AZLACTONES : RETROSPECT AND PROSPECT

Arya K. Mukerjee

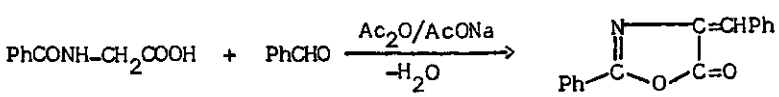
Chemistry Department, Faculty of Science,
Banaras Hindu University, Varanasi - 221005, India

Abstract- Interest in the chemistry of azlactones continues unabated because of their usefulness as intermediates in the synthesis of diverse products. The present review attempts to present the prolific development of recent years in this area and gives a critical and unified account of azlactones under the following headings :

1. INTRODUCTION
2. CYCLOCONDENSATION OF α-N-ACYLAMINO ACIDS AND RELATED SYNTHESES
3. REACTIONS OF 2-OXAZOLIN-5-ONES WITH A C-4 HYDROGEN ATOM
4. REACTIONS AT THE 4-C=C- BOND
5. DEHYDROAMINO ACIDS, PEPTIDES AND RELATED COMPOUNDS
6. CLEAVAGE OF THE 1,5-BOND AND RECYCLIZATION TO OTHER RINGS
7. REACTION OF THE C-2 METHYL GROUP
8. CYCLOADDITIONS
9. POLYMERIZATION
10. CONCLUDING REMARKS

1. INTRODUCTION

More than a century has passed since Plöchl reported the acetic anhydride-mediated condensation of hippuric acid with benzaldehyde. It was Erlenmeyer who first established the correct structure 2 and named the product as "Azlactone", a term which is still in vogue[1]. These heterocycles are usually known as 2-oxazolin-5-ones or simply 5(4H)-oxazolones. Interest in this class of compounds was revived

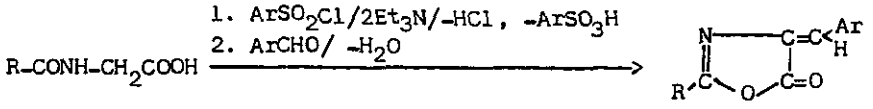


1 2

in connection with penicillin[2] which was erroneously assigned an oxazolone structure. Though penicillin has been shown to contain a β-lactam ring as an essential structural feature of its molecule, 2-oxazolin-5-ones continue to engage the attention of chemists because of their diverse reactions and usefulness as synthons[3-6]. The prodigious growth and current "research explosion" in this area prompted writing of the present article, envisaging a critical and unified account of the subject, based mostly on recent publications, and arranged under the following headings.

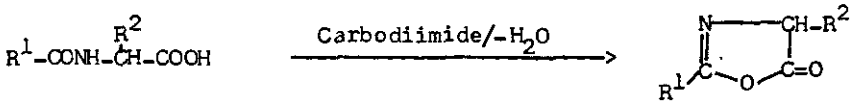
2. CYCLOCONDENSATION OF α-N-ACYLAMINO ACIDS AND RELATED SYNTHESES

A cyclizing agent, generally acetic anhydride, is used for the conversion of saturated as well as unsaturated α-N-acylamino acids into the corresponding 2-oxazolin-5-ones. There are several other reagents available for this purpose[6]. Recently, arylsulphonyl chlorides were employed for the synthesis of stereochemically pure azlactones (4)[7].



3 4, R = Ph or Me

Carbodiimides, which are extensively used in peptide synthesis, have been reported to bring about cyclization not only of the α-N-acylamino acids but also of t-butoxycarbonylamino- and/or benzyloxycarbonylamino acids (5), though yields are low, particularly in the case of the latter type of compounds[8]. The formation of 6 may bring about racemization, thereby adversely affecting a peptide synthesis, particularly in which the optical purity is desired.



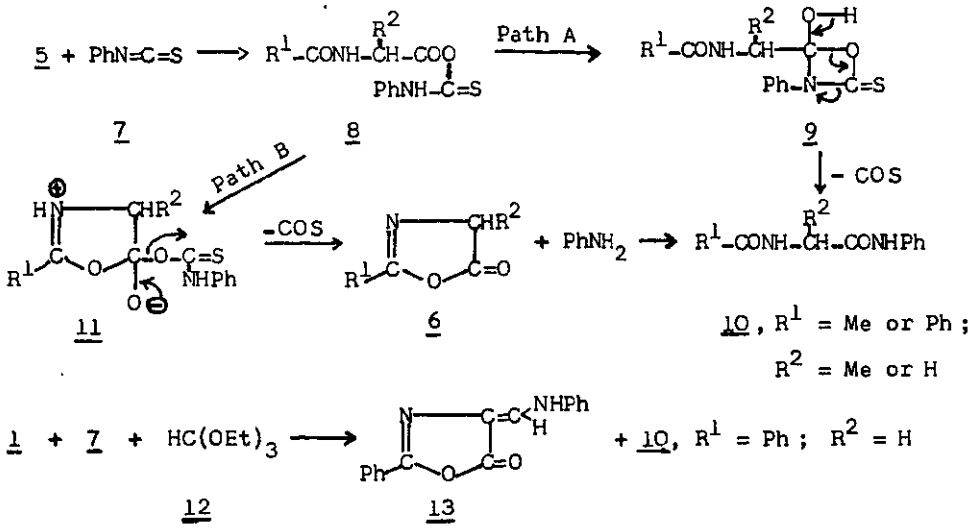
5 a, R^1 = alkyl or aryl ; R^2 = alkyl or aryl 6

b, R^1 = t-BuO; R^2 = alkyl or aryl

c, R^1 = $PhCH_2O$; R^2 = alkyl or aryl

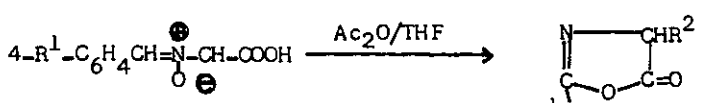
Recently, some α-N-acylamino acids (5) were found to afford the corresponding anilides (10), on heating with phenyl isothiocyanate in the presence of pyridine as a catalyst[9]. 2-Oxazolin-5-ones (6) were implicated in this reaction which has been substantiated by the isolation of 13 in the phenyl isothiocyanate-mediated cyclocondensation of hippuric acid in the presence of triethyl

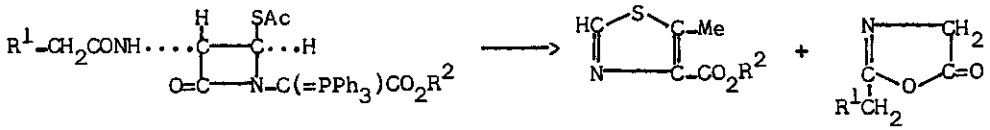
orthoformate (12)[10].



Erlenmeyer azlactone synthesis was often treated as an extension of the Perkin reaction. Though this view has been now revised and the saturated 5-oxazolone (6, R^2 = H) has been shown to be the intermediate, the polyphosphoric acid-mediated condensation of hippuric acid with some carbonyl compounds has been claimed to follow Perkin reaction[11]. The evidence adduced in its favour was that 6 (R^1 = Ph ; R^2 = H) could not be isolated. The cryoscopic studies[12] of hippuric acid in anhydrous sulphuric acid revealed the formation of 6 (R^1 = Ph ; R^2 = H) thereby indicating the possibility of similar cyclodehydration by PPA.

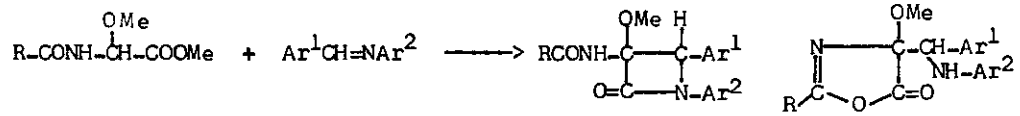
The condensation of α-amino acids with arylimidoyl chlorides[13] and/or triethyl orthobenzoate[5], silver oxide-aided cyclization of thioacylglycines[2,3], and the conversion of α-isocyanocarboxylic acid[14] into 2-oxazolin-5-ones are some examples in which the formation of the 1,2-bond takes place in contrast to the 1,5-bond formation described above. These have been reviewed earlier[6]. Recently, acetic anhydride-mediated cyclization of nitrones (14) was reported to give 15[15]. Besides, there are esoteric transformations of some heterocycles, affording 6. For example, the trans-β-lactams (16) were converted into thiazole-4-carboxylates (17) and 2-oxazolin-5-ones (18)[16].





16 17 18

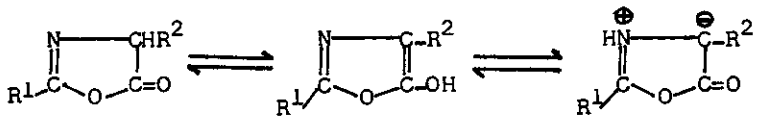
α-N-Acylamino acid esters do not seem to undergo base-mediated cyclization to 2-oxazolin-5-ones. An attempt to condense ethyl hippurate and benzaldehyde in the presence of sodium ethoxide was unsuccessful [17]. Recently, LDA-aided annulation of 19 with Schiff bases (20) was reported to give cephamycin analogs 21. On the basis of spectral data the oxazolone structure 22 was discarded [18], however, its intermediacy in the formation of 21 should not be ruled out altogether.



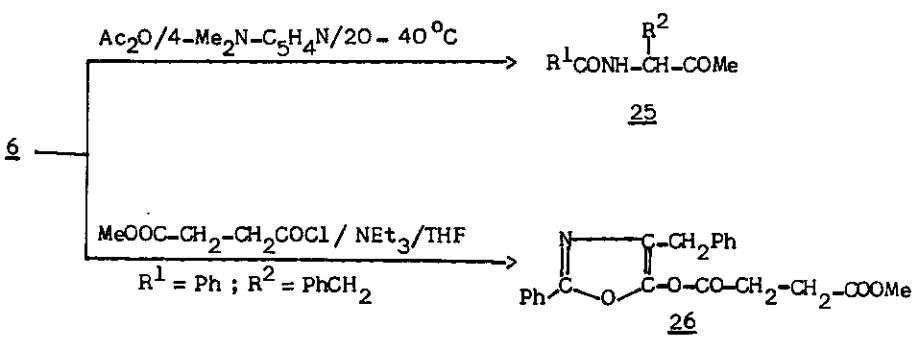
19 20 21 22

3. REACTIONS OF 2-OXAZOLIN-5-ONES WITH A C-4 HYDROGEN ATOM

2-Oxazolin-5-ones carrying at least one C-4 hydrogen atom behave as mesoionic compounds and exhibit tautomerism. 5-Hydroxyoxazoles (23) can be easily converted into 5-O-acyloxazoles which in their turn undergo base-aided O-C transacylation to afford products which are amenable to manipulations. Syntheses of 25 [19,20] and 28 [21] can be cited as examples. It is noteworthy that 28 is the key intermediate for the synthesis of angiotensin converting enzyme inhibitor analog of Bz-Phe-Gly-Pro [21].

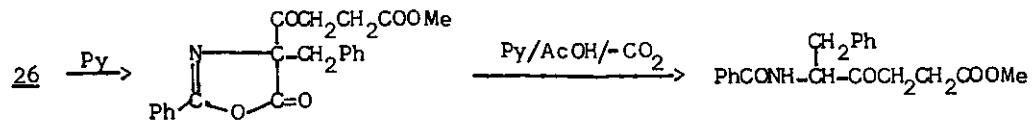


6 23 24



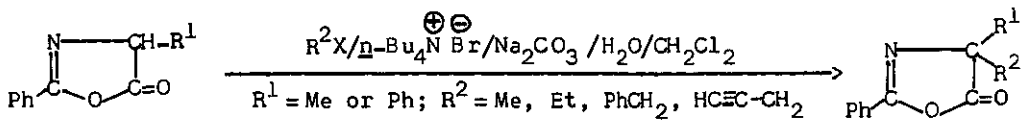
25

26

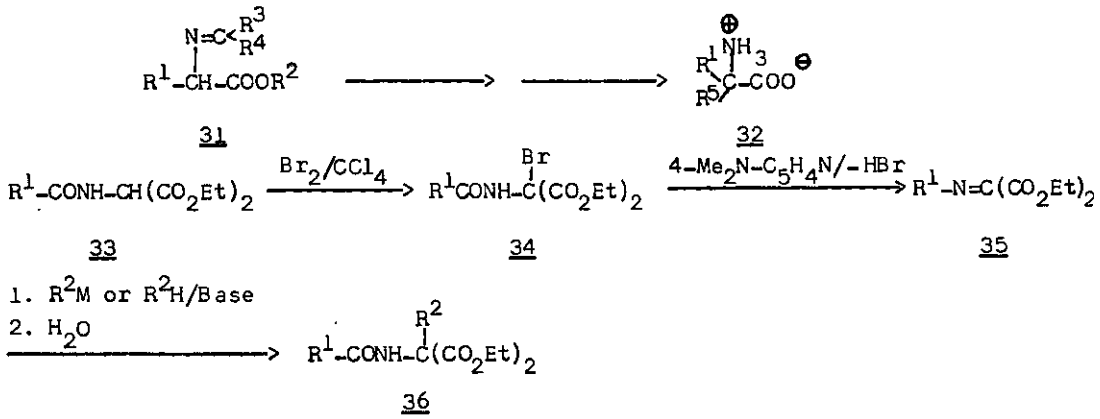


27 28

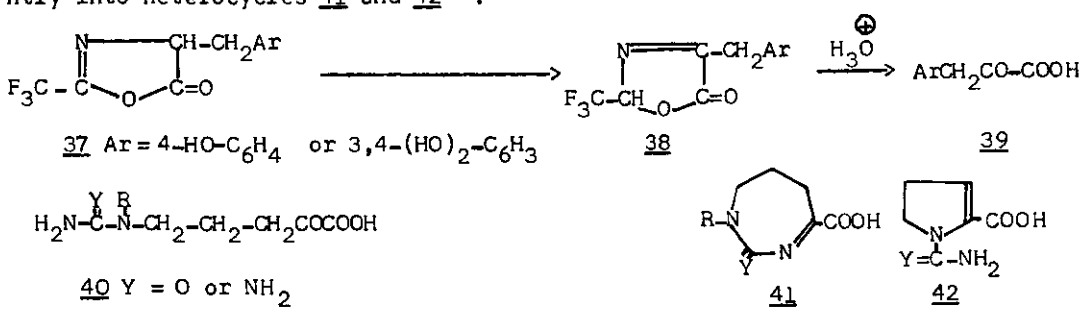
The carbanion 24 undergoes C-4 alkylation with suitable reagents. For example, 29 afforded 30 under phase transfer conditions[22]. A similar alkylation of



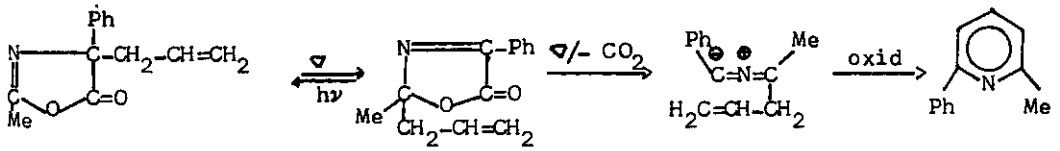
protected α-amino acid derivatives 31 is known in the literature[23]. Also, acylaminomalonic esters (33) can be used for this purpose[24].



Some 2-oxazolin-5-ones (37) undergo isomerisation to 3-oxazolin-5-ones (38) which can be converted into α-keto acids[25]. Recently, ω-guanidino-, and ω-ureido-α-amino acids were converted into the corresponding α-keto acids (40) and subsequently into heterocycles 41 and 42[26].

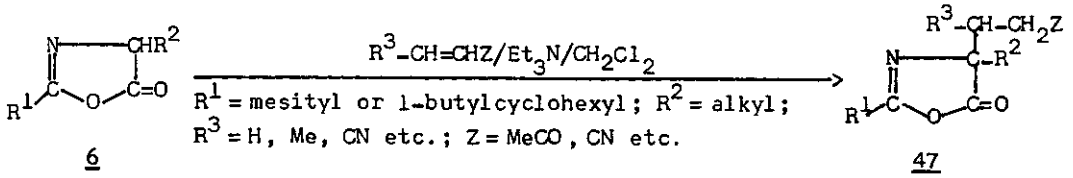


The isomerization of 43 to 44 via Cope rearrangement has been used to prepare 2,6-disubstituted pyridine (46)[27].

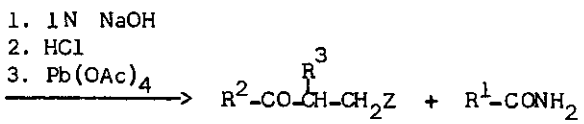


43 44 45 46

Recent studies on Michael addition of 2-oxazolin-5-ones have revealed that bulky substituents like mesityl or 1-butylcyclohexyl at C-2 favour triethylamine-catalyzed addition to activated olefins exclusively at the C-4 atom[28]. Some of these adducts have been converted into 1,4-dicarbonyl compounds 48 (Z = MeCO) or γ-oxonitriles (48, Z = CN).

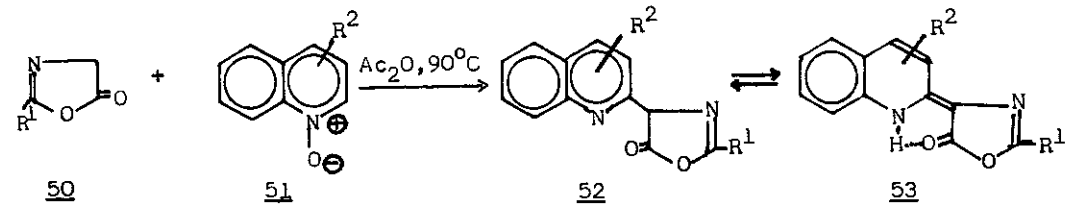


6 47



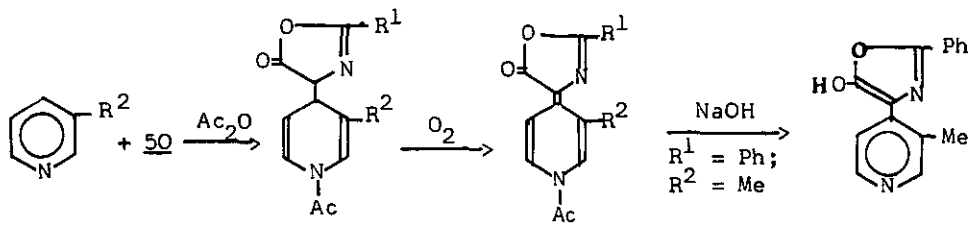
48 49

4-Unsubstituted 2-oxazolin-5-ones condense with aldehydes and imines, affording 4-alkyl(aryl)methylene-2-oxazolin-5-ones[29]. It has been found that ketimines give better result than the corresponding ketones. This may be of help in excercising certain amount of selectivity. Recently, addition of 4-unsubstituted 2-oxazolin-5-ones across the C=N bond of quinoline-1-oxides (51) was reported[30]. Similar reaction was observed with isoquinoline-2-oxides[30]. Pyridine, on the other hand, was attacked at the C-4 position under similar conditions[31].



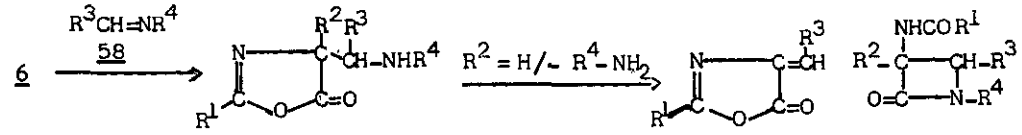
50 51 52 53

R^1 = Me or Ph; R^2 = H, 4-MeO, 4-Me, 4-Cl, 3-Br, etc.



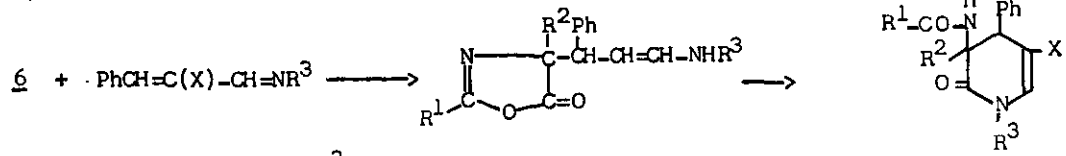
54 55 56 a, R^1 = Ph; R^2 = H 57
b, R^1 = Ph; R^2 = Me
c, R^1 = Me; R^2 = H

The reaction of 6 with some imines was reported to give β-lactams (61)[32,33]. However, addition of 6 (R^1 = Ph; R^2 = Me) to benzylideneaniline afforded 59 (R^1 = Ph; R^2 = Me; R^3 = R^4 = Ph) exclusively[34]. This was confirmed by the unambiguous synthesis of 61 (R^1 = Ph; R^2 = Me; R^3 = R^4 = Ph)[35]. It may be added that β-amino acids and their esters undergo cyclization to β-lactams only in the presence of some cyclocondensing agents which have been reviewed earlier[36].



59 60 61

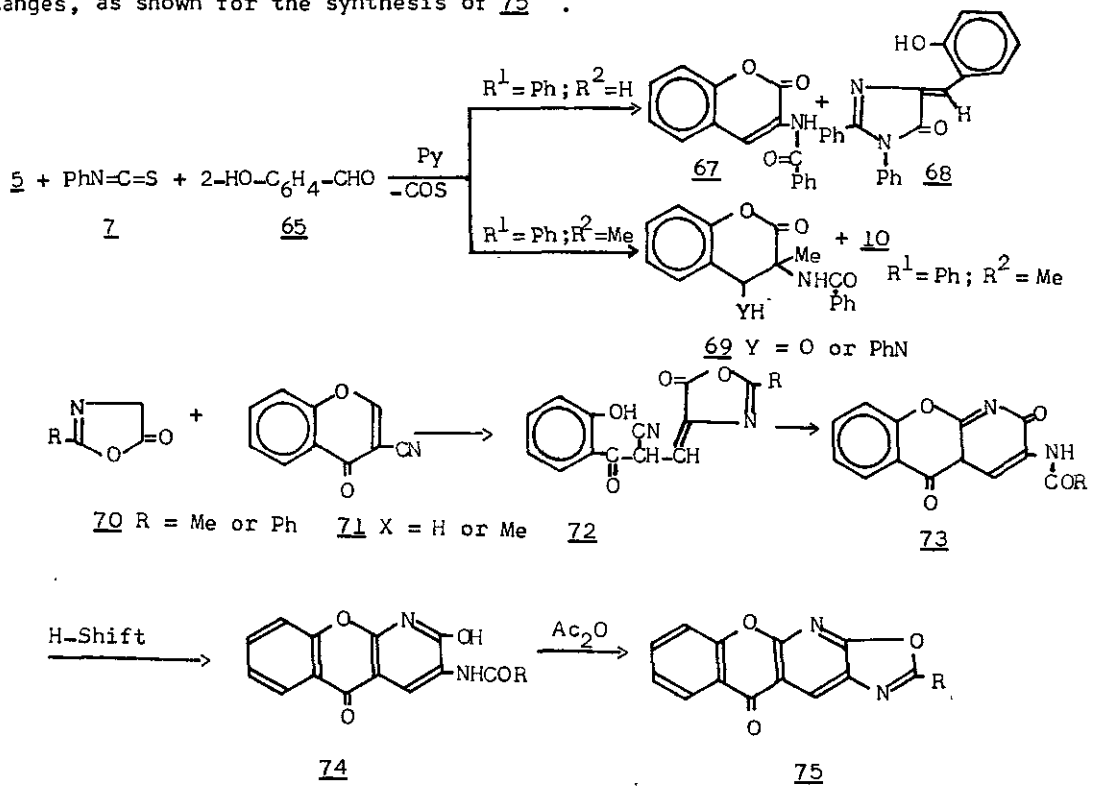
Michael adducts 63 derived from α,β-unsaturated imines (62) lead to the formation of δ-lactams (64)[37-40]. Similar addition with α,β-unsaturated aldehydes for the preparation of δ-lactones does not seem to have been tried.



62 X = H or Br; R^3 = alkyl or aryl 63 64

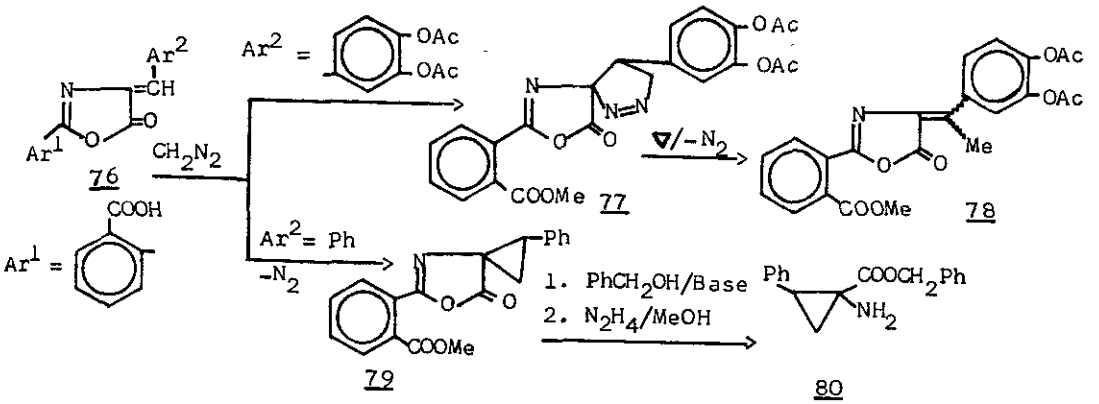
The condensation of 6 with salicylaldehyde or its imines affords coumarins (67) or dihydrocoumarins (69)[34], depending upon the absence or presence of a C-4 substituent. Recently, one-pot synthesis of 67 in moderate yield was achieved by heating hippuric acid and phenyl isothiocyanate in the presence of salicylaldehyde[41]. The 2-imidazolin-5-one (68) was obtained as a minor product. The reaction of 5 (R^1 = Ph; R^2 = Me) with 65, on the other hand, gave 69, only in trace amount, when heated in the presence of 7, the main product being 10. A vicinal reactive group, generated as a result of the reaction, can lead to subsequent

changes, as shown for the synthesis of 75[42].



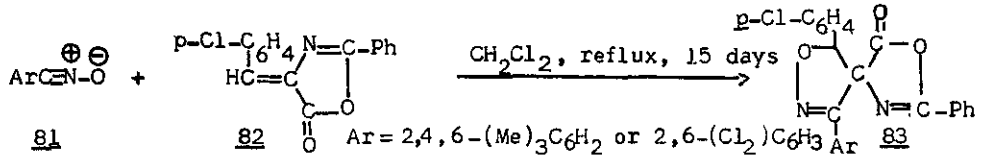
4. REACTIONS AT THE 4-C=C- BOND

4-Alkyl(aryl)methylene-2-oxazolin-5-ones can undergo reactions at the C=C- bond of 4-position with different reagents. For example, the addition of diazomethane has been studied by several workers in recent years[43-47]. The reaction may proceed by insertion of the carbene moiety or by the formation of pyrazoline ring.



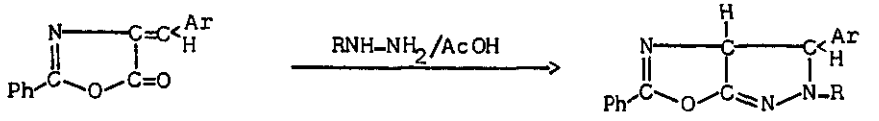
The addition is stereospecific only when the substituents are aryl groups[44]. Solvents have been reported to influence the reaction[45]. The adducts can be manipulated to give different products. Preparations of 78 and 79 are worth mentioning in this connection. The compound 79 was converted into 80 involving two steps[46]. A similar addition of some sulfur ylids is also known in the literature[48].

Stereospecific and regioselective cycloadditions of stable nitrile oxides (81) to unsaturated azlactones (82) were published recently[49].

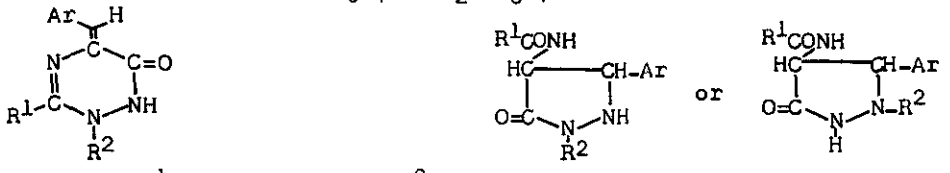


81 82 Ar = 2,4,6-$(Me)_3C_6H_2$ or 2,6-$(Cl_2)C_6H_3$ 83

Reactions involving the C=C- bond of 4-position with suitable binucleophiles can afford diverse products and are potentially important. Hydrazines were claimed to produce 85. Also, similar reaction with hydroxylamine was reported[50]. The products do not seem to have been thoroughly scrutinized. For example, hydrazines are known to give triazine (86)[51] or pyrazolone (87 or 88)[52,53], always envisaging 1,5-bond cleavage. On the other hand, hydroxylamine leads to the formation of diverse products which have been reviewed earlier[6].

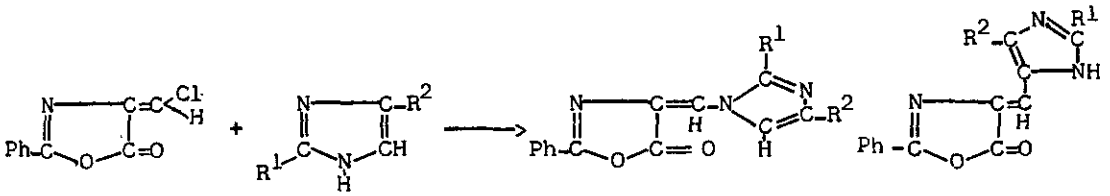


84 Ar = 4-HO-C_6H_4, 4-O_2N-C_6H_4; R = Ph or Ac 85



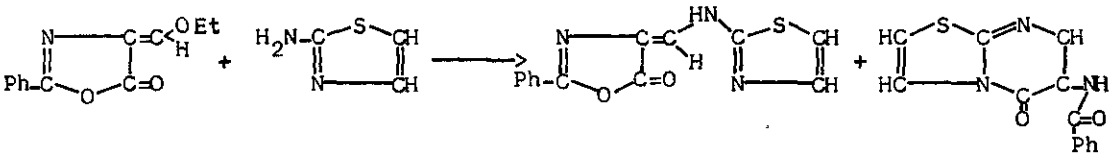
86 R^1 = alkyl or aryl; R^2 = Ph or H 87 88

4-Heteromethylene-2-oxazolin-5-ones have emerged as an important class of compounds. For example, 89 undergoes nucleophilic substitutions[54], and is used for the synthesis of different 4-arylmethylene-2-oxazolin-5-ones, 3-benzoylaminocoumarins etc. Imidazoles (90) were reported[55] to give 92, but the products have been found to be 91[56].



89 90 R^1 = H or Me; R^2 = H or Me 91 92

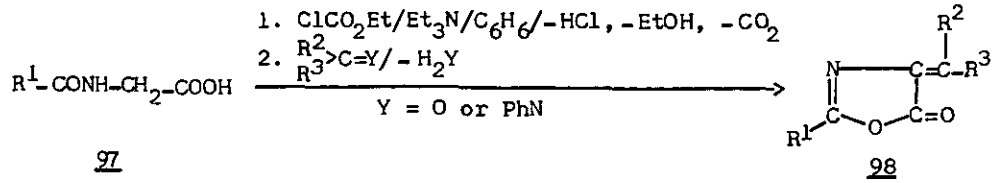
The alkoxy moiety in 93 is easily substituted by an active methylenic and suitable amino groups[2,57], and reactions with 1,2-, 1,3- and/or 1,4-binucleophiles afford different heterocycles. In such conversions, the replacement of the ethoxy group and subsequent intramolecular 1,5-bond cleavage are envisaged, as shown in the reaction of 93 with 94[57].



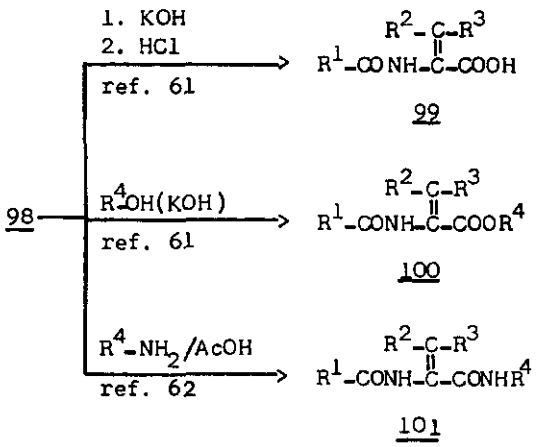
93 94 95 96

5. DEHYDROAMINO ACIDS, PEPTIDES AND RELATED COMPOUNDS

Some dehydroamino acids and/or esters, dehydropeptides as well as peptides exhibit biological activity. For example, methyl 2-acetamido-4-methoxybutenoate (100, R^1 = Me; R^2 = $MeOCH_2$; R^3 = H; R^4 = Me) acts as a plant growth promoter[58]. Similarly, several peptides and dehydropeptides possess antitumor property[59,60]. Dehydroamino acids are precursors of amino acids[3,6] and their preparation is of considerable importance. Recently, a method for the rapid synthesis of these intermediates was developed in which α-N-acylamino acids were cyclized with ethyl chloroformate and triethylamine in benzene, followed by condensation with aldehydes and/or suitable imines and the resultant azlactones (98) were subjected to stereospecific 1,5-bond cleavage without isolation[61]. It should be mentioned that aminolysis depends on the nature of the reactants and the reaction conditions, and it has been found that it becomes very fast in the presence of glacial acetic acid[62].

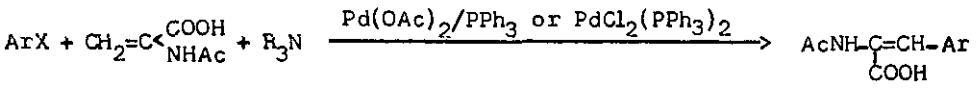


97 98



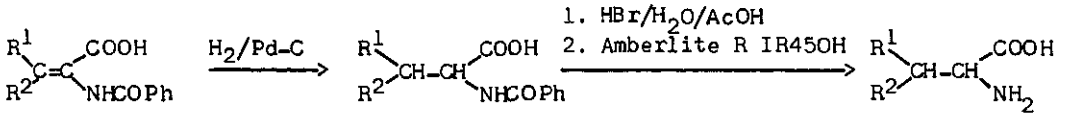
Recent studies on the mechanism of hydrolysis have revealed that the alkaline hydrolysis occurs through nucleophilic attack at the carbonyl carbon of 98, where as the acidic hydrolysis involves attack at the imino carbon[63]. Stereospecific hydrolysis, methanolysis[64] and aminolysis[65] are known in the literature.

Dehydroamino acids are amenable to various manipulations. Recently, palladium-catalyzed arylation of 102 was reported[66] to give 103.



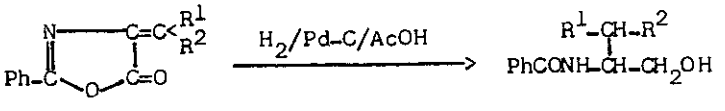
101 102 103

Stereospecific reduction of dehydroamino acids and peptides was developed in recent years. The Pd-catalyzed hydrogenation of 104, followed by hydrolysis, afforded the d,l-pairs of 106. The use of some rhodium compound, on the other hand, led to the asymmetric hydrogenation of dehydroamino acids[68] and peptides[69-71].

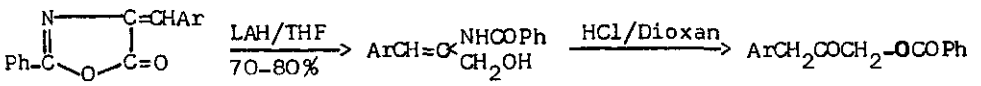


104 105 106

It is known that the catalytic reduction of unsaturated azlactones affords the corresponding saturated azlactones which are easily hydrolyzed to α-N-acylamino acids. Hydrogenation of 107 in the presence of acetic acid, however, led to the formation of α-N-acylamino alcohols (108) which are potentially important as antitumor agents[72]. The lithium aluminium hydride-mediated reduction of 109,

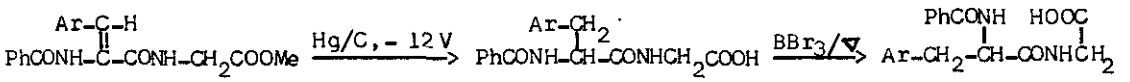


107 108



109 110 111

on the other hand, afforded 2-benzoylaminocinnamyl alcohols (110) which rearranged to give 111[73]. Electrochemical reduction of 112 is also worth mentioning in this connection[74]. It should be added that catechol derived peptides may be useful as metal chelators and enzyme inhibitors.

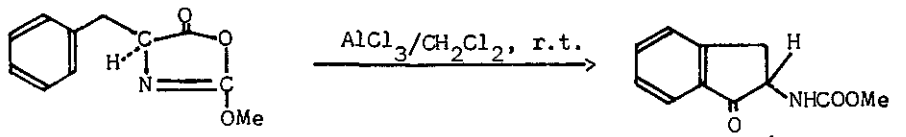


112 113 114

Ar = 2,3-$(MeO)_2C_6H_3$ Ar = 2,3-$(HO)_2C_6H_3$

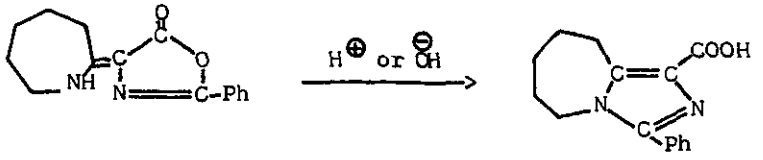
6. CLEAVAGE OF THE 1,5-BOND AND RECYCLIZATION TO OTHER RINGS

As already mentioned, azlactones undergo cleavage of the 1,5-bond with different reagents, affording diverse products. In some cases it may be accompanied by the formation of another ring. For example, 115 afforded 116, on treatment with aluminium chloride[75].



115 116

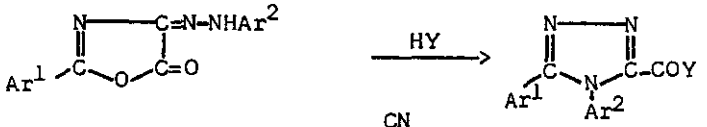
Reaction of some azlactones with an excess of diazomethane gave oxazine derivatives, besides other products, through cleavage of the 1,5-bond[76]. As already seen in the formation of 96, azlactones carrying amino substituents at a suitable position can be manipulated to afford different heterocycles. Hydrolysis of 117 gave 118[77]. It is noteworthy that 4-anilinomethylene-2-phenyl-2-oxazolin-5-one (13) underwent hydrolysis and alcoholysis but the resultant compounds failed to give an imidazole derivative. Also, the Conrad-Limpach cyclization to quinoline system was unsuccessful[78]. On the other hand, aminolysis of 119 afforded triazoles (120), some of which have been found to possess herbicidal property[80]. Similar



117 118

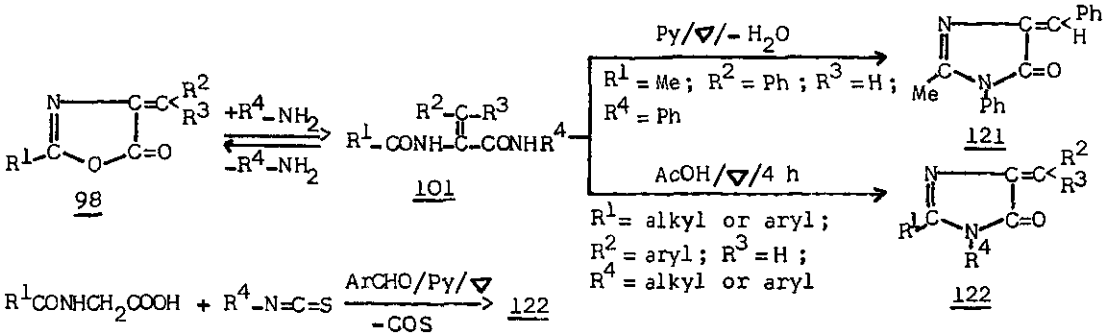
reaction of 119 with active methylenic compounds was also reported[81]. Earlier, 1,5-bond cleavage of unsaturated azlactones by an activated methylenic group was achieved[82].

Aminolysis of unsaturated azlactones (98) affords alkenamides (101)[62] which can be cyclized to 1,2-disubstituted 2-imidazolin-5-ones (122)[6,83], depending upon the



119 Y = NH_2 or RNH, $-CH(CN)-COOEt$, $NC-CH(CONHPh)-$, $NC-CH(COPh)-$, 120

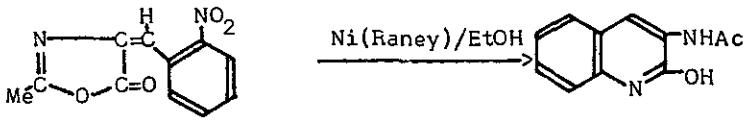
substituents present and the reaction conditions[84]. It has been observed that conversion of 101 into 122 can be carried out in boiling glacial acetic acid in the presence of a catalytic amount of fused sodium acetate or by heating at an elevated temperature, and it fails when R^2 or R^3 is an alkyl group. Also, some of the alkenamides (101) were cyclised to the corresponding unsaturated azlactones (98) under similar reaction conditions[84]. Contrary to the earlier report[85], it has been found that 4-benzylidene-2-methyl-2-oxazolin-5-one (98, R^1 = Me; R^2 = Ph; R^3 = H) affords 121, when heated with aniline in glacial acetic acid[84]. The yield was, however, low. It is noteworthy that 101 (R^1 = Me; R^2 = Ph; R^3 = H), unlike



98 101 121 122 97 123 122

other alkenamides, could be cyclised to 121 in boiling pyridine[84]. The yield was excellent. Though aminolysis of 98 was stereospecific, the cyclization of 101 always afforded the more stable (Z)-isomer of 122, and it was assumed that the corresponding (E)-form was thermolabile. Recently, isothiocyanate-mediated condensation of α-acylamino acids with suitable aromatic aldehydes was used for the one-flask synthesis of 122[86,87]. Similarly some 2-aroylamino-2-alkenoic acids afforded 2-imidazolin-5-ones (122) when heated with isothiocyanates using pyridine as a catalyst[88]. These transformations involve 2-oxazolin-5-ones (98) as intermediates.

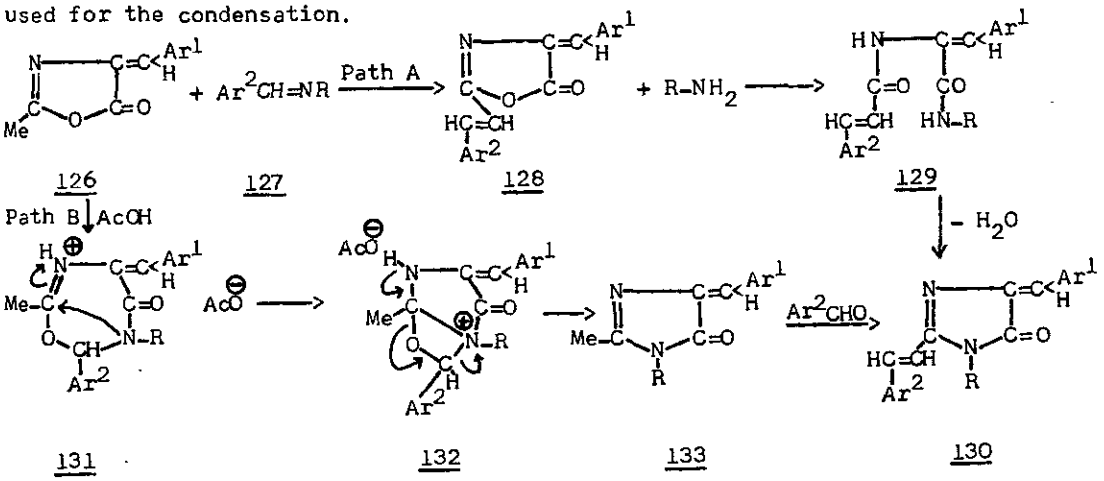
The conversion of (E)-4-(o-nitrobenzylidene)-2-methyl-2-oxazolin-5-one (124) to quinoline (125) was achieved by reduction with Raney nickel. The corresponding (Z)-isomer gave only the (Z)-4-(o-aminobenzylidene)-2-methyl-2-oxazolin-5-one[89].



124 125

7. REACTION OF THE C-2 METHYL GROUP

The activated methyl group of 126 can condense with suitable aldehydes. Recently, 126 was converted into 2-styryl-2-imidazolin-5-ones (130) by reaction with aromatic aldehydes, followed by aminolysis and cyclization[85]. The condensation was also successful with Schiff bases[90,91], and some of the styryl compounds 130 were isolated as cisoid-isomers which changed to the more stable transoid-form on heating[90]. The reaction can follow two different paths when Schiff bases are used for the condensation.

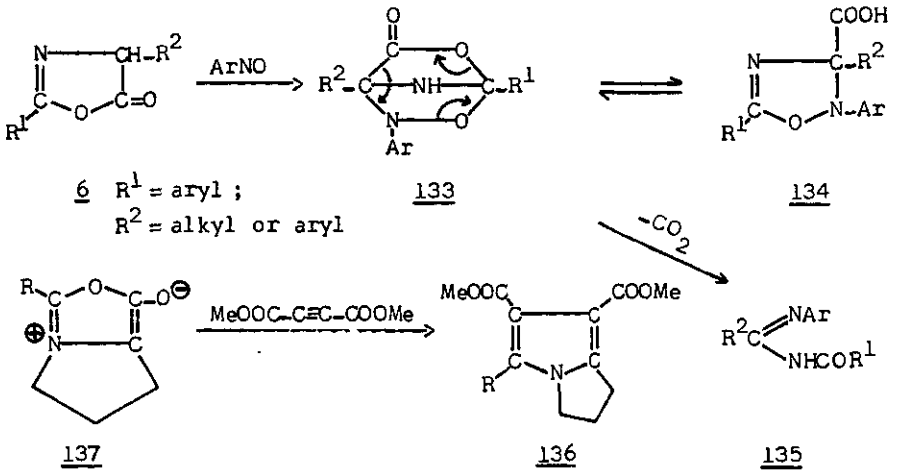


126 127 128 129

131 132 133 130

8. CYCLOADDITIONS

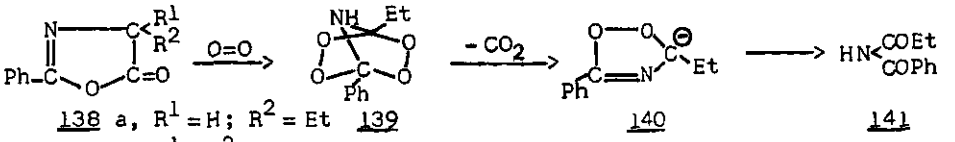
4-Substituted 2-oxazolin-5-ones (6) undergo cycloaddition reactions, some of which have been reviewed earlier[6]. Recently, nitroso compounds have been reported[92,93] to afford 135 on reaction with 6. 1,3-Dipolar cycloadditions of acetylenes with 6 are known in the literature and recently the proline-based oxazolone (137) was converted into 136[94].



6 R^1 = aryl ; R^2 = alkyl or aryl

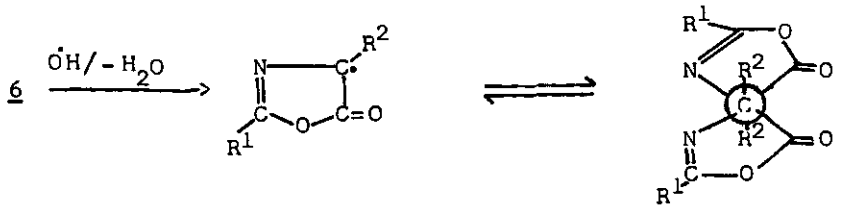
133 134 137 136 135

Similarly, 138a gave 141 on reaction with a superoxide in an aprotic solvent[95]. The compound 138b, however, afforded an α-amino acid derivative, as a result of nucleophilic attack of O_2^- at the carbonyl group. It should be mentioned in this connection that some of the mesoionic oxazolones form free radicals which give different products. Recently, nickel peroxide-mediated dimerization of 6 was observed[96]. Besides the racemic mixture and meso-isomer, other products were also isolated.



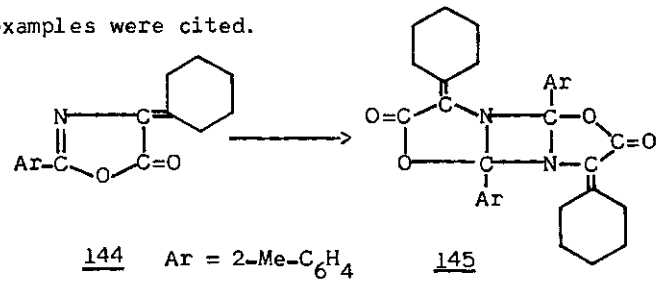
138 a, R^1 = H; R^2 = Et 139 140 141

b, R^1 = R^2 = Me



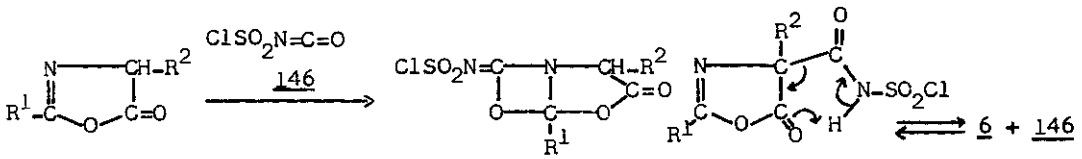
142 143

Some unusual cycloadditions involving the heterocyclic imino bond were reported recently. For example, solid phase photodimerization of 144 was achieved[97]. Several examples were cited.



144 Ar = 2-Me-C_6H_4 145

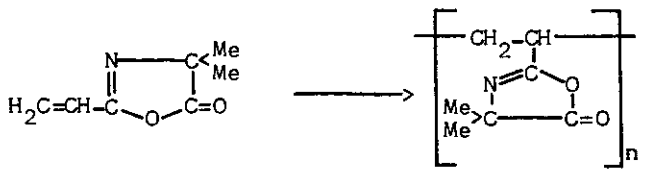
The reaction of 6 with chlorosulphonyl isocyanate (146) was reported to give 147, the structure of which was based on spectral data and on the formation of α-N-acylamino acid by hydrolysis[98]. These facts can also be explained by the structure 148 being in equilibrium with 6 and 146, especially in solution. The formation of 147 needs further verification by carrying out the reaction of 146 with a 4,4-disubstituted 2-oxazolin-5-one, for example 138b.



6 R^1 = Me or Ph; R^2 = Me or $PhCH_2$ 147 148

9. POLYMERIZATION

Azlactone-based polymers do not seem to have been widely studied. Recently, 149 was used for the preparation of polymeric compounds 150[99]. Some 2-oxazolin-5-ones



149 150

have found application in polyester-based materials[100-102]. 2-Alkenyl-2-oxazolin-5-ones were converted into polyamides having useful properties[103,104], besides moulding them to other products by the reaction of nucleophiles, particularly mercaptans[105,106], which afforded Michael adducts in some cases[106].

10. CONCLUDING REMARKS

Since their discovery, azlactones have emerged as a dependable class of synthetic intermediates, particularly for amino acids and related compounds. Vigorous

research over the years has widened their horizon as synthons. In view of their easy availability and diverse reactions, there is enormous possibility for using them as building blocks for various important commercial products, such as drugs, dyes, polymers etc. It would be worthwhile to explore the chemistry of these heterocycles further and to examine their scope in new frontiers, such as photobiology, solar energy etc.

REFERENCES

1. H.E. Carter, Org. Reactions, 1946, 3, 198.
2. J.W. Cornforth, "The Chemistry of Penicillins", H.T. Clarke, J.R. Johnson, and R. Robinson, Eds., Princeton University Press, 1949, p. 730.
3. J.W. Cornforth, "Heterocyclic Compounds", Vol. 5, R.C. Elderfield, Ed., John Wiley and Sons, New York, 1957, p. 298.
4. R. Filler, Adv. Heterocycl. Chem., 1965, 4, 75.
5. R. Filler and Y.S. Rao, Adv. Heterocycl. Chem., 1977, 21, 175.
6. A.K. Mukerjee and P. Kumar, Heterocycles, 1981, 16, 1995.
7. A.K. Mukerjee, P.K. Tripathy, and A. Jain (unpublished results).
8. N.L. Benoiton and F.M.F. Chen, Can. J. Chem., 1981, 59, 384; c.f. A. Paquet, F.M.F. Chen, and N.L. Benoiton, Can. J. Chem., 1984, 62, 1335.
9. R. Ashare, R.N. Ram, and A.K. Mukerjee, Indian J. Chem., 1984, 23B, 759.
10. R. Ashare and A.K. Mukerjee, Chem. Ind. (London), 1985, 165.
11. Y.S. Rao, J. Org. Chem., 1976, 41, 722.
12. J.L. O'Brien and C. Niemann, J. Am. Chem. Soc., 1957, 79, 80.
13. E.I. Boksiner, Zh. Org. Khim., 1972, 8, 604; C.A., 1972, 77, 5769.
14. D. Marquarding, Angew. Chem. Internat. Ed. Engl., 1973, 12, 79.
15. J. Graumann and W. Kliegel, Chem. Ztg., 1983, 107, 136; C.A., 1983, 99,88092.
16. J.R. Irving, E. Perrone, and R.J. Stoodley, Tetrahedron Lett., 1983, 24, 2501.
17. A.K. Mukerjee (unpublished result).
18. A.K. Bose, M.S. Khajavi, and M.S. Manhas, Synthesis, 1982, 407.
19. U. Redeker, N. Engel, and W. Steglich, Tetrahedron Lett., 1981, 22, 4263.
20. J.S. Mc Murray and D.F. Dyckes, J. Org. Chem., 1985, 50, 1112.
21. R.F. Meyer, E.D. Nicolaides, F.J. Tinney, E.A. Lunney, A. Holmes, M.L.Hoefle, R.D. Smith, A.D. Essenberg, H.R. Kaplan, and R.G. Almquist, J. Med. Chem., 1981, 24, 964.

22. M.L. Gelmi, D. Pocar, and L.M. Rossi, Synthesis, 1984, 763.

23. M.J. O'Donnel, B. LeClef, D.B. Rusterholz, L. Ghosez, J. Antonie, and M. Navarro, Tetrahedron Lett., 1982, 23, 4259.

24. R. Kober, W. Hammes, and W. Steglich, Angew. Chem. Internat. Ed. Engl., 1982, 21, 203.

25. C. Klein, G. Schulz, and W. Steglich, Liebigs Ann. Chem., 1983, 1638.

26. C. Klein, G. Schulz, and W. Steglich, Liebigs Ann. Chem., 1983, 1623.

27. A. Padwa, M. Akiba, L.A. Cohen, and J.G. MacDonald, J. Org. Chem., 1983, 48, 695.

28. H. Wegmann and W. Steglich, Chem. Ber., 1981, 114, 2580.

29. P. Kumar, H.D. Mishra, and A.K. Mukerjee, Synthesis, 1980, 836.

30. M.M. Yousif, S. Saeki, and M. Hamana, J. Heterocycl. Chem., 1980, 17, 1029.

31. K. Hirota, M. Shimamura, M. Ikeda, and S. Ohmori, J. Heterocycl. Chem., 1982, 19, 1551.

32. B. Sain, J.N. Baruah, and J.S. Sandhu, J. Heterocycl. Chem., 1984, 21, 257; B. Sain and J.S. Sandhu, Heterocycles, 1985, 23, 1611.

33. K.K. Prasad and T. Petrzilka, Helv. Chim. Acta, 1975, 58, 2504.

34. P. Kumar and A.K. Mukerjee, Indian J. Chem., 1981, 20B, 418.

35. P. Kumar and A.K. Mukerjee, Indian J. Chem., 1981, 20B, 420.

36. A.K. Mukerjee and A.K. Singh, Tetrahedron, 1978, 34, 1731.

37. B. Sain, J.N. Baruah, and J.S. Sandhu, J. Heterocycl. Chem., 1982, 19, 1511.

38. B. Sain, G. Thyagarajan, and J.S. Sandhu, Can. J. Chem., 1980, 58, 2034.

39. D. Konwar, J.S. Sandhu, and J.N. Baruah, Indian J. Chem., 1983, 22B, 1248.

40. B. Sain, J.N. Baruah, and J.S. Sandhu, J. Chem. Soc. Perkin Trans. 1, 1985, 773.

41. R. Ashare and A.K. Mukerjee, Indian J. Chem., (in press).

42. C.K. Ghosh, N. Tiwari, and C. Morin, Indian J. Chem., 1982, 21B, 881.

43. S.W. King, J.M. Riordan, E.M. Holt, and C.H. Stammer, J. Org. Chem., 1982, 47, 3270.

44. I. Arenal, M. Bernabe, E.F. Alvarez, M.L. Izquierdo, and S. Penades, J. Heterocycl. Chem., 1983, 20, 607.

45. C. Cativiela, M.D. Diaz de Villegas, J.A. Mayoral, and E. Melendez, J. Org. Chem., 1984, 49, 1436.

46. M. Suzuki, S.D. Kumar, and C.H. Stammer., J. Org. Chem., 1983, 48, 4769.

47. C. Cativiela, M.D. Diaz de Villegas, and E. Melendez, J. Heterocycl. Chem., 1985, 22, 1655.

48. O. Tsuge, M. Noguchi, and H. Moriyama, Heterocycles, 1981, 16, 209; Heterocycles, 1982, 19, 1823.

49. N.G. Argyropoulos and E. Coutouli-Argyropoulou, J. Heterocycl. Chem., 1984, 21, 1397.

50. M.A. El-Maghraby and A.A.E. Hassan, J. Indian Chem. Soc., 1982, 59, 867.

51. J.H. Jones and M.J. Witty, J. Chem. Soc. Perkin Trans. 1, 1980, 858.

52. D.S. Iyengar, K.K. Prasad, and R.V. Venkataratnam, Aust. J. Chem., 1974, 27, 2439.

53. K. Nalepa, Acta Univ. Placki Olomuc, Fac. Rerum. Nat., 1984, 79; C.A., 1985, 103, 22554.

54. H. Behringer and K. Falkenberg, Chem. Ber., 1963, 96, 1428.

55. H. Behringer and P. Duesberg, Chem. Ber., 1963, 96, 381.

56. C.J. Bish and J.H. Jones, Tetrahedron Lett., 1984, 25, 679.

57. O. Tsuge and M. Noguchi, Heterocycles, 1981, 16, 2149; c.f. I. Hermeez, A. Harvath, L. Vasvari-Debreczy, and Z. Meszaros, Synthesis, 1984, 152.

58. D.D. Keith and M. Weigele, U.S. Patent, 4216008 (1980); C.A., 1981, 94, 16083.

59. E. Etschenberg, H. Jacobi, and W. Opitz, German Patent, 2904512 (1980); C.A., 1981, 94, 47753.

60. E. Etschenberg, W. Opitz, and S. Raddatz, U.S. Patent, 4310517 (1982); C.A. 1982, 97, 72781.

61. P.K. Tripathy and A.K. Mukerjee, Synthesis, 1984, 418.

62. P.K. Tripathy and A.K. Mukerjee, Synthesis, 1985, 285.

63. J. Suh, E. Lee, Y.C. Myoung, M. Kim, and S. Kim, J. Org. Chem., 1985, 50, 977.

64. C. Cativiela, M.D. Diaz de Villegas, J.A. Mayoral, and E. Melendez, Synthesis, 1983, 899.

65. C. Cativiela, J.I. Gracia, and E. Melendez, Synthesis, 1982, 763.

66. M. Cutolo, V. Fiandanese, F. Naso, and O. Sciacovelli, Tetrahedron Lett., 1983, 24, 4603.

67. C. Cativiela and E. Melendez, Synthesis, 1981, 805.

68. C. Cativiela, J.A. Mayoral, E. Melendez, L.A. Oro, M.T. Pinillos, and R. Uson, J. Org. Chem., 1984, 49, 2502; C. Cativiela, J. Fernandez, J.A. Mayoral, E. Melendez, L.A. Oro, M.T. Pinillos, and R. Uson, An. Quin. Ser. C, 1983, 79, 188; C.A., 1985, 102, 7051.

69. U. Schmidt, A. Lieberknecht, H. Griesser, and F. Bartkowiak, Angew Chem., 1984, 96, 310; I. Ojima, N. Yoda, M. Yatabe, T. Tanaka, and T. Kogure, Tetrahedron, 1984, 40, 1255.

70. J.P. Poulin and H.B. Kagan, J. Chem. Soc. Chem. Commun., 1982, 1261; I. Ojima, T. Kogure, N. Yoda, T. Suzuki, M. Yatabe, and T. Tanaka, J. Org. Chem., 1982, 47, 1329.

71. Chiral amino acids/dipeptides via a novel photooxidative cleavage of trisubstituted imidazoles were recently reported: B.H. Lipshutz and M.C.Morey, J. Am. Chem. Soc., 1984, 106, 457.

72. R.B. Bates and K.D. Janda, Synthesis, 1984, 310.

73. S.S. Naim, M. Husain, and N.H. Khan, Synthesis, 1985, 48.

74. C.D'Silva and K.T. Doughlas, J. Org. Chem., 1983, 48, 263.

75. D.E. McClure, B. Arison, J.H. Jones, and J.J. Baldwin, J. Org. Chem., 1981, 46, 2431.

76. I.A. Blair and L.N. Mander, Aust. J. Chem., 1979, 32, 1055.

77. R.G. Glushkov and O. Yu. Magidson, Zh. Obshch. Khim., 1960, 30, 1855; C.A., 1961, 55, 7430.

78. P.K. Tripathy and A.K. Mukerjee, Indian J. Chem., (in press).

79. A.M. Khalil, I.I.Abd-El-Gawad,and H.M. Hassan, Aust. J. Chem., 1974, 27, 2509.

80. Kureha Chemical Industry Co. Ltd., Japan Patent, 58185572 (1983); C.A., 1984, 100, 156607.

81. M.A.E. Khalifa, G.H. Tammam, R.M. Abdel-Motabb, and M.H. Elnagdi, Heterocycles, 1983, 20, 45.

82. H.D. Stachel, K.K. Harigel, H. Poschenrieder, and H. Burghard, J. Heterocycl. Chem., 1980, 17, 1195.

83. C.K. Ghosh and C. Bandyopadhyay, Indian J. Chem., 1984, 23B, 1048.

84. P.K. Tripathy and A.K. Mukerjee, Indian J. Chem., (in press).

85. M.Z.Badr, H.A.H. Elsherief, and M.E.Tadros, Bull.Chem.Soc.Japan, 1982,55,2267.

86. R. Ashare and A.K. Mukerjee, Chem. Ind. (London), 1985, 627.

87. R. Ashare and A.K. Mukerjee, Indian J. Chem., (in press).

88. R. Ashare and A.K. Mukerjee, Chem. Ind. (London), 1985, 378.

89. A.A. Mazurov, S.A. Andronati, and V.V. Antonenko, Khim. Geterotsikl.Soedin., C.A., 1985, 103, 141871.

90. A.K. Mukerjee and P. Kumar, Can. J. Chem., 1982, 60, 317.

91. M.S. Reddy, P. Hanumanthu, and C.V. Ratnam, Indian J. Chem., 1982, 21B, 646.

92. H. Rodriguez, H. Pavez, A. Marquez, and P. Navarrete, Tetrahedron, 1983, 39, 23.

93. P.J. Bhuyan, B. Sain, and J.S. Sandhu, Indian J. Chem., 1984, 23B, 973.

94. D. Laduree, J.C. Lancelot and M. Robba, Tetrahedron Lett., 1985, 26, 1295.

95. C.A. Chuaqui, S. Delaney, and J. Meritt, Tetrahedron, 1983, 39, 2947.

96. A. Marquez, C.A. Chuaqui, H. Rodriguez, and L. Zagal, Tetrahedron, 1985, 41, 2341.

97. D. Lawrenz, S. Mohr, and B. Wendlander, J. Chem. Soc. Chem. Commun., 1984, 863.

98. D.N. Dhar and R. Raghunathan, Indian J. Chem., 1984, 23B, 761.

99. L.D. Taylor, H.S. Kolesinski, A.C. Mehta, L. Locatell, and P.S. Larson, Makromol. Chem-Rap. Comm., 1982, 3, 779.

100. Teijin Ltd. Japan Patent, 80164218 (1980); C.A., 1981, 94, 193100.

101. S.C. Li, U.S. Patent, 4266040 (1981); C.A., 1981, 95, 63252.

102. Teijin Ltd., Japan Patent, 8202330 (1982); C.A., 1982, 96, 163390; Japan Patent, 5991120 (1984); C.A., 1984, 101, 172327.

103. J.K. Rasmussen, F.J. Palensky, and S.M. Heilmann, European Patent, 105665 (1984); C.A., 1984, 101, 131733.

104. S.M. Heilmann, F.J. Palensky, and J.K. Rasmussen, European Patent, 105666 (1984); C.A., 1984, 101, 132584.

105. S.M. Heilmann, J.K. Rasmussen, F.J. Palensky, and H.K. Smith, J. Polym. Sci. Polym. Chem. Ed., 1984, 22, 1179.

106. J.K. Rasmussen, S.M. Heilmann, L.R. Krepski, and H.K. Smith, Polym. Prepn., 1984, 25, 33.

Received, 2nd June, 1986