Intramolecular Insertion of Cyclopropylidenes into N–H Bonds and into C–H Bonds Adjacent to Nitrogen

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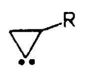
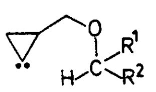
Summary Reaction of the amino-methyl- (V) and amino-ethyl-dibromocyclopropanes (IX, R^3 = H) with methyl-lithium leads to 3- and 2-azabicyclo[3.1.0]hexanes (VI) and (X) respectively in competition with the formation of allenes.

ALKYL substituted *gem*-dibromocyclopropanes generally react with methyl-lithium to give high yields of substituted allenes, by rearrangement of an intermediate carbenoid related to the cyclopropylidene (I).[1] However, the introduction of an oxygen atom as in (II) can activate the adjacent C–H bond towards a competitive carbenoid insertion, leading to (III).[2] In addition, introduction of an alcohol group as in (IV) causes competitive O-H insertion to produce a 2-oxabicyclo[3.1.0]hexane.[3]

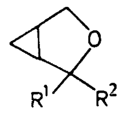
Reaction of (Va) with methyl-lithium in ether at 25—35 °C followed by quenching with H_2O leads to (VIa) and (VII, R = NMe_2) (*ca.* 1:1, 18%), but the major product is



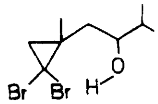
(I)



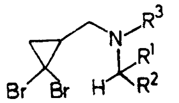
(II)



(III)

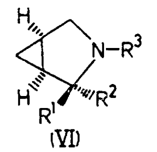


(IV)



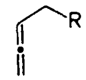
(V)

(a) $R^1 = R^2 = H, R^3 = Me$
(b) $R^1 = Me, R^2 = H, R^3 = Et$
(d) $R^1 = R^2 = Me, R^3 = Pr^i$
(e) $R^1 = R^2 = Me, R^3 = H$

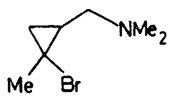


(VI)

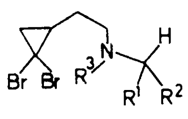
(a) $R^1 = R^2 = H, R^3 = Me$
(b) $R^1 = Me, R^2 = H, R^3 = Et$
(c) $R^1 = H, R^2 = Me, R^3 = Et$
(d) $R^1 = R^2 = Me, R^3 = Pr^i$
(e) $R^1 = R^2 = Me, R^3 = H$



(VII)

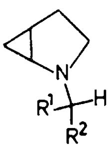


(VIII)



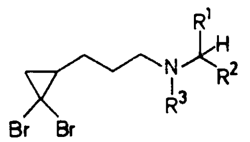
(IX)

(a) $R^1 = R^2 = Me, R^3 = Pr^i$
(b) $R^1 = R^2 = Me, R^3 = H$
(c) $R^1 = R^2 = R^3 = H$



(X)

(b) $R^1 = R^2 = Me$
(c) $R^1 = R^2 = H$



(XI)

the methylated derivative (VIII). However, (Vb) is converted into the isomers (VIb), (VIc),† and (VII, R = NEt_2) (*ca.* 5 : 3 : 3, 68%). In the case of (Vd), the insertion product (VId) is formed in high yield together with only a small quantity of the allene (VII, R = NPr^i_2) (*ca.* 6 : 1, 81% total). Thus the ease of insertion into C–H bonds adjacent to nitrogen[4] follows the order: tertiary > secondary > primary, as in the case of oxygen derivatives (II).

Reaction of (IXa) with MeLi leads to the allene (VII, R = $CH_2NPr^i_2$) (60%) and no insertion products are detected. However, (IXb) and (IXc) give no allenic product, but instead the two 2-azabicyclo[3.1.0]hexanes (Xb) (51%) and (Xc) (55%) respectively, derived by a carbenoid insertion into the N–H bond; the former showed in the n.m.r. spectrum τ 7·0 (m, 1H), 7·2 (dt, *J* 2·75 and 6 Hz, 1H), 7·57 (septet, *J* 6·5 Hz, 1H), 7·9—8·2 (m, 3H), 8·58 (dd, *J* 8 and 6 Hz, further split into t, *J* 4·5 Hz, 1H), 8·77 (d, *J* 6·5 Hz, 3H), 8·9 (d, *J* 6·5 Hz, 3H), 9·35 (ddd, *J* 2·75, 4·5, and 6 Hz, 1H), 9·9 (dt, *J* 8 and 6 Hz, 1H).

These results suggest that a 1,6-relationship between the carbene (carbenoid) and the hydrogen atom is necessary in order that an insertion should occur. Support for this was obtained in the conversion of (Ve) into (VIe) by reaction with methyl-lithium, when the allene and the product of N–H insertion are not observed. However, reaction of (XI, $R^1 = R^2 = Me$, $R^3 = Pr^i$) with MeLi leads only to the allene (VII, R = $CH_2CH_2NPr^i_2$), and no insertion at the $-CH_2-$ adjacent to nitrogen is observed; in contrast, (XI, $R^1 = R^2 = Me$, $R^3 = H$) and (XI, $R^1 = R^2 = R^3 = H$) lead to complex product mixtures which contain only small amounts of allene.

The above results provide relatively simple routes to a variety of substituted 2- and 3-azabicyclo[3.1.0]hexanes[5] and the scope of the reaction is being investigated further.

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† The n.m.r. spectra of 3-azabicyclo[3.1.0]hexanes were in good agreement with the detailed analysis by D. Wendisch and W. Naegele, *Org. Magnetic Resonance*, 1970, **2**, 619.

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[4] A related insertion α to nitrogen leading to a tricyclic derivative has been discussed: R. F. Boswell and R. G. Bass, *J. Org. Chem.*, 1975, **40**, 2419.
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