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Synthesis of Oxazepinones from Vinyloxiranes and Chlorosulfonyl Isocyanate

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A facile synthesis of oxazepinone derivatives is reported by the interaction of vinyloxiranes and chlorosulfonyl isocyanate. A 1,5 to 1,7 - dipolar rearrangement of the initially formed adduct, followed by ring closure is proposed.

Oxiranes are reported[1] to undergo ring enlargement cycloaddition reaction with heterocumulenes (alkyl and aryl isocyanates) in polar solvents and in presence of catalyst, to yield the corresponding five-membered oxazolidine derivatives. However, these reactions lack selectivity and some times lead to unexpected side products. Murthy and Dhar[2] reported a regio- and stereospecific reaction of oxiranes and chlorosulfonyl isocyanate (CSI) to yield the corresponding oxazolidine and dioxolane derivatives. Formation of a 1,5 - dipolar intermediate was proposed by these authors.[2] A similar mechanism has been put forward by Lorincz et al.[3] for the reaction of CSI with oxiranes at low temperature (-78 ^{o}C). A 1,5 to 1,7 - dipolar rearrangement in the above mentioned case may yield a novel seven-membered heterocyclic system. However, it is well known that the nature of the substituents and the reaction conditions influence the course of the reaction and nature of the products in the case of CSI and oxiranes.[2,3] We have successfully carried out the reaction of vinyloxiranes (1) with CSI and obtained oxazepinone derivatives (5).

Oxazepinone (5a), mp 99 ^{o}C, was obtained in good yield (98%) by mixing equimolar quantities of CSI and 1a (R = H, R^1 = C_6H_5) at 0-5 ^{o}C in dry dichloromethane, followed by aqueous work-up. The structure of 5a followed from its spectral[4] characteristics. Its ^{1}H-NMR spectrum contained a doublet at δ 2.20, double triplet at δ 5.90, and a double doublet at δ 6.70, which is in good agreement with the assigned structure, viz., 3,4-dihydro-4-phenyl-1,3-oxazepin-2-one.

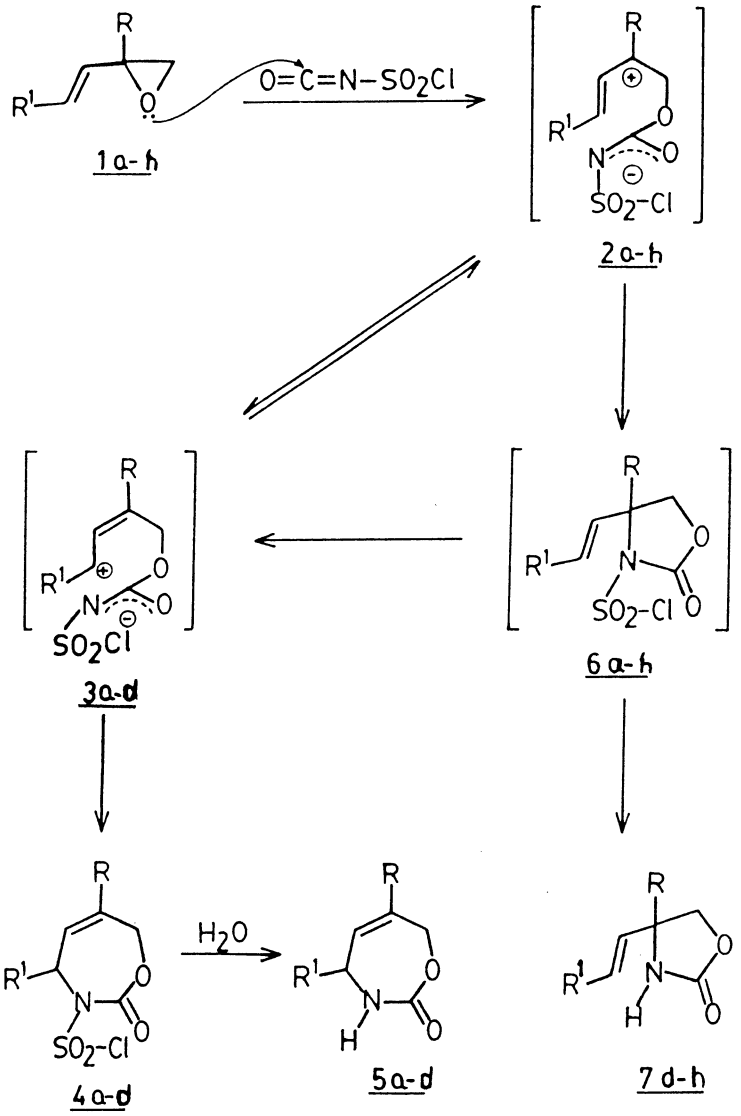
It has been reported[5] that seven-membered heterocyclic compounds, namely, azepines, oxazepines, thiepines, diazepines, triazepines, oxadiazepines, and their benzologues exist in a flexible boat conformation. The

^{1}H-chemical shifts for these heterocyclic ring protons lie in the vinyl proton region (δ 4.50 - 6.80) due to their non-planar polyene character. However, the relative stabilities of the two boat conformations and the ^{1}H-chemical shift values of the ring protons of these heterocycles depend very much on the nature and position of the substituents, heteroatoms, and the exocyclic double bonds present in the ring structure. In the present case oxazepinone (5a) has 4-H ring proton resonance at a higher magnetic field (δ 2.20) as compared to acyclic C_6H_5-CH-N- moiety and the olefinic protons resonances (δ 5.90 - 6.70) in the vinyl proton region. This indicates that oxazepinone 5a exist in the boat conformation identical with other seven-membered heterocycles.

Oxazepinones 5b (mp 128 ^{o}C, 97% yield) and 5c (mp 60 ^{o}C, 96% yield) are formed in a similar manner from CSI and the corresponding oxiranes 1b (R = H, R^1 = CH_3) and 1c (R = C_6H_5, R^1 = $(MeO)_2C_6H_3$) respectively. In the case of 1d (R = C_6H_5, R^1 = MeO-C_6H_4), on treatment with CSI, gave oxazepinone (5d,[6] mp 64 ^{o}C, 51% yield) and oxazolidinone (7d,[6] mp 73 ^{o}C, 48% yield). On the other hand oxiranes 1e (R = R^1 = C_6H_5), 1f (R = C_6H_5, R^1 = p-$NO_2C_6H_4$), 1g (derived from diosgeninone), and 1h (derived from cholestenone) upon reaction with CSI gave oxazolidinones (7e-h)[7] as the sole products in moderate yields (70-80 %).

The ring protons of 5b-d show an up field ^{1}H-chemical shift in their NMR spectra similar to that of 5a, which is probably due to their non-planar ring structure. The ^{1}H-NMR chemical shift correlation of the ring protons of 5d and 7d in conjunction with their characteristic carbonyl stretching frequencies confirms the structure of 5.

A mechanism which accounts for the formation of 5 would involve an electrophilic attack of CSI on the epoxide oxygen atom forming a 1,5 - dipolar intermediate (2), which undergoes resonance stabilization to the 1,7 - dipolar species (3), followed by ring closure. The ring closure of 2 give rise to 7 through the intermediacy of 6 (scheme). It was not possible to isolate the intermediates 4 and 6 probably due to their instability. During isolation these intermediates 4 and 6 undergo hydrolysis to form 5 and 7 respectively. Stability arising due to electronic factors favours the complete conversion of 2a-c to 3a-c, which in turn cyclize to form 5a-c. In other words the positive charge formed at the C-7 is stabilized by the aryl or methyl moieties in the case of 3a-c. However, in the case of 1d substituent effect at C-5 and C-7 are the same, thus 2d and 3d are formed in an almost equal ratio. Similar explanation would hold for the formation of only 7e-h from 1e-h.



a: R = H, R^1 = C_6H_5. b: R = H, R^1 = CH_3. c: R = C_6H_5, R^1 = $(MeO)_2C_6H_3$
d: R = C_6H_5, R^1 = $MeOC_6H_4$. e: R = R^1 = C_6H_5. f: R = C_6H_5, R^1 = $p\text{-}NO_2C_6H_4$.
g: R-R^1 = $-C_{24}H_{39}O_2-$. h: R-R^1 = $-C_{24}H_{43}-$.

Scheme 1.

References

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2) K. S. K. Murthy and D. N. Dhar, *Synth. Commun.*, 14, 687 (1984); *J. Heterocycl. Chem.*, 21, 1721 (1984).

3) T. Lorincz, J. Erden, R. Nadar, and A. de. Meijer, *Synth. Commun.*, 16, 123 (1986).

4) Oxazepinone 5a: mp 99 °C; IR (KBr), ν_{max}: 3320, 1720, 1600, 1540, 1240, 1050, 760, 700 cm^{-1}; MS, m/e (rel. int.): 189 (M^+, 9), 145 (7), 131 (8), 130 (19), 117 (7), 115 (12), 104 (10), 103 (8), 101 (8), 90 (10), 77 (20), 58 (90), 43 (100); ^{1}H-NMR ($CDCl_3$), δ: 2.20 (d, 1H, J = 7.00 Hz), 4.25 (d, 2H, J = 9.40 Hz), 4.50 (b, 1H, NH), 5.99 (dt, 1H, J = 14.00 and 9.40 Hz), 6.70 (dd, 1H, J = 14.00 and 7.00 Hz), and 7.00-8.00 (m, 5H); ^{13}C-NHR ($(CD_3)_2SO$), δ: 52.33, 65.17 (C-4 and C-7), 126.28, 126.55, 127.69, 128.61, 129.59, 130.67 (phenyl carbons), 136.25 (olefinic carbons), 155.59 (carbonyl carbon); Anal Found: C, 69.61; H, 6.10; N, 7.18%. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.85; N, 7.40%.

5) A. Steigel, J. Sauer, D. A. Kleir, and G. Binsch, *J. Am. Chem. Soc.*, 94, 2770 (1972).

6) Oxazepinone 5d: mp 64 °C; IR (KBr), ν_{max}: 3400, 1750, 1610, 1520, 1260, 1180, 1040, 770, 710 cm^{-1}; MS, m/e (rel. int.): 295 (M^+,2), 267 (13), 220 (5), 192 (20), 176 (10), 169 (70), 121 (20), 92 (30), 77 (50), 57 (60), 43 (100); ^{1}H-NMR ($CDCl_3$), δ: 2.30 (d, 1H, J = 7.5 Hz), 3.50 (s, 2H,), 3.95 (s, 3H), 4.15 (b, 1H, NH), 6.85 (d, 1H, J = 7.5 Hz), 7.50-7.90 (m, 9H); Anal Found: C, 72.95; H, 5.42; N, 4.33%. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74%.
Oxazolidinone 7d: mp 73 °C; IR (KBr), ν_{max}: 3450-3400, 2960, 1810, 1690, 1610, 1260, 1170, 1060, 770, 710 cm^{-1}; MS, m/e (rel. int.): 295 (M^+, 5), 267 (6) 251 (15), 220 (10), 188 (30), 175 (45), 165 (75), 120 (40), 107 (35), 92 (50), 77 (40), 57 (80), 43 (100); ^{1}H-NMR ($CDCl_3$), δ: 3.25 (s, 2H), 3.95 (s, 3H), 4.04 (b, 1H, NH), 6.95-7.95 (m, 11H); Anal Found: C, 72.64; H, 5.51; N, 4.43%. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74%.

7) Oxazolidinone 7f: mp 90 °C; IR (KBr), ν_{max}: 3400, 1770, 1600, 1530, 1440, 1230, 810 cm^{-1}; MS, m/e (rel. int.): 320 (M^+,2), 280 (3), 264 (5), 252 (4), 230 (10), 228 (12), 193 (20), 170 (10), 169 (70), 153 (40), 141 (60), 105 (20), 77 (65), 43 (100); ^{1}H-NMR ($CDCl_3$), δ: 3.40 (s, 2H), 4.50 (b, 1H, NH), 6.70 (d, 1H, J = 12.50 Hz), 6.95 (d, 1H, J = 12.50 Hz), and 7.30-8.10 (m, 9H); Anal Found: C, 65.52; H, 4.31; N, 9.21%. Calcd for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.54; N, 9.02%.

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