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NEIGHBOURING GROUP PARTICIPATION IN ELECTROPHILIC ADDITION TO ACETYLENES. 5-METHYLENE OXAZOLINES FROM 3-BENZAMIDOPROPYNE.

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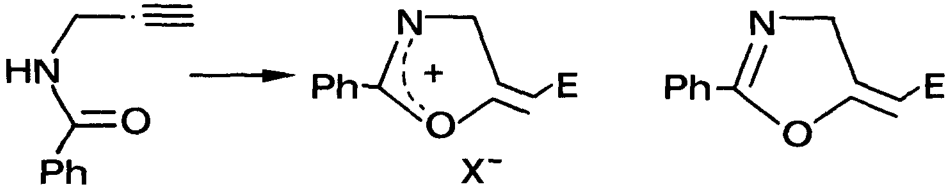
Summary. Benzamido group participates in addition of various electrophiles to triple bond leading to 5-methylene oxazolines.

The pronounced tendency of a neighbouring benzamido group to participate in electrophilic additions to carbon-carbon double bonds has been widely investigated:oxazolines[1], oxazines[2] and spirobi-heterocyclic[3] compounds have been obtained by this route, depending on the structure of the substrate. By contrast the participation of the benzamido group in electrophilic addition to acetylenes has received much less attention.[4]

We wish to report here the reaction of 3-benzamidopropyne **1** with bromine, iodine and methyl(bismethylthio)sulphonium $(MeS)_2\overset{+}{S}Me$ hexachloroantimonate[5] which leads to stable 5-methylene oxazolines **3**.



1 **2** **3**

a, E = Br ; X = Br_3
b, E = I ; X = I_3
c, E = SMe; X = $SbCl_6$

a, E = Br
b, E = I
c, E = SMe

The reaction with bromine and iodine, carried out in chloroform at room temperature requires two equivalents of the halogen.

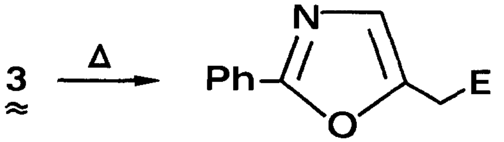
Perbromide **2a**[7] and periodide **2b** oxazolinium salts precipitate from the solutions in almost quantitative yield. Similarly the hexachloroantimonate **2c** is obtained by mixing equimolar amounts of **1** and the $(MeS)_2\overset{+}{S}Me$ salt in methylene chloride.[8]

Treatment of **2c** with $NaHCO_3$ solution and of **2a** and **2b** with Na_2SO_3-$NaHCO_3$ solution affords the corresponding free bases **3a-c**.[9]

The ir[10] and the nmr spectra (table) clearly indicate the same cyclic structure **3** for the compounds obtained; in particular the ^{13}C nmr data show the presence of a monosubstituted vinylic carbon whose chemical shift varies in **3a-c** according to the well known heavy atom effect.[11]

The methylene oxazolines **3** are stable either in acid or in alkaline media, however a fast exo-endo migration of the double bond occurs upon heating at 150°C. Thus **3a** and **3c** can be easily converted to 5-bromomethyl-2-phenyloxazole **4a** and 5-methylthiomethyl-2-phenyloxazole **4b** respectively.[12] Attempts to isomerize **3b** failed and extensive decomposition was observed.

Compound **4a** was also synthesized by bromination of 5-methyl-2-phenyloxazole with N-bromosuccinimide thus confirming the proposed structure.



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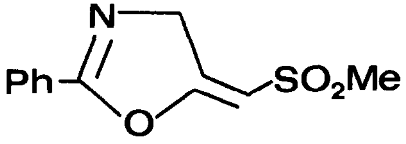
a, E = Br

b, E = SMe



5

Bromirenium, iodirenium and thirenium ions have been postulated in addition of bromo, iodo and sulphenic electrophiles to alkynes.[13] Thirenium ions have also been isolated as stable salts.[14] The E configuration of compounds **3** is suggested by the anti mode of ring opening of **6** by the neighbouring benzamido group. Further evidence arises from the observed magnitude of the deshielding of the 4-methylene protons of **5**[15] in respect to **3c** (table).

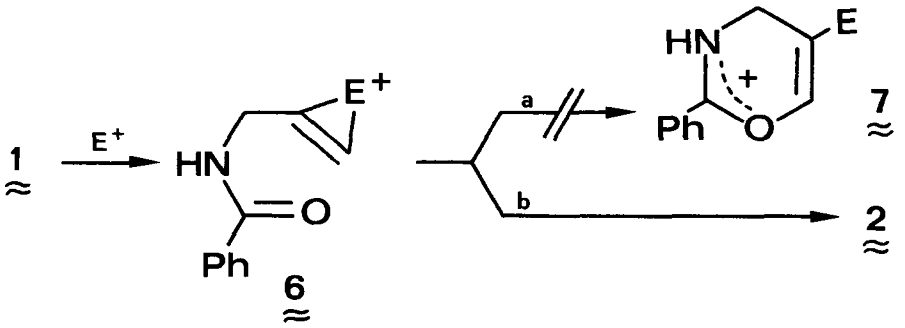
T A B L E

^{1}H and ^{13}C nmr parameters for compounds **3a**–c and **5**.

Chemical shifts in δ in $CDCl_3$ solutions at room temperature;J in Hz.

	^{1}H				^{13}C					
	Ph	CH	CH_2	Me	Ph	2-C	4-C	5-C	exo-C	Me
3a	8 0-7 3	6 02 (t) J=3 3	4 67 (d)	–	132 1 (d),128 6(d) 128 1 (d),127 5 (s)	163 6(s)	59 2(t)	155 6(s)	81 5 (d)	–
3b	8 0-7 4	5 77 (t) J=3 2	4 62 (d)	–	132 0(d),128 5(d) 127 9(d),126 5 (s)	163 7(s)	61 2(t)	157 9(s)	47 2 (d)	–
3c	8 0-7 3	5 80 (t) J=3 0	4 74 (d)	2 24(s)	131 8(d),128 5 (d) 128 0(d),126 6 (s)	163 4(s)	57 7(t)	159 7(s)	95 3 (d)	18 1(q)
5	8 2-7 4	6 27 (t) J=3 0	5 18(d)	3 07(s)						

In principle two reaction paths for cyclization can be expected:one leading to the oxazine derivatives **7** and the other to the oxazolines **2**. Preferential anti-Markownikov ring opening (path a) of intermediates similar to **6** has been established in various instances. The observed regiospecificity of the attack by the neighbouring benzamido group at the internal ethylenic carbon of **6** (path b) may be due to entropy factors which favour the 5-membered over the 6-membered ring closure. Moreover the low nucleophilicity of the oxygen atom may lead to a ring opening of the three membered intermediate with a developed S_N1 character giving Markownikov-type products.



The absence of the "normal" addition products indicates that neighbouring benzamido is a remarkable participating group also in addition to carbon-carbon triple bond.

The effect of substituents on the regioselectivity of the reaction as well as the participation of other neighbouring groups are currently in progress.

References and Notes

1. L.Goodman, S.Winstein and R.Boschan, *J.Amer.Chem.Soc.*, **80**, 4312 (1958).
2. S.P.McManus and R.A.Hames, *Tetrahedron Letters*, 4549 (1973).
3. G.Stagno d'Alcontres, C.Caristi, A.Ferlazzo and M.Gattuso, *J.C.S.Perkin I*, 1694 (1976).
4. F.Eloy, A.Deryckere, *Chim.Ther.*, **8**, 437 (1973).
5. The aptitude of methyl(bismethylthio) sulphonium ions to transfer a $Me\overset{+}{S}$ mojety to insaturated substrates has been reported.[6]
6. G.Capozzi, V.Lucchini and G.Modena, *Rev.Chem.Intermediates*, **2**, 347 (1979).
7. Compound **2a** behaves as a brominating agent:with acetone it gives bromoacetone and the corresponding hydrobromide.
8. Melting points: **2a** 100-103, **2b** 140-143; **2c** 111-113°C. Satisfactory elemental analyses were obtained for all the compounds described.
9. Melting points: **3a** 94-96; **3b** 116; **3c** 47-49°C.
10. NH stretching is absent.
11. J.B.Stothers in "Carbon-13 NMR Spectroscopy", Academic Press, N.Y., 1972.
12. ¹H nmr in $CDCl_3$: **4a**, δ 8.1-7.4(m, 5H), 7.18(broad s, 1H), 4.57(broad s, 2H), **4b** δ 8.3-7.3 (m, 5H), 7.03(broad s, 1H), 3.72(broad s, 2H), 2.12(s, 3H).
13. For a review see: G.H.Schmid in "The chemistry of the carbon-carbon triple bond", S. Patai ed., Y.Wiley, N.Y., 1978.
14. G.Capozzi, V.Lucchini, G.Modena and P.Scrimin, *Tetrahedron Letters*, 911 (1977).
15. Compound **5** was obtained by oxidation of **3c** with trifluoroperacetic acid; it easily decompose and cannot be isolated in the pure state.

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