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DIRECTED FUNCTIONALIZATION OF TRANS-1,2-DICHLOROCYCLOHEXANE BY ETHOXYCARBONYLNITRENE

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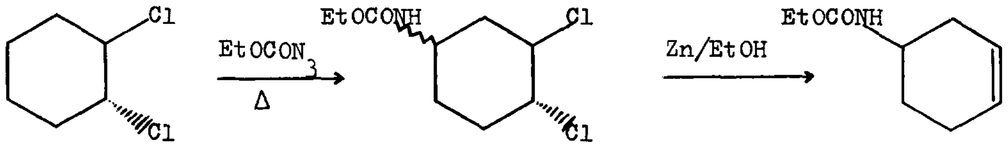
The decomposition of ethyl azidoformate in cyclohexene has been thoroughly investigated and it is known that a mixture of products is formed where N-carbethoxy-7-azabicyclo[4.1.0]heptane and 1-cyclohexenylurethan are the main products.[1]

It has been reported on the influence of halogenated solvents, and particularly chlorinated solvents, in affecting both the yields of insertion products and the insertion selectivity, probably due to stabilization of the singlet nitrene in a nitrene-solvent complex,[2-4] according to the proposal of Gleiter and Hoffmann.[5]

The complexing ability of chlorine atoms was used here to functionalize a peculiar position of a protected cyclohexene such as trans-1,2-dichlorocyclohexane 1, prepared by chlorine addition to cyclohexene.[6] We could actually obtain the transformation outlined below, in good yield.



1 2 3

Ethyl N-(trans-3,4-dichlorocyclohexyl)carbamate 2 was formed as the main product (77% by column chromatography, SiO_2, petroleum ether and then Et_2O) colourless viscous liquid in the thermolysis at 110° for 12 h of $EtOCON_3$ in trans-1,2-dichlorocyclohexane (volume ratio = 1:10): IR ($CHCl_3$) 3440 and 1710 cm^{-1}; NMR ($CDCl_3$) δ 1.8-2.2 (m), 4.1 (q+m); MS m/e 239 (M), 241 (M+2), 243 (M+4). 2 was dechlorinated by overnight reflux with Zn in EtOH. Ethyl N-(4-cyclohexenyl)carbamate 3 was formed in 85% yield; the identity of the product was established by comparison of g.l.c. retention times and IR, NMR, and mass spectra with those of an authentic specimen, prepared according to a reported procedure.[1]

Both chlorine atoms are required to obtain a single product in the reaction with ethoxycarbonylnitrene, the thermolysis of $EtOCON_3$ in chlorocyclohexane giving a mixture of isomeric urethans. In order to exclude that a deactivation effect of the chlorine atoms on the adjacent C-H bonds operate, we thermolyzed ethyl azidoformate at 110° for 12 h in 1,3-dichloropropane 4, 1,4-dichlorobutane 5, and 1,5-dichloropentane 6. All substrates gave the urethans arising from EtOCON insertion into the β and γ C-H bonds in 13-19% yields. 1,5-dichloropentane afforded both expected products (9 and 10) in the statistical ratio of 2/1 (Table I).

On the basis of these data we believe that the selectivity and the higher yield observed in trans-1,2-dichlorocyclohexane can be attributed to complexation of ethoxycarbonylnitrene by the two chlorine atoms on adjacent carbon atoms. Such a complex might approach preferentially the γ C-H bonds of another molecule of the substrate. Investigation on the behaviour of other dichloro compounds are in progress.

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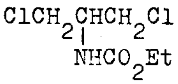
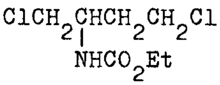
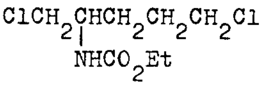
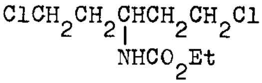
Table I. Urethans obtained from the thermolysis of $EtOCON_3$ in 1,3-dichloropropane 4, 1,4-dichlorobutane 5, and 1,5-dichloropentane 6.[a]

Compound	Products	Yield %[b]	IR($CHCl_3$) cm^{-1}	NMR($CDCl_3$) δ,ppm	MS, m/e
4	 $ClCH_2\underset{\substack{\mid\\ NHCO_2Et}}{C}HCH_2Cl$ 7	13	3420 1720	1.2(t,3H) 3.6–3.8(d+m,5H) 4.1(q,2H) 5.0(broad,1H)	201(M+2) 199(M,2%) 150(100%) 78(87%)
5	 $ClCH_2\underset{\substack{\mid\\ NHCO_2Et}}{C}HCH_2CH_2Cl$ 8	19	3420 1710	1.2(t,3H) 2.0(m,2H) 3.6(m,5H) 4.2(q,2H) 4.9(broad,1H)	215(M+2) 213(M,<1%) 164(100%) 150(29%) 92(52%) 78(58%)
6	 $ClCH_2\underset{\substack{\mid\\ NHCO_2Et}}{C}HCH_2CH_2CH_2Cl$ 9	11	3420 1710	1.3(t+m,5H) 1.9(m,2H) 3.6(m,4H) 3.9(m,1H) 4.1(q,2H) 4.9(broad,1H)	229(M+2) 227(M,<1%) 178(100%) 150(36%) 106(48%) 78(52%)
	+				
	 $ClCH_2CH_2\underset{\substack{\mid\\ NHCO_2Et}}{C}HCH_2CH_2Cl$ 10	5.5	3420 1710	1.3(t,3H) 2.0(q,4H) 3.6(t,4H) 4.0(m,1H) 4.1(q,2H) 4.6(broad,1H)	229(M+2) 227(M,<1%) 164(100%) 92(51%)

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[a] Volume ratio of $EtOCON_3$ to dichloroalkane = 1:10

[b] From $EtOCON_3$; products isolated by column chromatography

References

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