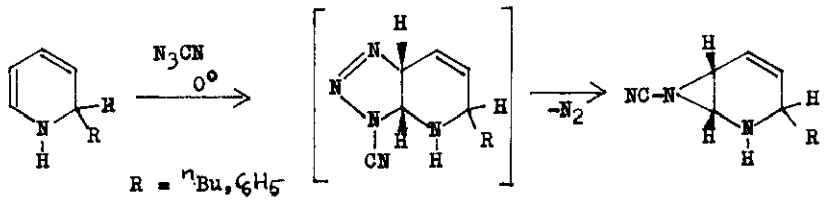


33 45%

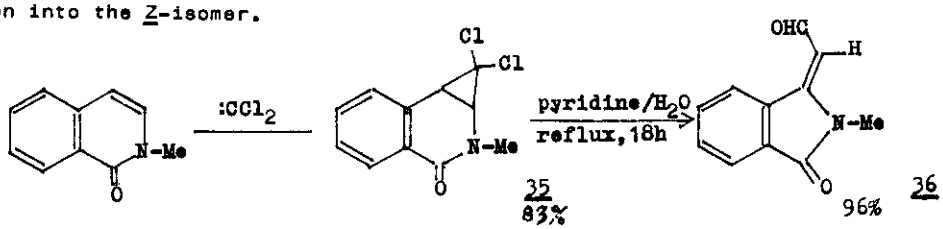
34 17%

Among reactions which do not proceed at the N atom, the following ones can be mentioned.

1,3-Dipolar cycloaddition of 1,2-dihydropyridines with cyanogen azide affords diazabicyclohept-4-enes[31]:



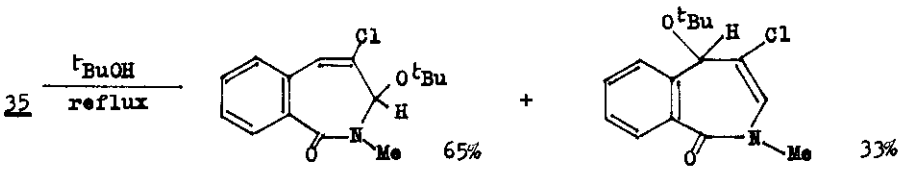
N-Methylisoquinolone reacts with dichlorocarbene to give 1:1 adduct 35, which refluxed in pyridine/H_2O yielded exclusively E-3-formylmethine-2-methylisoindolinone 36.[32-34] The E stereochemistry was established by its photochemical transformation into the Z-isomer.



35 83%

96% 36

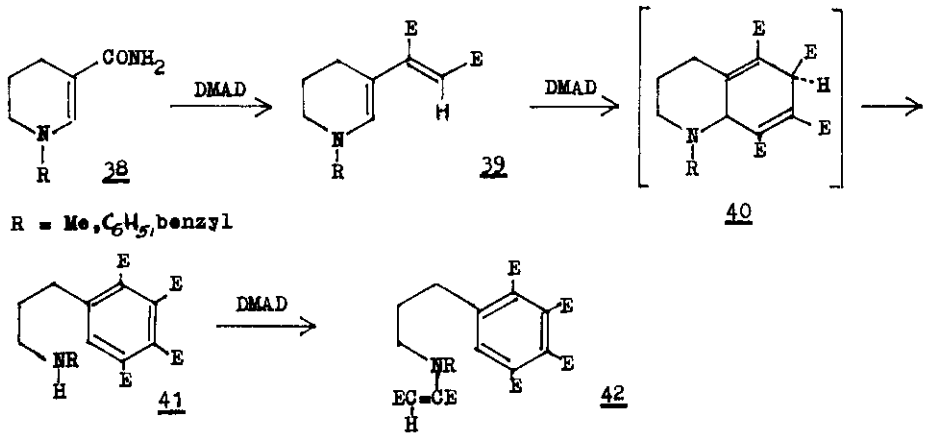
The adduct 35 upon treatment with alcohols yielded 2-benzazepinone derivatives, e.g.:



65% 33%

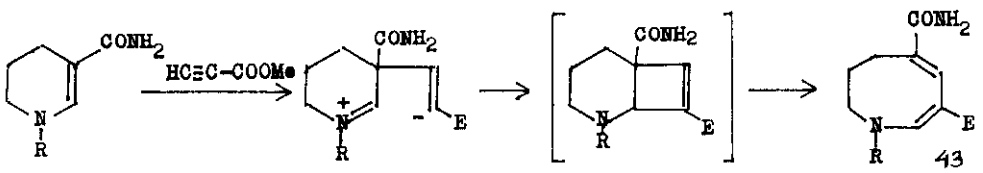
Acheson et al. investigated cycloadditions of dihydropyridines[35]. These compounds can behave as dienes or as enamines; reacting with DMAD they afford 1,2-dihydroazocines, cyclobutapyridines and benzene derivatives[36,37].

Some N-substituted tetrahydronicotinamides 38 yield with DMAD 39 /Z-isomers/ via the carboxamide elimination. 39 undergoes subsequent cycloaddition to DMAD forming the intermediate 40, which aromatizes into 41. This undergoes Michael-type addition with DMAD to give 42.[35]



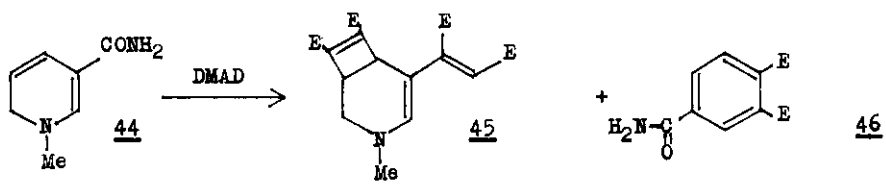
R = Me, C_6H_5, benzyl

On the other hand, with methyl propiolate the electrophilic attack at C-3 takes place, no carboxamide elimination occurs and the reaction results in tetrahydroazocine 43, thus providing a new route to this class of heterocycles[35]:

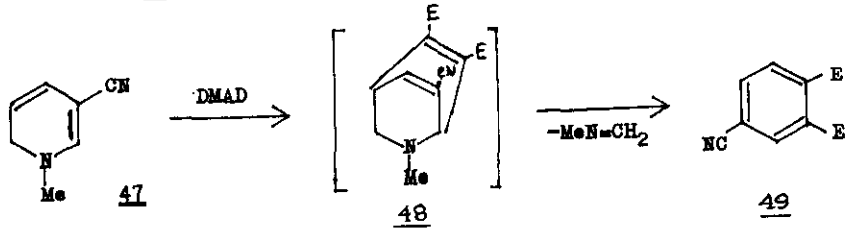


Some 1,2-dihydropyridines behave as enamines, in the reaction with DMAD they yield primary cyclobuta[b]pyridines, which ring ppen to give azocines[36,37], while a number of 1,4-dihydropyridines afford stable cyclobuta[b]pyridines, which do not ring open[38-40].

44 upon treatment with DMAD yields 45 together with 46. The reaction may be explained by vinylogous enaminic character of 3,4 double bond of 44; the four-membered ring is formed, and subsequent electrophilic attack by another acetylene molecule at position 5, followed by amide elimination leads to 45[41].
A successive Diels-Alder addition and retrogression gives rise to the dimethyl phthalate derivative 46[41].

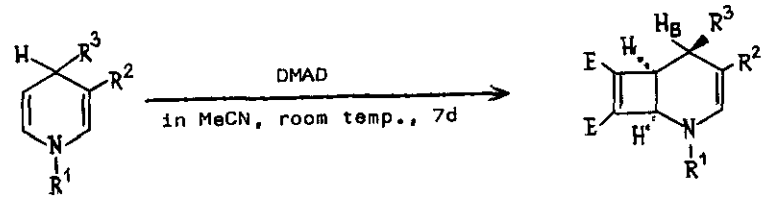


The reaction of 47 with DMAD proceeds as follows:[41]



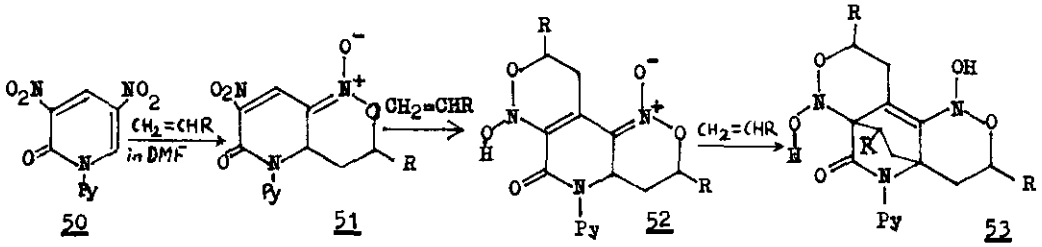
47 48 49

The reaction of 1,4-dihydropyridines with DMAD gives rise to cyclobutapyridines, e.g.[38]:



	a	b
R_1	CH_2-C_6H_5	$CH_2C_6H_5$
R^2	CO-N/C_6H_5/Et	CN
R^3	H_A	H_A
	32%	52%

Matsumura reported the reaction of an electron deficient 50 with electron rich olefins. The reaction yields first a 1:1 molar adduct 51, which in the subsequent cycloaddition reaction affords 1:2 and 1:3 molar cycloadducts 52 and 53, resp.:[42]

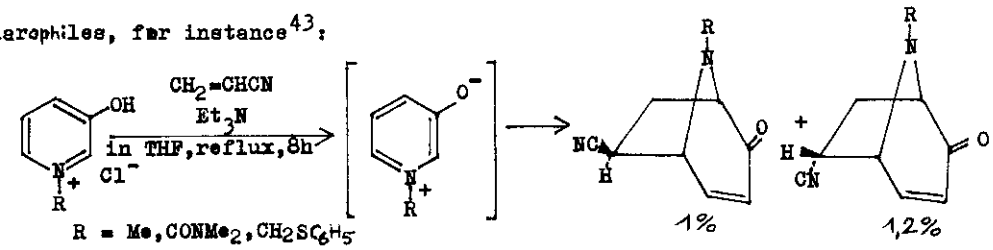


50 51 52 53

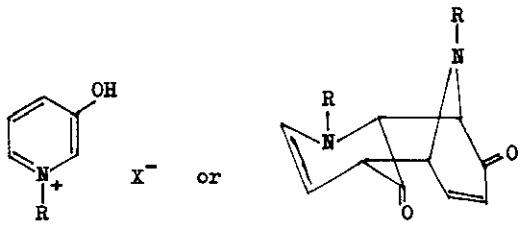
Py = 2-pyridyl; R = p-MeO-C_6H_4

1,3-Dipolar cycloadditions of six-membered heteroaromatic betaines are a useful route for synthesis of heterocyclic compounds. Katritzky describes the cycloaddition reactions of N-substituted 3-hydroxypyridinium betaines to various dipo-

larophiles, for instance[43]:



1,3-Cycloaddition reactions of 1-heteroaryl-3-hydroxypyridinium betaines 56 with allyl alcohol resulted in tricyclic products 57. The starting betaines were generated in situ either from their salts 54 or from their dimers 55[44].

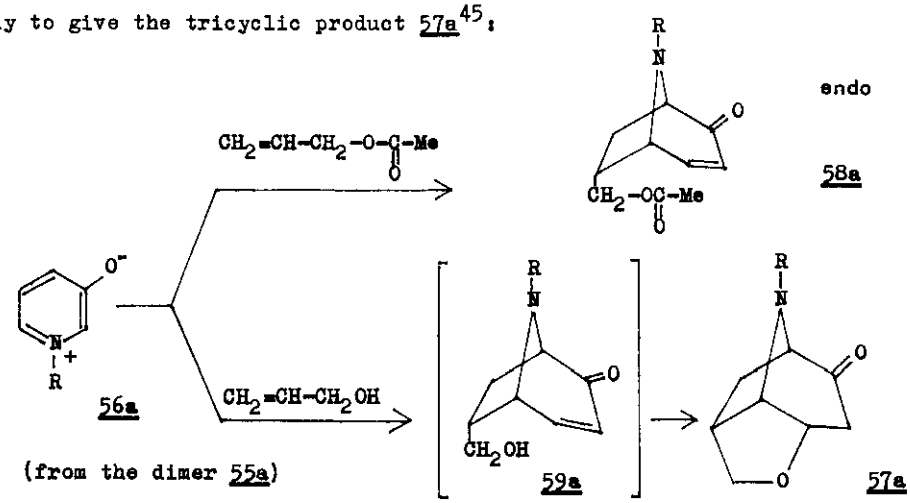


54 55

a b

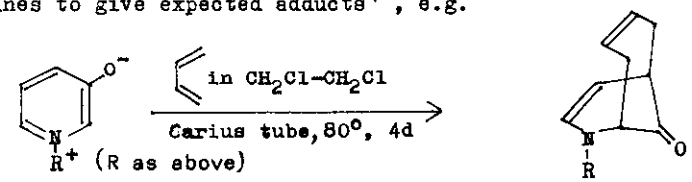
R = 5-NO_2-2-pyridyl , 4,6-Me_2-pyrimidin-2-yl

Pyridinium betaine 56a yields with allyl acetate the normal endo-cycloadduct 58a, while in the case of allyl alcohol the intermediate 59a cyclizes spontaneously to give the tricyclic product 57a[45]:



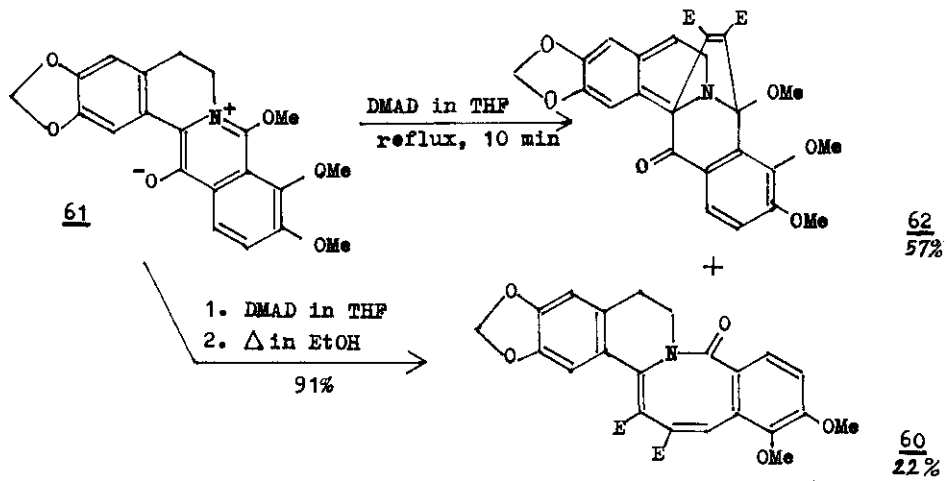
Reactions with other dipolarophiles, such as 2- and 4-vinylpyridines, vinyl acetate, ethyl phenylpropiolate, are described[44].

In the case of butadiene, the reaction proceeds across the 2,4 positions of betaines to give expected adducts[46], e.g.



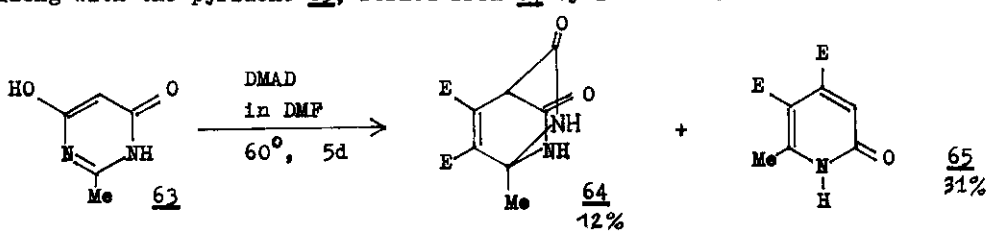
The kinetic rates, as well as the regio- amd stereoselectivity of the reactions of 1-substituted 3-hydroxypyridinium betaines have been correlated by FMO theory by Katritzky et al.[47]

Another example of 1,3-dipolar cycloaddition of heteroaromatic betaines is a simple synthesis of a new heterocyclic system 60, which was reported by Hanaoka et al.[48] 8-Methoxyberberine phenol-betaine 61 reacts with DMAD to give the cycloadduct 62 together with the azocine 60.



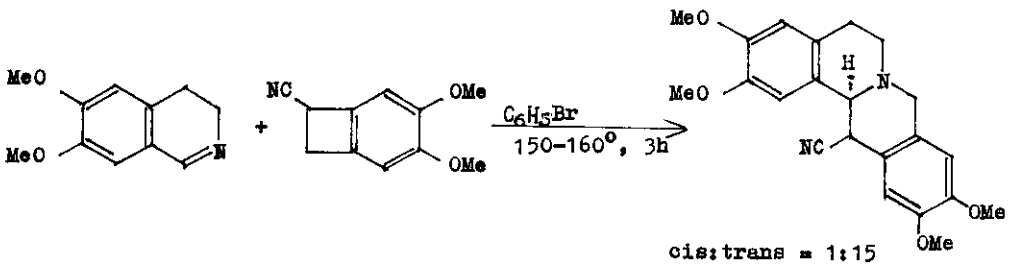
Using unsymmetrical acetylenes, the reverse regioselectivity of reaction, contrary to the general regiospecifity of cycloadditions of heteroaromatic betaines[49,50], was found, e.g. in the reaction with methyl propiolate.[48]

Davies et al. studied the cycloadditions across the pyrimidine nucleus. 4,6-Dihydroxy-2-methylpyrimidine 63 upon treatment with DMAD gave the adduct 64 along with the pyridone 65, formed from 64 by a retro Diels-Alder reaction:[51]



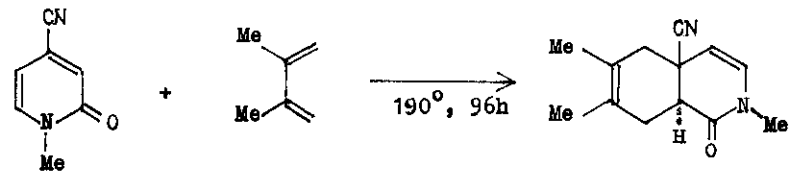
Diels-Alder reactions

Numerous examples of Diels-Alder reactions of piridines are known.[8] Among the large number of cycloadditions examined by Kametani et al.[52-54] the following reaction was performed[55]:



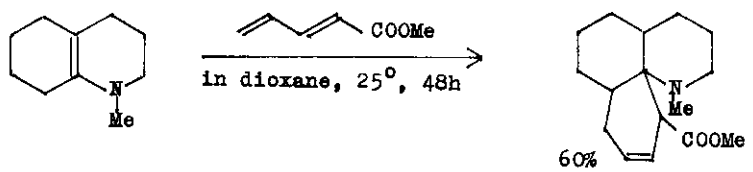
cis:trans = 1:15

Kato described the Diels-Alder reaction providing a convenient route for isoquinolines:[56]



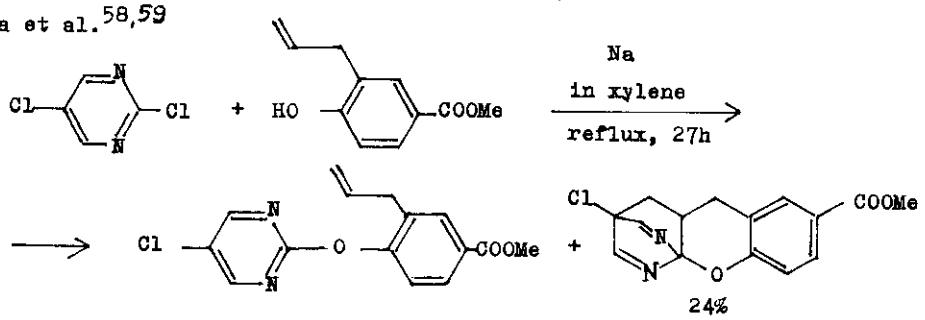
7.5%

The following cycloaddition reaction was reported by Schumann and Vidic[57]:



60%

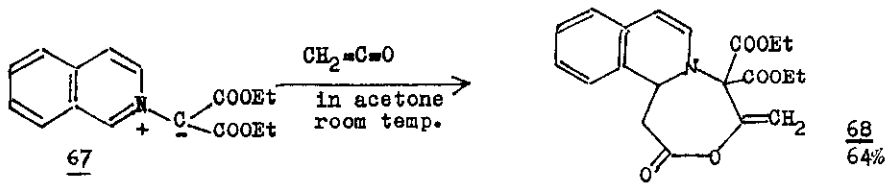
Intramolecular cycloaddition of 2(2-allylphenoxy)pyrimidines was reported by Jojima et al.[58,59]



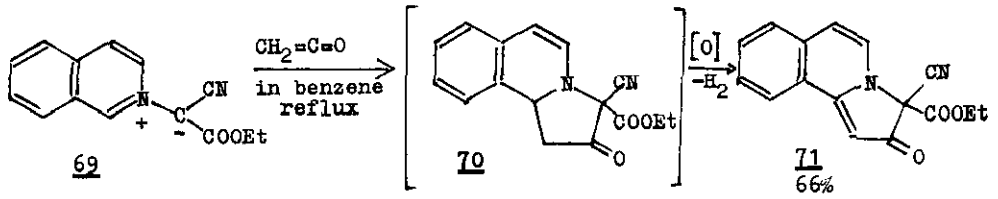
24%

2. Cycloadditions of pyridinium N-methylides

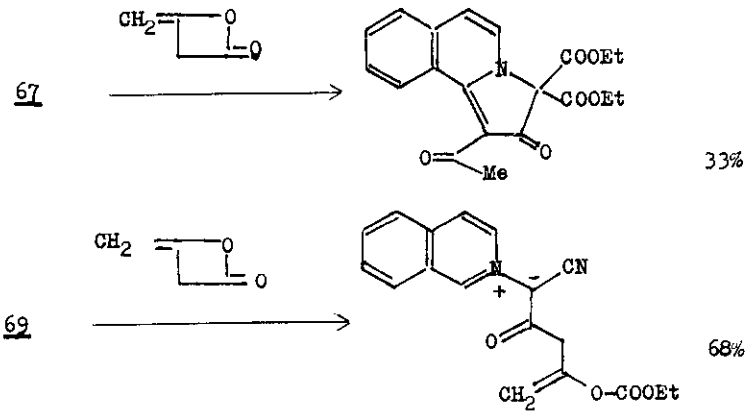
Kato et al. reported the reaction of N-methylide 67 with ketene giving rise to 1:2 molar cycloadduct 68[60]



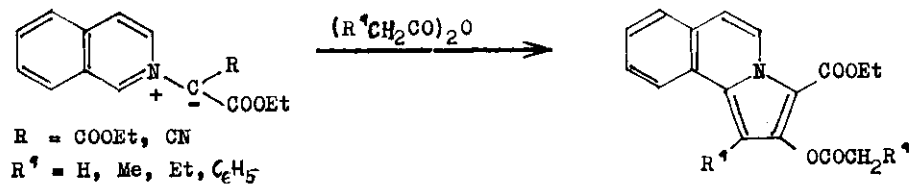
Similar reaction of N-methylide 69 gives the cycloadduct 70 as an intermediate, readily oxidized to 71[60-62]



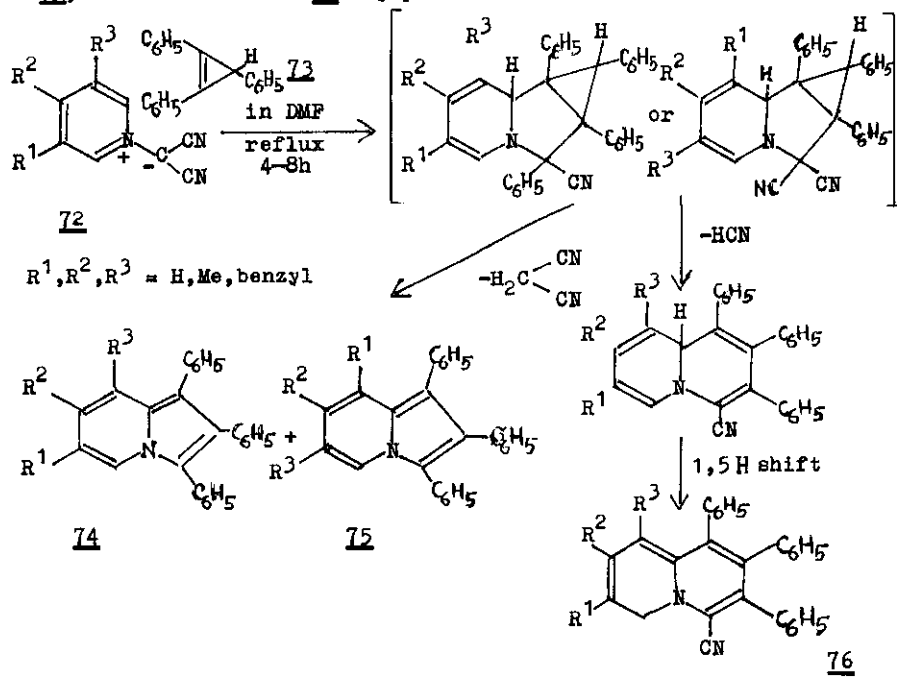
The reactions with diketene proceed in the following way[63]:



Isoquinolinium N-methylides react with acid anhydrides to give pyrroloisoquinolines[64]:

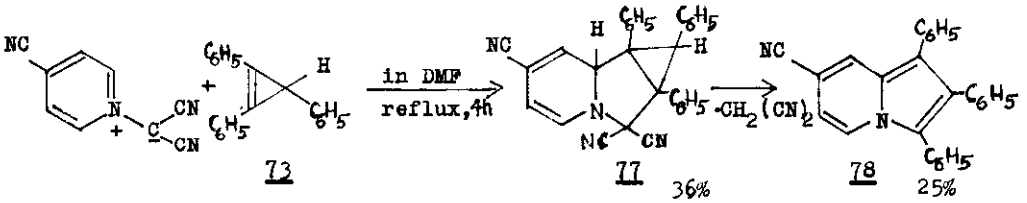


The 1,3-cycloaddition of pyridinium dicyano-N-methylides 72 with triphenylcyclopropene 73 was described by Matsumoto et al.[65] The corresponding 1,2,3-triphenylindolizines 74 and 75 are produced; however, depending on the structures of 72, the formation of 76 may predominate:

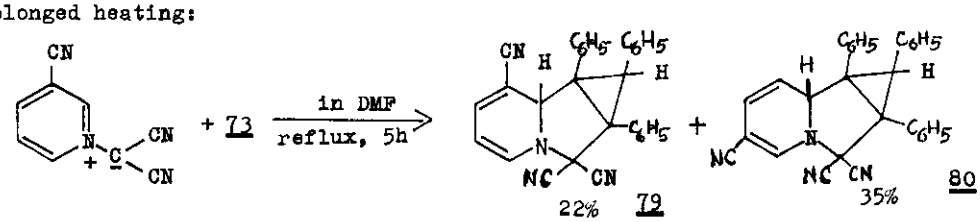


Similar reactions were carried out on isoquinolines[65].

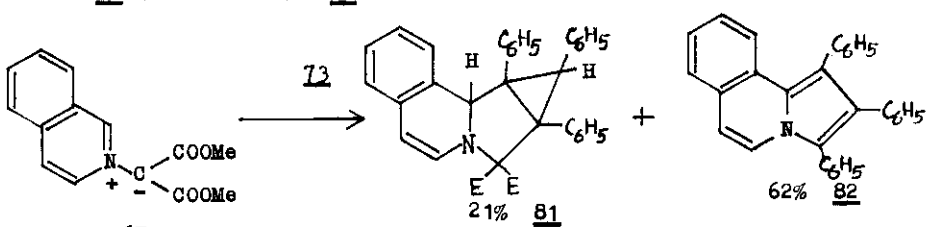
Indolizines and quinolizines are obtained in the cycloaddition reaction of cyclopropenes to 1,3-dipoles and the subsequent opening of the three-membered ring of the primary adducts. So far, little is known on the isolation of the primary adducts; Matsumoto and Uchida[66] studied the reaction of 4-cyanopiridinium dicyano-N-methylide with triphenylcyclopropene 73, giving rise to 1:1 adduct 77 and indolizine 78:



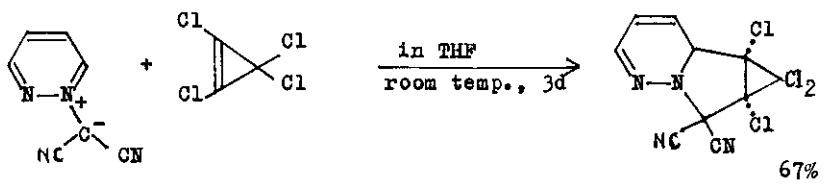
3-Cyanopyridinium dicyano-N-methylide reacts with 73 under the same conditions to give the isomeric adducts 79 and 80; no indolizine was formed even upon prolonged heating:



Reaction of isoquinolinium bis(methoxycarbonyl)methylide with 73 afforded 1:1 adduct 81 and indolizine 82[66]

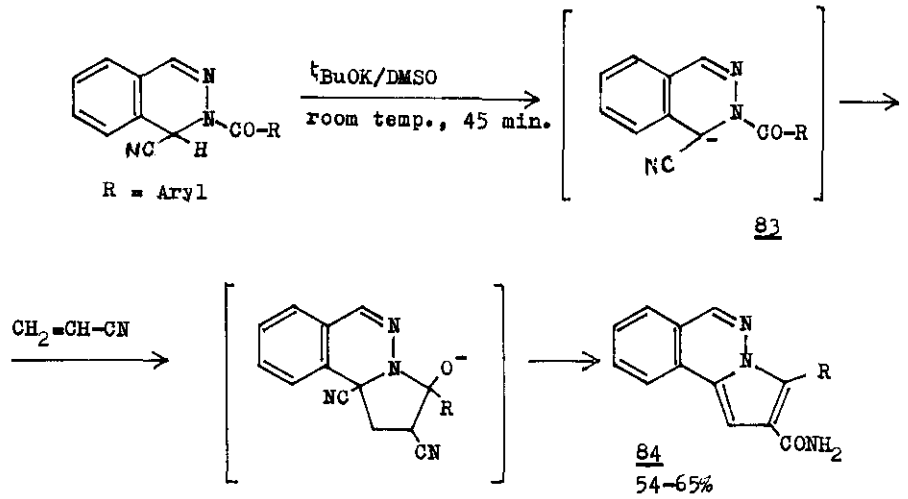


Ohsawa et al.[67] in the investigations of primary tricyclic adducts of this type examined the 1,3-dipolar cycloaddition of pyridazinium N-ylides with tetrahalocycloalkenes, for instance:



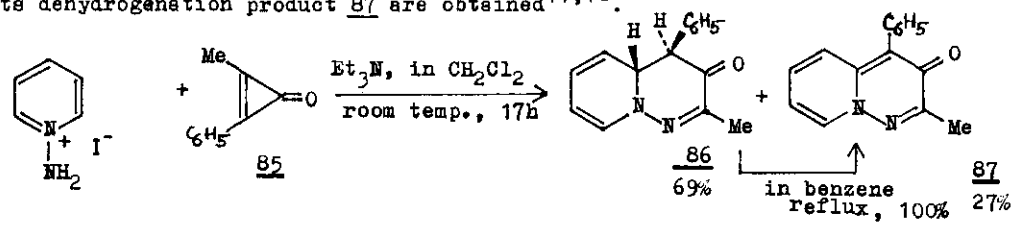
When cyclopropenones react with pyridinium N-ylides, the primary tricyclic adducts are unstable and bicyclic products are formed.[65,68,69]

The phthalazine Reissert compounds upon treatment with potassium butoxide in DMSO afford carbanion 83, which adds acrylonitrile to give 84[70]:



3. Cycloadditions of pyridinium N-imino-ylides

In the reaction with cyclopropenones, pyridinium N-imines act often as nucleophiles, [71-73] however 1,3-dipolar cycloadditions of these compounds were also observed[68, 74-76]. Kascheres et al.[77] described the reactions of pyridinium N-imines with methylphenylcyclopropenone and dipropylcyclopropenone. In the reaction of pyridinium N-imine iodide with 85, the 1:1 adduct 86 and its dehydrogenation product 87 are obtained[77,78].

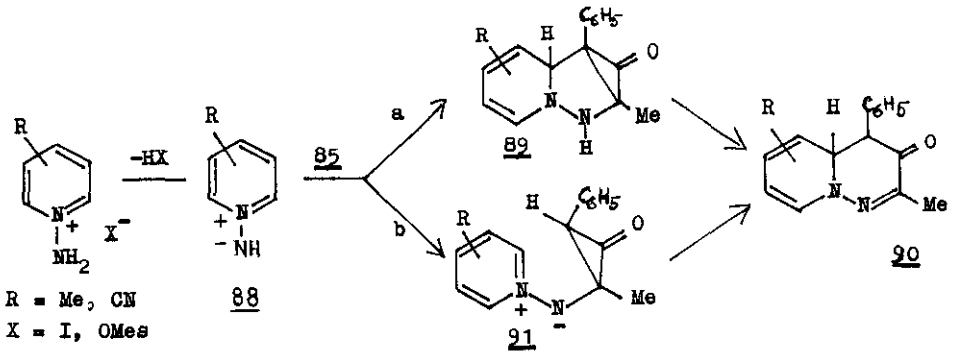


Reactions of substituted pyridinium N-imine salts proceed in a similar way.

Possible pathways of the above reactions are:

Path a involves initial 1,3-dipolar cycleaddition of pyridinium N-imine 88 to 85 resulting in 89, followed by opening of the cyclopropanone ring, with transfer of the amino hydrogen to give 90.

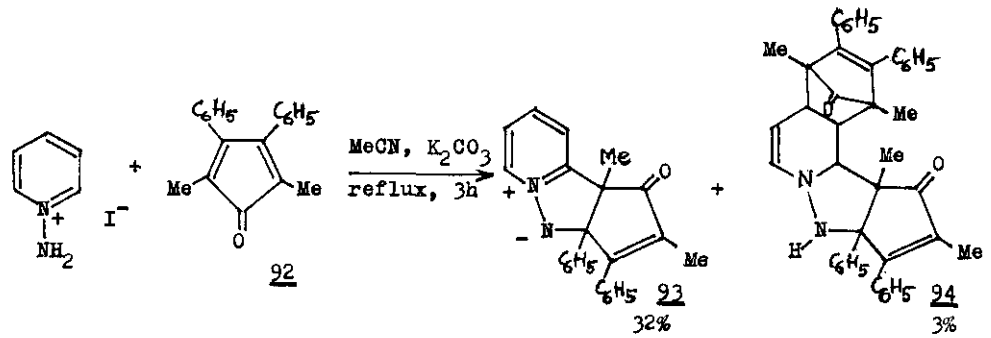
An alternative path b involves nucleophilic addition of 88 to 85 with hydrogen transfer, followed by intramolecular 1,5-dipolar cyclization of 91[77].



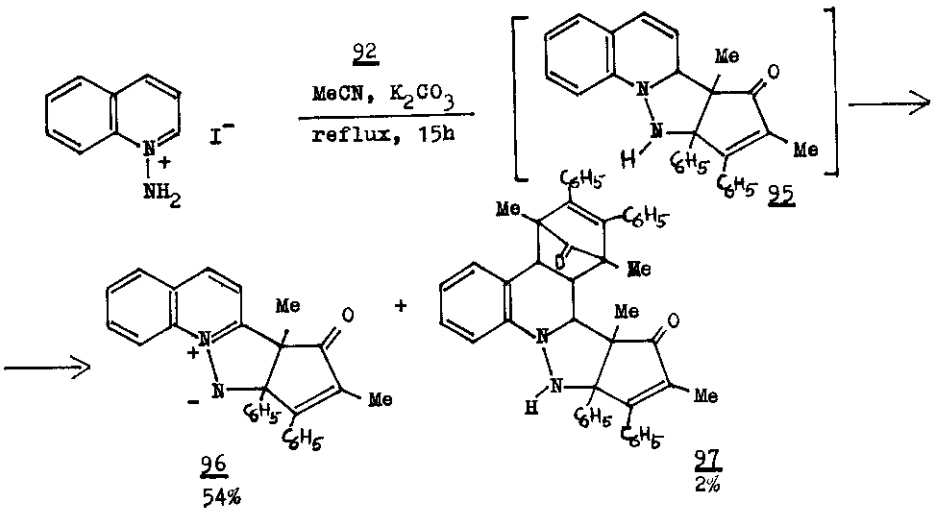
R = Me, CN
X = I, OMes

Although the isolated dihydrointermediate 86 is trans, initial formation of a cis-dihydrointermediate cannot be ruled out, as under the basic conditions utilized, the isomerization might be expected. For this reason the stereochemistry in 90 is not specified.

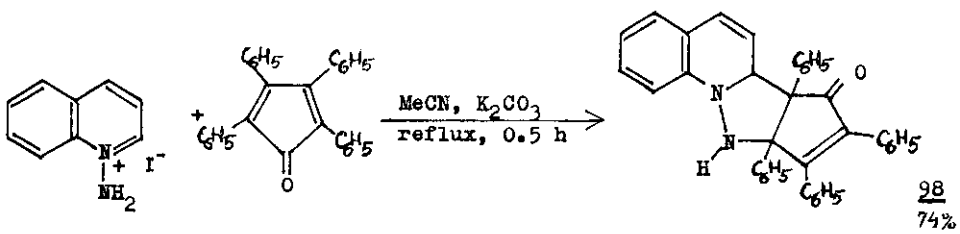
Yamashita and Masumura reported the reaction of pyridinium N-imine iodide with 2,5-dimethyl-3,4-diphenylcyclopentadienone 92, yielding the ylide 93 together with the 1:2 adduct 94[79]:



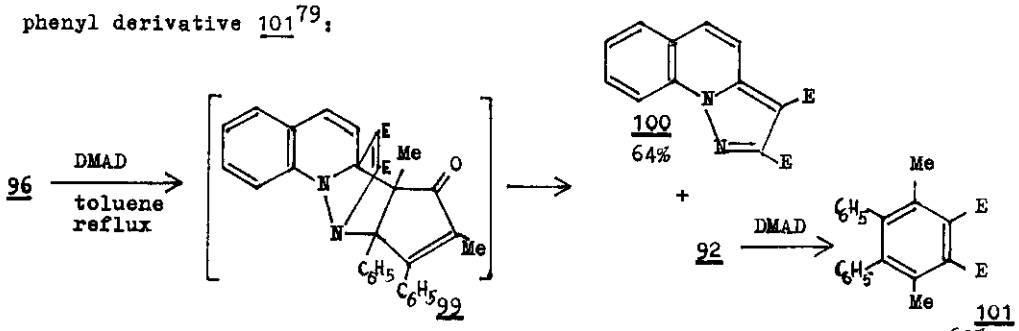
A similar reaction carried out on quinolinium N-imine iodide gave a dehydrogenation product 96 of an unisolable 1:1 adduct 95, along with the 1:2 adduct 97, providing from the Diels-Alder reaction of 95 with 92:



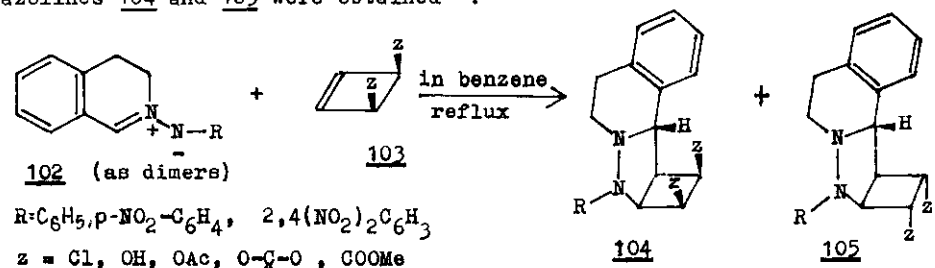
However, in the reaction with tetracyclone, the 1:1 adduct 98 could be isolated:



Ylides 93 and 96 are interesting examples of stable pyridinium and quinolinium N-imino-ylides, their stability being probably due to the construction in a five-membered ring, as well as to the presence of bulky substituents. Ylide 96 treated with DMAD yields 1:1 adduct 99, which in the retro 1,3-dipolar cycloaddition gives 100 and 92, affording with excess of DMAD the o-terphenyl derivative 101[79]:



The syn-anti isomerism of azomethine imines and azomethine oxides reactions with cis-3,4-disubstituted cyclobutanes was examined. In reaction of dimers of 102 and cyclobutenes 103 in boiling benzene, the exo-syn and exo-anti pyrazolines 104 and 105 were obtained[80]:



102 (as dimers) 103 104 105

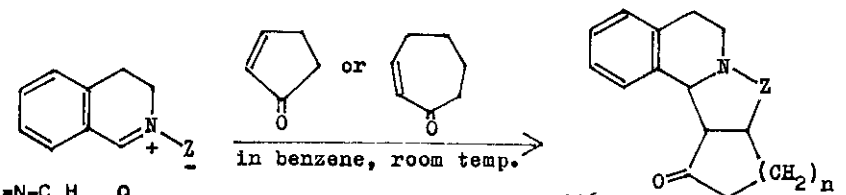
R=C_6H_5, p-NO_2-C_6H_4, 2,4$(NO_2)_2C_6H_3$

z = Cl, OH, OAc, O-C(=O)-O, COOMe

The exo-syn adducts 104 were characterized by tlc, their R_F being smaller than that of corresponding exo-anti adducts 105, syn-compounds posessing a larger dipole moment[81]. No endo adducts were detected.

Gandolfi et al.[82] studied 1,3-dipolar cycloreversions of isoxazolidines and pyrazolidines, these reactions being much less investigated than 1,3-cycloadditions. Cycloreversion reactions of isoxazolidines were reported by Bianchi[83] and Joucla[84], and only one example of cycloreversion of pyrazolidines by Burger[85].

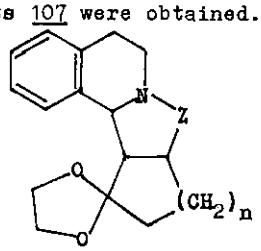
The adducts 106 to be cycloreversed were obtained in the reaction of 3,4-dihydroisoquinolinium ylides with cyclopent-2-enone and cyclohept-2-enone[82]:



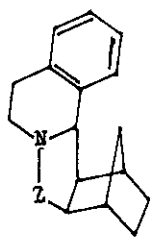
Z=N-C_6H_5, O

106 n = 1 or 3

In an analogous manner, using ketals of the above α,β-unsaturated ketones, the adducts 107 were obtained.



107

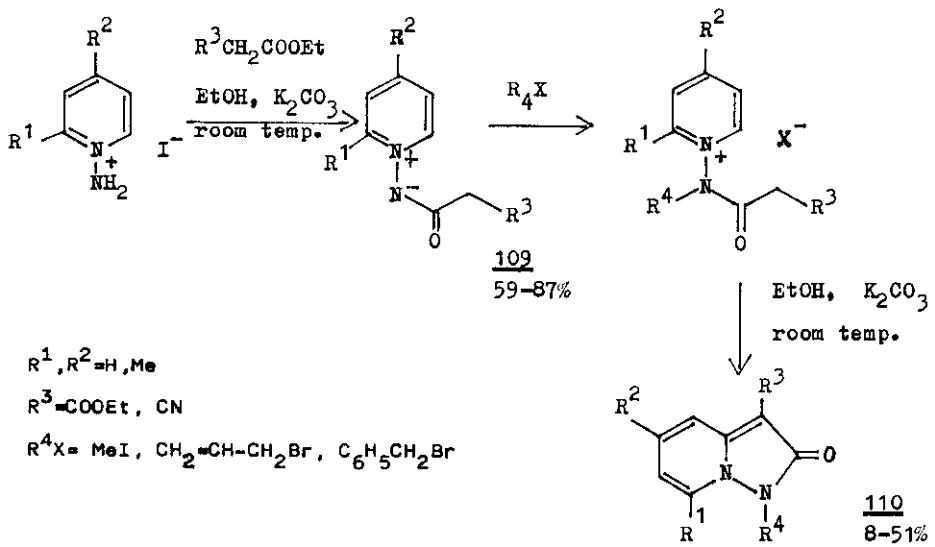


108

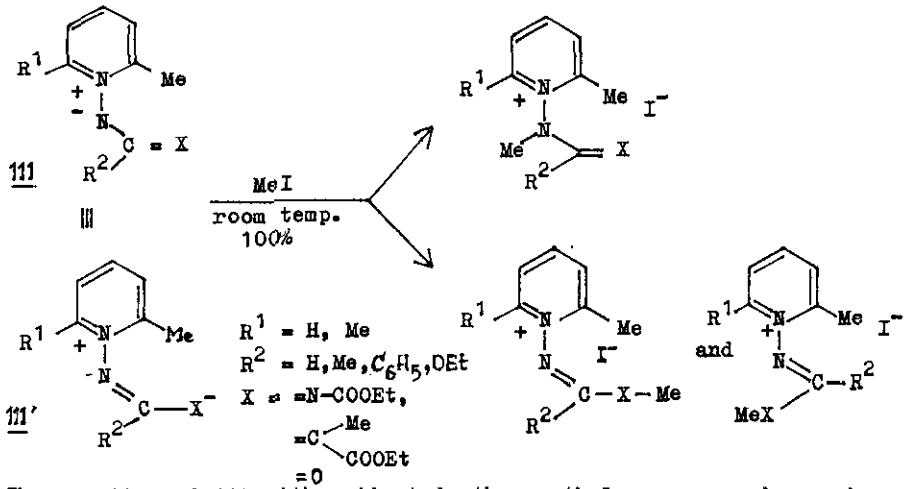
Cycloreversion reactions were carried out using norbornene as a 1,3-dipole scavenger. Cycloadducts 106 and 107 heated with norbornene in benzene gave adducts of the type 108.

The easier fragmentation of the adducts with α,β-unsaturated ketones as compared with that of the corresponding ketals can be explained on the basis of conjugation gain in the cycloreversion transition state of the former compounds.

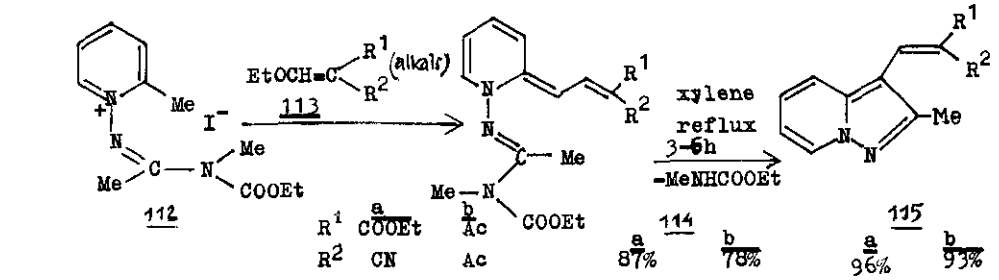
Kakehi et al.[86] described the reaction of substituted pyridinium N-imines with diethyl malonate and ethyl cyanoacetate yielding pyridinium N-imino-ylides 109. These quaternize readily to give pyridinium salts, which with potassium carbonate undergo cyclization resulting in 110:



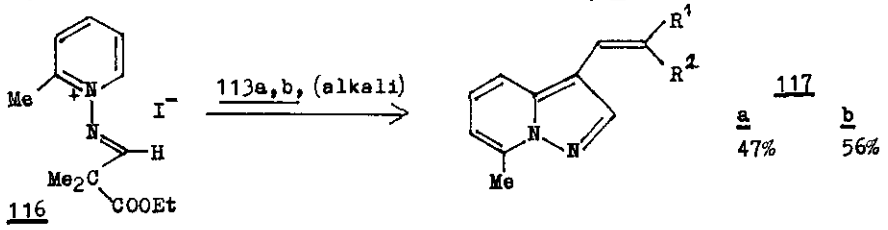
2-Picolinium N-imino-ylides (acting as 1,3-dipoles 111 or as 1,5-dipoles 111′) were methylated with MeI to give the corresponding 2-picolinium salts[87] used in cycloaddition reactions.



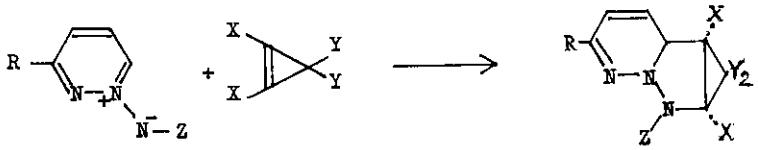
The reaction of 112 with activated ethoxymethylene compounds, such as 113, in the presence of alkali gave the expected 2-allylidene-1,2-dihydropyridine derivative 114, which heated in xylene afforded 115, along with ethyl N-methylcarbamate:



On the other hand, 116 with the same reagents did not yield allylidene derivatives, but was converted into pyrazolopyridines 117[87]:

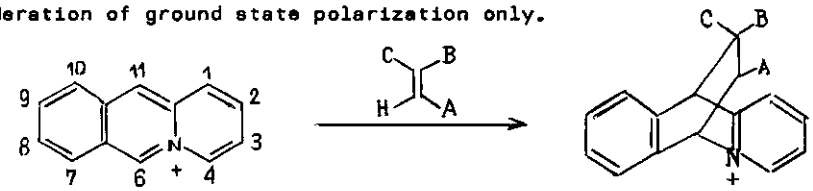


Ohsawa et al. examined the reaction of pyridazinium N-imino-ylides with tetrahalocycloalkenes affording primary tricyclic adducts[67,91,92]:

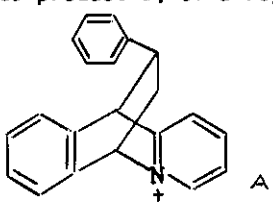


R = H, C_6H_5, OEt ; Z = Ac, COC_6H_5, COOEt
X = Y = Cl X = Y = Br X = Br Y = F

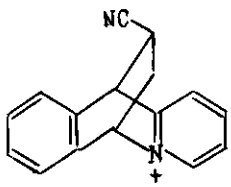
Westerman and Bradsher examined regiochemistry of polar cycloadditions studying the reactions of acridizinium ion with unsymmetrical alkenes.[94,95] Polar cycloadditions show a remarkable stereospecifity.[96-99] For alkenes with electron-withdrawing groups, the regiochemistry of addition cannot be predicted by consideration of ground state polarization only.



The alkenes used were styrene, indene, acrylonitrile etc. In the addition with styrene, its β carbon atom becomes bonded to the electrophilic center of the acridizinium ion, as it can be predicted from the rules of electrophilic addition, and the product A is formed. However, the reaction with acrylonitrile affords product B, of a regiochemistry opposite to that predicted.



A



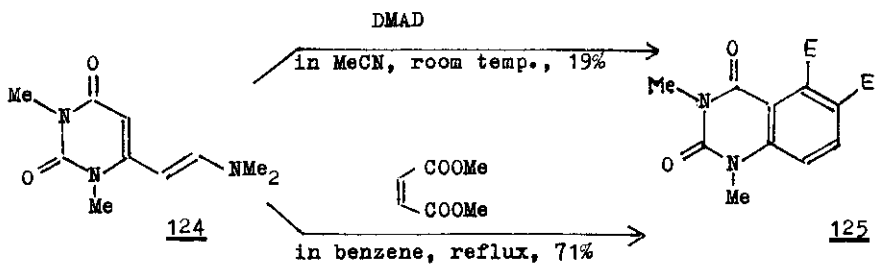
B

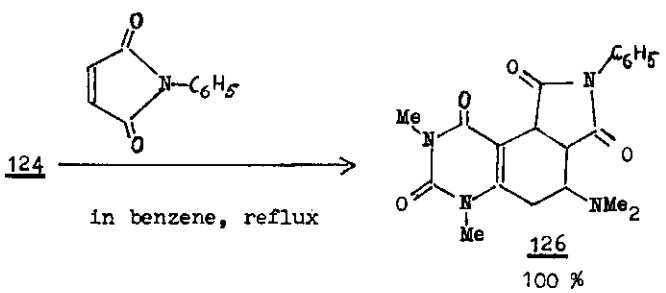
According to the theory of Houk,[100] in such cases of anomalous regiochemistry, the frontier orbital theory ought to be used to rationalize the orientation. In the above reaction the β carbon atom with the largest HOMO coefficient of the acrylonitrile should become bonded to the 6 position of the acridizinium ion, where the LUMO coefficient is the largest.

In polar cycloadditions two stages are involved, the first being an interaction of HOMO of the donor with LUMO of the acceptor, the initial interaction

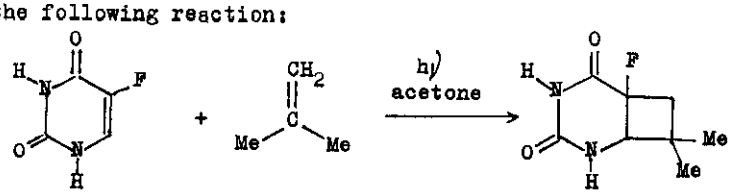
being in the nature of a charge-transfer complex formation. The great regioselectivity, which distinguishes cationic polar cycloadditions from other types of cycloaddition with inverse electron demand is due to the fact that cations have a strong tendency towards the formation of charge-transfer complexes.[101]

Other examples of cycloadditions of acridizinium ion are given by Fields[102]. Vinyluracil 124 is a reactive heterocyclic diene in the Diels-Alder reactions, giving rise to quinazoline-5- and-6-carboxylic acids. Senda et al.[103] reported the reaction of 124 with DMAD, dimethyl maleate or dimethyl fumarate, resulting in quinazolinedione 125. Similar reaction of 124 with N-phenylmaleimide gave the 1:1 adduct 126.

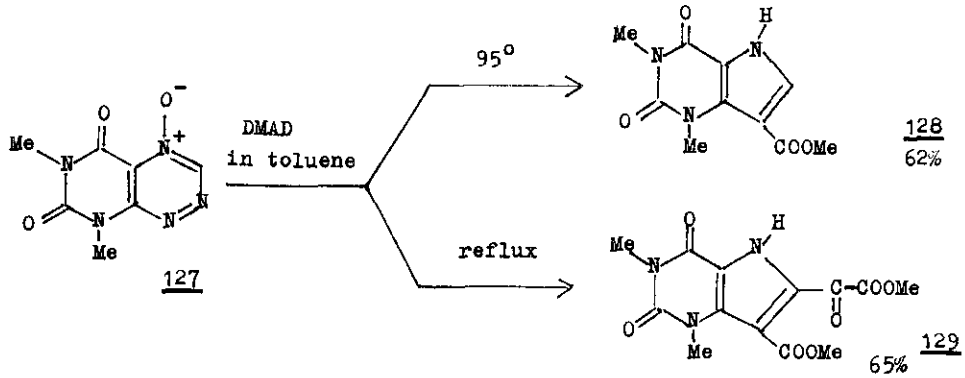




In the photocycloaddition of uracil with olefins, the substitution of 5H for F remarkably enhances the regioselectivity[104]. Greenlee et al.[105,106-108] reported the following reaction:

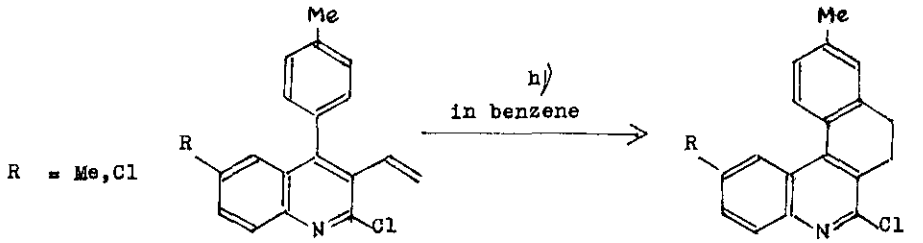


The 1,3-dipolar cycloaddition reactions of fervenulin-4-oxide, as well as of its 3-alkyl derivatives were investigated by Senga et al.[109]. The reaction of 127 with DMAD in toluene at 95° afforded pyrrolo[3,2d]pyrimidine 128, while in refluxing toluene the unexpected pyrrolo[3,2d]pyrimidine 129 was formed.

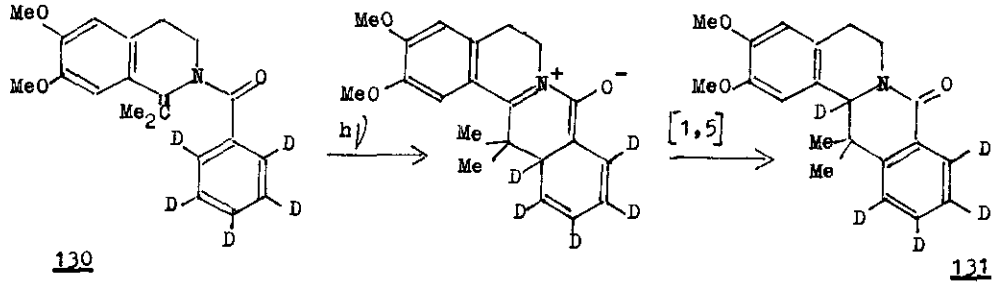


Similar reactions were carried out with methyl propiolate and ethyl phenylpropiolate[109].

Photocyclization being a useful method in organic synthesis, some examples of this reaction should be included here. Thus, Veeramani et al.[110] reported reactions of 3-vinyl-4-phenylquinolines, for instance:

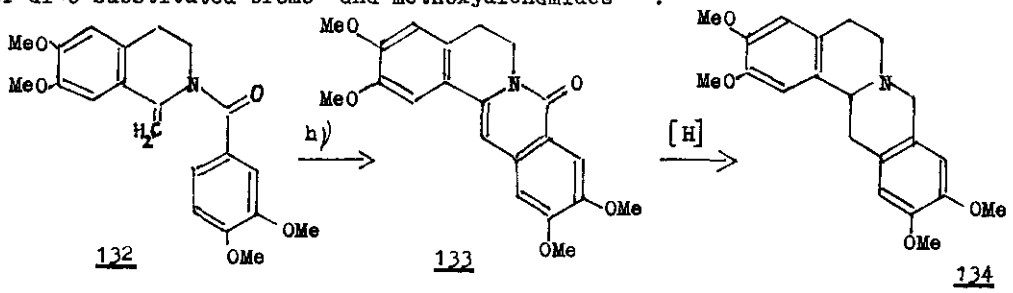


Lenz showed, that in the irradiation of the compound 130, containing a perdeuteriobenzoyl group an o-deuteron was transferred in a [1,5]-shift with the formation of 131[6,111]:

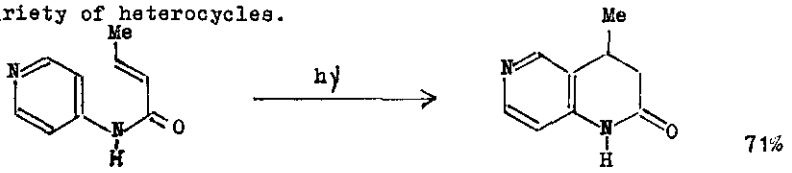


Numerous examples of this type of photocyclization involving [1,5]-group migrations were described by Ninomiya et al.[112]

Kametani et al. studied conversion of 132 via the oxyprotoberberine 133 to naturally occuring dl-xylopinine 134[113], as well as investigated reactions of di-o-substituted bromo- and methoxydienamides[114].



The following conversion, described by Ogata et al.[115], where pyridine ring can be replaced by other heterocyclic systems can serve as useful synthetic route to a variety of heterocycles.



REFERENCES

1. E.C. Taylor and I.J. Turchi, Chem.Rev., 1979, 79, 181.
2. T.Uchida and K. Matsumoto, Synth., 1976, 209.
3. W. Oppolzer, Angew.Chem., 1977, 89, 10.
4. K.N. Houk, Topics in Curr.Chem., 1979, 79, 1.
5. N. Dennis, A.N. Katritzky and Y. Takeuchi, Angew.Chem., 1976, 88, 41.
6. G.R. Lenz, Synth., 1978, 489.
7. V. Šimánek and V. Preininger, Heterocycles, 1977, 6, 475.
8. S.M. Weinreb and J.I.Levin, Heterocycles, 1979, 12, 949.
9. W. Śliwa and H. Zamarlik, Heterocycles, 1979, 12, 529.
10. K. Burger, K. Einhellig, W.D. Roth and E. Daltrozzo, Chem.Ber., 1977, 110, 605.
11. K. Burger and W.D. Roth, Synth., 1975, 731.
12. M. Kurabayashi and Ch. Grundmann, Bull.Chem.Soc.Jap., 1978, 51, 1484.
13. R.M.Acheson and G. Procter, J.C.S.Perkin I, 1979, 2171; R.M.Acheson and N.F.Elmore, Adv.Het.Chem., vol.23, Acad.Press 1978, 263
14. R.M.Acheson, J.D.Wallis and J. Wooland, J.C.S.Perkin I, 1979, 584.
15. R.M.Acheson and R. Flowerday, J.C.S.Perkin I, 1975, 394; R.M. Acheson, G.Procter and S.R. Critchley, Chem.Comm., 1976, 692.
16. M. Sakamoto, K. Miyazawa, K.Kuwabara and Y. Tomimatsu, Heterocycles, 1979, 12, 231.
17. J. Bödeker and K. Courault, Tetr., 1978, 34, 101.
18. T.Kato and S.Masuda, Chem.Pharm.Bull., 1975, 23, 2251
19. C.N. Filer, F.F. Granchelli, P. Perri and J.L. Neumeyer, J.Org.Chem., 1979, 44, 285.
20. M. Yoshida, Y. Ishiguro, T. Yamamori, M. Aoyama, T. Endo, H. Noda, R. Funakoshi, S. Saeki and M. Hamana, 11th Congress of Heterocyclic Chemistry, Kanazawa, Japan 1978, Heterocycles, 1979, 12, 167; M.Hamana, private information.
21. R.A. Abramovitch, Heterocyclic Chem. Symposium, 29th Southeastern ACS Meeting, Tampa, Florida, 1977, Plenary Lecture No.1.
22. R.A. Abramovitch and J. Shinkai, J.Amer.Chem.Soc., 1974, 96, 5265.
23. R.A. Abramovitch and J. Shinkai, J.Amer.Chem.Soc., 1975, 97, 3227.
24. R.A. Abramovitch and J. Shinkai, Chem. Comm., 1973, 569.
25. R.A. Abramovitch, G. Grims, R.B. Rogers and J. Shinkai, J.Amer.Chem.Soc., 1976, 98, 5671.

26. S. Takahashi and H. Kano, J.Org.Chem., 1965, 30, 1118.
27. S.R. Challand, S.F. Gait, M.J. Rance and C.W. Rees, J.C.S.Perkin I, 1975, 26.
28. P. Canonne, G. Lemay and R.S. Abramovitch, Heterocycles, 1978, 9, 1217.
29. G.S.S. Murthi and S.K. Gangopadhyay, Indian J.Chem., 1979, 17B, 20.
30. T. Uchida, S. Tsubokawa, K, Harihara and K. Matsumoto, J.Het.Chem., 1978, 15, 1303.
31. T.A. Ondrus, E.E. Knaus and C.S. Giam, J.Het.Chem., 1979, 16, 409.
32. H.A. Soetens and U.K. Pandit, Heterocycles, 1978, 11, Spec., 75.
33. W. Flitch and H. Peters, Chem.Ber., 1970, 103, 805.
34. A. Marsili, V. Scartoni, I. Morelli and P. Pierangeli, J.C.S.Perkin I, 1977, 959.
35. R.M. Acheson and G. Paglietti, Heterocycles, 1979, 12, 695.
36. R.M. Acheson, G. Paglietti and P.A. Tasker, J.C.S.Perkin I, 1974, 2496.
37. R.M. Acheson and G. Paglietti, Chem.Comm., 1973, 665.
38. R.M. Acheson, N.D. Wright and P.A. Tasker, J.C.S.Perkin I, 1972, 2918.
39. R.M. Acheson and G. Paglietti, J.C.S.Perkin I, 1976, 45.
40. P.G. Lehman, Tetr.Lett., 1972, 4863.
41. R.M. Acheson and G. Paglietti, J.C.S.Perkin I, 1979, 591.
42. E. Matsumura, M. Ariga and Y. Tohda, Heterocycles, 1979, 12, 160.
43. A.R. Katritzky, J. Banerji, A. Boonyarakvanich, A.T. Cutler, N. Dennis, S.Q.Abbas Rizvi, G.J. Sabongi and H. Wilde, J.C.S.Perkin I, 1979, 399.
44. A.R. Katritzky, N. Dennis, G.J. Sabongi and L. Turker, J.C.S.Perkin I, 1979, 1525.
45. N. Dennis, B. Ibrahim and A.R. Katritzky, J.C.S.Perkin I, 1976, 2296.
46. N. Dennis, A.R. Katritzky, G.J. Sabounji and L. Turker, J.C.S.Perkin I, 1977, 1930.
47. A.R. Katritzky, N. Dennis, M. Chaillet, Ch. Larrieu and M. El Mouhtadi, J.C.S.Perkin I, 1979, 408.
48. M. Hanaoka, A. Wada, S. Yasuda, C. Mukai and T. Imanishi, Heterocycles, 1979, 12, 511.
49. N. Dennis, A.R. Katritzky and Y. Takeuchi, Angew.Chem.,Intern.Ed.Engl., 1976, 15, 1.

50. N. Dennis, B. Ibrahim and A.R. Katritzky, J.C.S.Perkin I, 1976, 2307.
51. L.B. Davies, O.A. Leci, P.G. Sammes and R.A. Watt, J.C.S.Perkin I, 1978, 1293.
52. T. Kametani, T. Takahashi, K. Ogasawara and K. Fukumoto, Tetr., 1974, 30, 1047.
53. T. Kametani, Y. Katoh and K. Fukumoto, J.C.S.Perkin I, 1974, 1712.
54. T. Kametani, M. Kajiwara, T. Takahashi and K. Fukumoto, J.C.S.Perkin I, 1975, 737.
55. T. Kametani, T. Takahashi, T. Honda, K. Ogasawara and K. Fukumoto, J.Org.Chem., 1974, 39, 447.
56. H. Kato, R. Fujita, H. Hongo and H. Tomisawa, Heterocycles, 1979, 12, 1.
57. D. Schumann and H.J. Vidic, Tetr., 1971, 27, 4091.
58. T. Jojima, H. Takeshiba and T. Kinoto, Heterocycles, 1979, 12, 665.
59. H. Neunhoeffer and G. Werner, Ann., 1974, 1190.
60. T. Kato, T. Chiba, S. Tanaka and T. Sasaki, Heterocycles, 1978, 11, Spec., 227.
61. I. Zugravescu, M. Constantinescu, G. Surpateanu, A. Lablanche-Combier and L. Devos, Rev.Roum.Chim., 1978, 24, 1089.
62. G. Surpateanu, M. Constantinescu and I. Zugravescu, Rev.Roum.Chim., 1978, 23, 1449.
63. T. Kato, T. Chiba and S. Tanaka, J.Het.Chem., 1976, 13, 461.
64. T. Kato, T. Chiba and T. Sasaki, Heterocycles, 1979, 12, 925.
65. K. Matsumoto and T. Uchida, Synth., 1978, 207.
66. K. Matsumoto and T. Uchida, Heterocycles, 1979, 12, 661.
67. A. Ohsawa, I. Wada, H. Igeta, T. Akimoto, A. Tsuji and Y.Iitaka, Tetr.Lett., 1978, 4121.
68. K. Matsumoto and Y. Kono, Chem.Comm., 1976, 1045.
69. A. Kascheres and D. Marchi Jr., Chem.Comm., 1976, 275.
70. B.C. Uff and R.S. Budhram, Synth., 1978, 206.
71. T. Sasaki, K, Kanematsu and A. Kakehi, J.Org.Chem., 1972, 37, 3106.
72. T. Sasaki, K. Kanematsu and A. Kakehi, J.Org.Chem., 1971, 36, 2451.
73. A. Kascheres and D. Marchi Jr., J.Org.Chem., 1975, 40, 2985.
74. A. Kascheres and D. Marchi Jr., Chem.Comm., 1976, 275.

75. Y. Tamura, Y. Sumida, Y. Miki and M. Ikeda, J.C.S.Perkin I, 1975, 406.

76. A. Kascheres, C. Kascheres, J.A.R. Rodrigues and A.A. Santana, J.Org.Chem., 1976, 41, 3546.

77. A. Kascheres, D. Marchi Jr. and J.A.R. Rodrigues, J.Org.Chem., 1978, 43, 2892.

78. A. Kakehi, S. Ito, T. Manabe, H. Amano and Y. Shimaoka, J.Org.Chem., 1976, 41, 2739.

79. Y. Yamashita and M. Masumura, Tetr.Lett., 1979, 1765.

80. R. Gandolfi, M. Ratti, L. Toma and C. De Micheli, Heterocycles, 1979, 12, 897.

81. G.Bianchi,C.DeMicheli,O.Gamba and R.Gandolfi, J.C.S.Perkin I,1974,137.

82. R.Gandolfi, L.Toma and C.DeMicheli, Heterocycles, 1979,12,5.

83. D.F.Hunt, G.C.Farrant and G.T.Rodeheaver, J.Organomet.Chem., 1972, 38, 349.

84. M. Joucla, J. Hamelin and R. Carrie, Tetr., 1974, 30, 1121; Bull.Soc.Chim. Fr., 1973, 3116.

85. K. Burger, H. Schickander and C. Zettl, Angew.Chem.,Intern.Ed.Engl., 1967, 6, 733.

86. A. Kakehi, S. Ito, Y. Konno and T. Maeda, Bull.Chem.Soc.Jap., 1978, 51, 251.

87. A. Kakehi, S. Ito, K. Uchiyama and K. Kondo, J.Org.Chem., 1978, 34, 2896.

88. A.Kakehi, S.Ito, T.Funahashi and N.Ogasawara, Chem.Lett., 1975, 919.

89. A.Kakehi, S.Ito, K.Uchiyama and K.Kondo, Chem.Lett., 1977, 545.

90. A.Kakehi, S.Ito, T.Funahashi and N.Ogasawara, Bull.Chem.Soc.Jpn., 1976, 49, 2250.

91. M.P. Neumann and J.J.Lohmann, Angew.Chem., 1977, 89, 331.

92. H.D. Martin and M. Hekman, Angew.Chem., 1972, 84, 995.

93. G.Germain, P.Main and M.M.Woolfson, Acta Cryst., 1971, A27, 368.

94. I.J. Westerman and C.K. Bradsher, J.Org.Chem., 1978, 43, 3002.

95. C.K. Bradsher, C.R. Miles, N.A. Porter and I.J. Westerman, Tetr.Lett., 1972, 4969.

96. R.R. Schmidt, Angew.Chem.,Intern.Ed.Engl., 1973, 12, 212.

97. C.K. Bradsher, Adv.Heterocycl.Chem., 1974, 16, 289.
98. C.K. Bradsher and F.H.Day, J.Het.Chem., 1974, 11, 23.
99. F.M. Day, C.K. Bradsher and T.K. Chen, J.Org.Chem., 1975, 40, 1195.
100. K.N. Houk, J.Amer.Chem.Soc., 1973, 95, 4092, 4094, 7287.
101. C.K. Bradsher, G.L.B. Carlson, N.A. Porter, I.J. Westerman and T.G. Wallis, J.Org.Chem., 1978, 43, 822.
102. D.L. Fields, J.Org.Chem., 1971, 36, 3002.
103. S. Senda, K. Hirota, T. Asao and Y. Toyota, 11th Congress of Heterocyclic Chemistry, Kanazawa, Japan 1978, Abstracts of Papers, Heterocycles, 1979, 12, 197.
104. A.J. Wexler and J.S. Swenton, J.Amer.Chem.Soc., 1976, 98, 1602.
105. M.L. Greenlee, E.L. Fritzen Jr. and J.S. Swenton, J.Org.Chem., 1978, 43, 4512.
106. A.J. Wexler, J.A. Hyatt, P.W. Raynolds, C. Cotrell and J.S. Swenton, J. Amer.Chem.Soc., 1978, 100, 512.
107. R.O. Loufty and P. De Mayo, J.Amer.Chem.Soc., 1977, 99, 3559.
108. S. Shaik and N.D. Epiotis, J.Amer.Chem.Soc., 1978, 100, 18.
109. K. Senga, M. Ichiba and S. Nishigaki, Heterocycles, 1978, 9, 793; 1979, 12, 209
110. K. Veeramani, K. Paramasivam, S. Ramakrishnasubramanian and P. Shanmugam, Synth., 1978, 855.
111. G.R. Lenz, J.Org.Chem., 1976, 41, 2201.
112. I. Minomiya, T. Kiguchi and T. Naito, Chem.Comm., 1974, 81.
113. T. Kametani, T. Honda, T. Sugai and K. Fukumoto, Heterocycles, 1976, 4, 927.
114. T. Kametani, T. Sugai, Y. Shoji, T. Honda, F. Satoh and K. Fukumoto, J.C.S.Perkin I, 1977, 1151.
115. M. Ogata and H. Matsumoto, Chem.Pharm.Bull., 1972, 20, 2264.

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