HETEROCYCLES, Vol. 24, No. 11, 1986

ONE CARBON UNIT TRANSFER TO ENAMINES THROUGH OXAZOLIDINES AND TETRAHYDRO-2H-1,3-OXAZINE

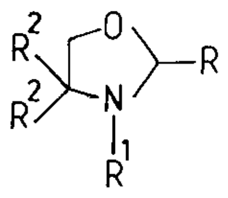
Harjit Singh*, Rakesh Sarin, and Kamaljit Singh
Department of Chemistry, Guru Nanak Dev University
Amritsar-143005, India

Abstract - Oxazolidines and tetrahydro-2H-1,3-oxazine undergo acid catalysed transfer of C_2 carbon unit inbetween two nucleophilic carbons of stabilised enamines.

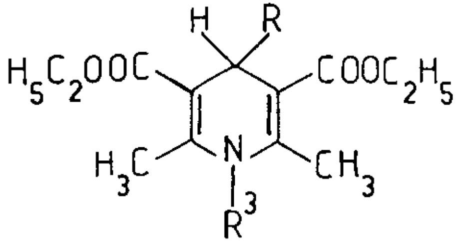
Like THF model 1-methyl-3-tosyl/acetyl imidazolidine derivatives[1], oxazolidines and thiazolidines irrespective of the presence or absence of electron donating group at nitrogen, demonstrate carbonyl group oxidation level carbon transfer character to binucleophiles, i.e. C, N; N, N etc.[2] The N^5,N^{10}-methylenetetrahydrofolate induced reductive methylation[3] of 2'-deoxyuridylate to 2'-deoxythymidylate involves the initial transfer of $CH_2(C_2)$ of imidazolidine ring, at formaldehyde level to enamine β-carbon (C_5)[4] of uracil moiety. Consequently, for understanding the mechanistic features, the investigation of such carbon transfer reactions on enamines are significant.[5] Here we report that oxazolidines and tetrahydro-2H-1,3-oxazine perform acid catalysed transfer of C_2 carbon unit inbetween nucleophilic carbons of two molecules of relatively stable enamines and form methylene bis-enamine adducts which may undergo further transformations.

Ethyl β-aminocrotonate, a relatively stable enamine[6], with 2-phenyl-3,4,4-trimethyloxazolidine (1a) or 2-phenyl-4,4-dimethyloxazolidine (1b) in acetonitrile at room temperature in the presence of a catalytic amount of acetic acid furnish diethyl 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxylate (2a). Likewise, 3-phenyloxazolidine (1c) and ethyl β-aminocrotonate yield diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (2b) (Table). Ethyl β-anilinocrotonate also reacts with (1a), (1b) and (1c) to furnish corresponding dihydropyridine derivatives, 2c and 2d, respectively (Table).

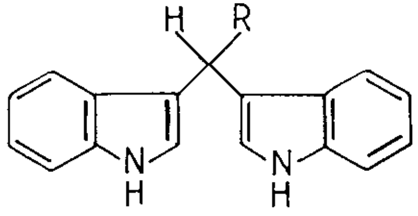
Evidently, alkylidene imines, (6, R=H, Ph; R^5=COOEt; R^3=H, Ph; R^6=Me), generated through β-elimination of (5), which are tautomers of the initial adducts (4) formed from protonated oxazolidines and enamines, react with a second molecule of enamine to form adducts which through cycloelimination finally yield 2a - 2d. In case of a similar reaction of oxazolidine with an enamine lacking H at nitrogen corresponding 7 is formed through cycloaddition reaction of the initial adduct (4)[7] which cannot exist as tautomer (5). Thus the absence or presence of H at nitrogen of enamine directs the course of its reaction with an oxazolidine (Scheme).



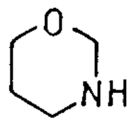
	R	R¹	R²
1a	C_6H_5	CH_3	CH_3
1b	C_6H_5	H	CH_3
1c	H	C_6H_5	H



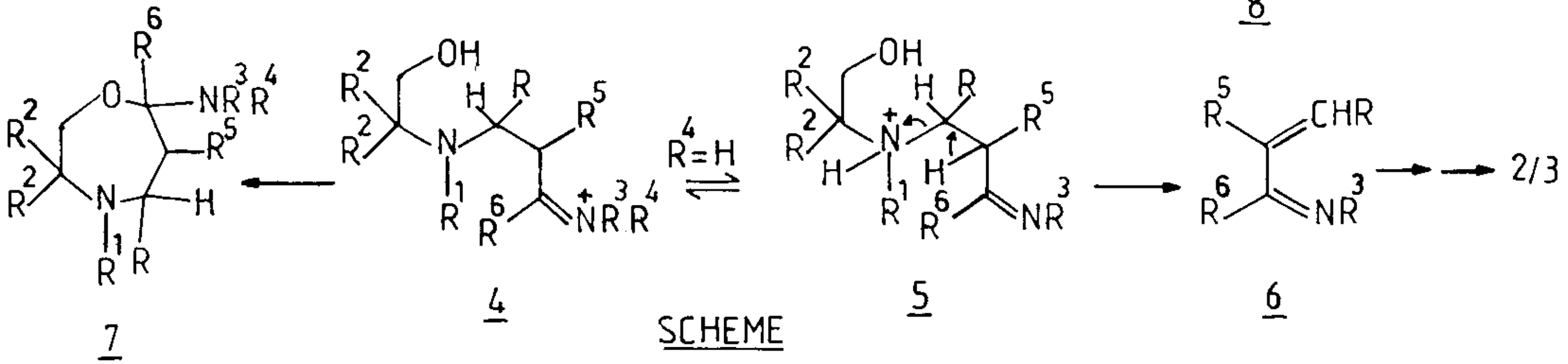
	R	R³
2a	C_6H_5	H
2b	H	H
2c	C_6H_5	C_6H_5
2d	H	C_6H_5



	R
3a	C_6H_5
3b	H

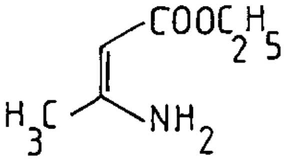
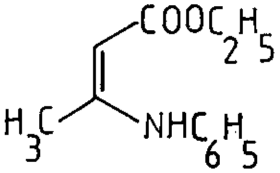
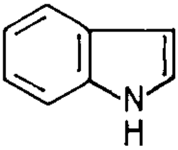


8



SCHEME

Table: Reactions of Enamines with oxazolidines and tetrahydro-2H-1,3-oxazine

Reagent	Enamine	Product[a]	m.p.(°c)	Time(h)	Yield(%)
1a		2a	156	6.0[b]	73
1b		2a	-do-	4.5[b]	70
1c		2b	182.5	3.0[b]	80
8		2b	-do-	0.1[b]	90
1a		2c	155	6.0[b]	40
1b		2c	-do-	8.0[b]	35
1c		2d	99	2.5[b]	70
8		2d	-do-	0.7[b]	65
1a		3a	127	8.0[c]	53
1b		3a	-do-	18.0[d]	55
1c		3b	164	12.0[b]	55
8		3b	-do-	3.0[d]	70

a - For all the compounds satisfactory spectral data and/or comparison with authentic samples have been obtained. b - In CH_3CN/CH_3COOH at room temperature. c - In refluxing CH_3CN/CF_3COOH. d - In refluxing CH_3CN/CH_3COOH.

Indole undergoes electrophilic reactions at position 3 and has an enamine character. It reacts with 2-phenyl-3,4-trimethyloxazolidine (1a)/2-phenyl-4,4-dimethyloxazolidine (1b) in refluxing acetonitrile under acidic conditions to furnish 3,3'-phenylmethylene-bis(1H-indole) (3a). In a similar reaction, 3-phenyloxazolidine (1c) and indole furnish 3,3'-methylene-bis(1H-indole) (3b) (Table). These products are analogs of streptindole, a genotoxic metabolite.[8]

The carbonyl character of saturated C_2 unit of tetrahydro-2H-1,3-oxazines and functionalization of C_2-alkyl chain of their precursor 5,6-dihydro-2H-1,3-oxazines has been demonstrated.[9] By the same argument as was advanced for oxazolidines[2], tetrahydro-2H-1,3-oxazines could also act as carbon transfer agents. Thus we have found that tetrahydro-2H-1,3-oxazine (8) reacts advantageously (Table) with ethyl β-aminocrotonate, ethyl β-anilinocrotonate and indole in acetonitrile in the presence of acetic acid to furnish 2b, 2d and 3b respectively. Further synthetic utility of tetrahydro-2H-1,3-oxazines is being investigated.

ACKNOWLEDGEMENT

We are thankful to UGC and CSIR for financial assistance.

REFERENCES

1 H.C.Hiemstra, H. Bieräugel, M.Wijnberg and U.K.Pandit, Tetrahedron, 1983, 39, 3981 and references therein.

2 H.Singh and R.Sarin, Heterocycles, 1985, 23, 107 and unpublished results.

3 D.W.Young in 'Chemistry and Biology of Pteridines' ed. J.A. Blair, Walter de Gruyter and Co., Berlin, 1983, 321.

4 G.Lauer, W.Schäfer and A.Schweig, Tetrahedron Letters, 1975, 3939.

5 P.F.C.v.d. Meij, R.D.Lohmann, E.R.D.Waard, T.B.R.A. Chen. and U.K.Pandit, J.Chem.Soc. Chem. Commun., 1985, 1229.

6 G.DE Stevens, H.M.Blatter and R.W.J. Carney, Angew. Chem. Int.Ed.Engl., 1966, 5, 35

7 H.Griengl, G.Prischl and A.Bleikolm, Liebigs Ann. Chem., 1980, 1573.

8 T.Osawa and M.Namiki, Tetrahedron Letters, 1983, 24, 4719.

9 A.I.Meyers, A.Nabeya, H.W.Adickes, I.R.Politzer, G.R.Malone, A.C. Kovelesky, R.L.Nolen and R.C.Portnoy, J.Org. Chem., 1973, 38, 36.

Received, 30th June, 1986