

Tetrahedron Letters 40 (1999) 29-32

TETRAHEDRON LETTERS

Reactions of Halodiazirines with Potassium Ethyl Xanthate

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Received 25 September 1998; revised 12 October 1998; accepted 13 October 1998

Abstract: Aryl halodiazarines are reduced by potassium ethyl xanthate to give benzonitrile as the major product along with significant amounts of a novel heterocyclic product, 3-phenyl-5-ethoxy-1,2,4-thiadiazole. A mechanism involving fragmentation of an N-substituted diazirine is considered. © 1998 Elsevier Science Ltd. All rights reserved.

The mechanisms by which halodiazirines of general type 1 react with nucleophiles remains an area of fascination.^{1, 2} The $S_N 2'$ mechanism for reaction of 1 with azide ion is now well documented,³ as is the $S_{RN}1$ mechanism.⁴ Recently, Moss has found an unusual variation of the $S_{RN}1$ mechanism using acetate ion.⁵ Bertrand has found that phosphines react to give an unusual delocalized phosphonium salt.⁶ In other words, azide, fluoride, acetate, phosphines, thiophenoxide, and organometallic reagents give, in many instances, very different types of products by a number of mechanistic processes which are still not completely understood. Some of these processes studied by us and others are summarized below.



With the goal of better understanding the reaction of sulfur containing nucleophiles with 1, we have now carried out a study of the reaction of phenylbromodiazirine, 2, with potassium ethyl xanthate, 3. A fascinating series of color changes accompany this reaction which occurs readily at room temperature. Over the course of the reaction, the mixture changes from light yellow to green, to blue, to violet, and finally, to red. Benzonitrile is the major product formed in this reaction (87%), along with a significant amount (13%) of the heterocycle $5.^7$ The structure of this product was assigned by standard spectroscopic methods.⁸ The



atom connectivity was established using ¹⁵N NMR and ¹³C NMR on a sample of the heterocycle prepared from the triply labeled substrate 2^* , which gives a product 5^* . The ¹⁵N-¹⁵N coupling in 5^* is relatively small (1.3 Hz; two bond coupling) and the ¹⁵N atoms are both coupled in expected fashion to the additional ¹³C atoms in both rings.^{9,10} Additionally, 5 undergoes a facile substitution reaction with methoxide ion at room temperature to form the analogous methoxy derivative 7. This substitution reaction presumably proceeds via the conjugated sulfur stabilized anionic intermediate 6.



The fate of the second nitrogen atom in the benzonitrile forming reaction, as well as the sulfur atom in the process that leads to 5 is also of interest. The second nitrogen atom ends up partially as the thioamide, 8 (20%). Monitoring the reaction by 15 N NMR in DMSO-d₆ shows that 8 is not a primary product, but is formed during the aqueous workup. Also formed is a small amount of the ethylated xanthate 9. Finally, elemental sulfur is also formed in high yield.



Since benzonitrile is the major aromatic product formed, at first glance, the process might seem to be analogous to the reaction of thiophenoxide with halodiazirines.¹¹ However, the kinetic behavior is substantially different from any behavior that we have previously observed. Typical phenylbromodiazirine rate data are shown below. Phenylbromodiazirine disappears in a first order process when an excess of xanthate is used. However, phenylchlorodiazirine, which gives the same products as phenylbromodiazirine, does not disappear in a first order process. The reaction of phenylchlorodiazirine and other arylchlorodiazirines appears to be autocatalytic, and a typical plot is shown below for phenylchlorodiazirine. The xanthate reaction therefore contrasts with the thiophenoxide reaction, which is first order in chlorodiazirine in the S_N2' process,³ and shows an induction period under photoinitiated $S_{RN}1$ conditions.⁴



The mechanism of the reaction of xanthate ion with halodiazirines warrants some comment. Electronwithdrawing substituents on the aryl group speed up the reaction but the effect is not large. With respect to the leaving group, the reactivity of phenylfluorodiazirine has been compared to that of *p*-tolylchlorodiazirine, 12, by means of a direct competition experiment. During the time required for *p*-tolylchlorodiazirine to react completely with potassium ethyl xanthate (40 hours), phenylfluorodiazirine present in the mixture is completely unreacted. In a separate competition experiment, phenylchlorodiazirine reacts completely with xanthate leaving *p*-tolylfluorodiazirine, 11, untouched. By way of contrast, relative rates of the electron transfer initiated S_{RN1} reaction of azide ion with the fluorodiazirine 11 is only 2.6 times less reactive than the chlorodiazirine 12. The step that determines relative reactivity in the S_{RN1} reaction involves an electron transfer to the competing halodiazirines to give intermediates such as 13. Since the carbon-halogen bond is not being broken in the formation of 11, electron transfer to fluorodiazirines vs. chlorodiazirines is a relatively unselective reaction. This contrasts with the very selective reaction of xanthate with chlorodiazirines at the exclusion of fluorodiazirines. Hence the xanthate reaction does not appear to be an electron transfer initiated process.



While the complete mechanism of the xanthate reaction is uncertain, the partial mechanism presented below merits consideration. Formation of the substitution product 14 by some mechanism could be followed by fragmentation of the weak N-N bond of this formally antiaromatic compound. Further N-C bond fragmentation would give benzonitrile and the sulfur stabilized nitrene 15. While, at first glance, this fragmentation to a nitrene intermediate might seem to be unreasonable, computational studies (HF/6-31G⁺) suggest that fragmentation of the methyl analog of 14 to CH₃CN and the nitrene 15 is not an unfavorable process; it is essentially thermoneutral. Rearrangement of this nitrene forms the necessary N-C bond required in the nitrogen containing product 8. Cyclization of a biradical 16 (or the nitrene 17) would result

in 18 (or the zwitterionic analog). Further cyclization and sulfur extrusion would generate the heterocyclic compound 5.



There are a number of other questions that need to be answered. What is the origin of the ethylated xanthate 9? Why do arylchlorodiazirines show non-first order behavior? What is responsible for the color changes that accompany the reaction? These questions, which are currently under investigation, suggest that a variety of fascinating reactive intermediates and products are derived from reaction of xanthate ion with halodiazirines.

Acknowledgment is made to the National Science Foundation for support of this research.

References and Notes

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