Pergamon

Tetrahedron Letters, Vol. 38, No. 51, pp. 8793-8794, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10418-X

[3+2]-Cycloaddition Reactions of Alkynyl(phenyl)iodonium Triflates with Ethyl Diazoacetate, N-t-Butyl-α-phenyl Nitrone and t-Butylnitrileoxide as 1,3-Dipoles

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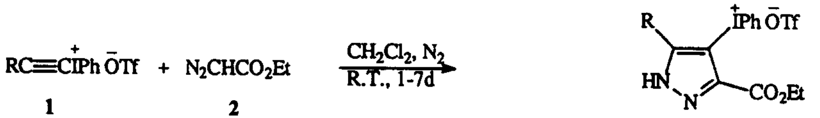
Abstract: The [3+2]-cycloaddition of various β-substituted ethynyliodonium salts, $RC{\equiv}C\overset{+}{I}\overset{-}{O}Tf$, with ethyl diazoacetate, N-t-butyl-α-phenyl nitrone and t-butylnitrile oxide results in single regioisomeric pyrroles, dihydroisoxazoles, and isoxazoles respectively in moderate yields. © 1997 Elsevier Science Ltd.

Cycloadditions are among the most important and useful synthetic reactions in organic chemistry.[1] Appropriately substituted olefins and alkynes readily undergo Diels-Alder as well as 1,3-dipolar cycloadditions resulting in synthetically useful carbocycles and heterocycles, respectively. Alkynyliodonium salts represent a relatively recent class of electron deficient acetylenes with useful synthetic applications.[2] Whereas the Diels-Alder cycloaddition chemistry of alkynyliodonium salts has been explored[3] in some detail, there are only two limited reports[4] on the 1,3-dipolar cycloaddition of these species. Such 1,3-dipolar cycloadditions of alkynyliodonium salts are of interest both from a mechanistic perspective[5] as well as synthetically in the formation of diverse heterocycles.[6] Hence, herein we report the [3+2]-cycloadditions of β-functionalized ethynyl(phenyl) iodonium triflates with three different types of 1,3-dipoles.

Interaction of alkynyliodonium salts **1** with ethyl diazoacetate, **2**, resulted, after a 1,3-hydrogen shift, in the iodonium substituted pyrroles **3** in reasonable isolated yields (Scheme 1).



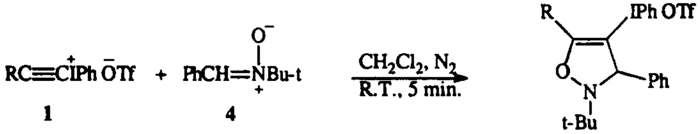
Scheme 1

3a: R = Me_3Si (76%); b: R = CN (57%); c: R = t-BuC(O) (63%)

The products were characterized by multinuclear NMR, IR and elemental analysis and/or HMS.[7,8] For **3a** an X-ray structure determination was carried out,[5a,8] thereby unambiguously establishing not only the structure but also the regiochemistry of the cycloadducts. The regiochemistry of addition is in accord with both electronic (frontier MO) and steric expectations.[5,9,10] Similarly, interaction of **1** with N-t-butyl-α-phenyl nitrone, **4**, gave dihydroisoxazoles **5** in moderate yields (Scheme 2).

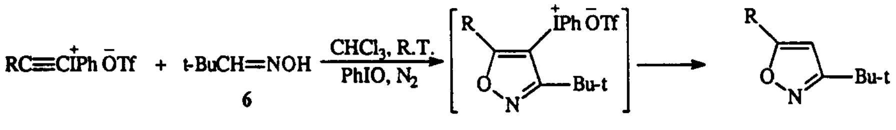
Likewise, reaction of **1** with *in situ* formed t-butyl-nitrile oxide resulted in isoxazoles **8** in reasonable yields (Scheme 3). As iodonium salts react[2] with nucleophiles or bases generally employed for the formation of nitrile oxides, the *in situ* oxidation of oxime **6** with idososobenzene was used in a one pot procedure for the formation of the required nitrile oxide (Scheme 3). However, this also resulted in the oxidation of the initially formed adduct **7** and loss of the iodonium moiety in the product isoxazoles **8**.

Both **5** and **8** were identified by spectral and physical means[7,8] and are in congruence with spectral data of related known[11] isoxazoles.

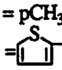


Scheme 2

5a: R = Me (58%);
b: R = Me_3Si (56%);
c: R = t-BuC(O) (44%)



Scheme 3 **7**

8a: R = MeOC(O) (48%)
b: R = t-BuC(O)(38%);
c: R = $pCH_3C_6H_4SO_2$ (52%)
d: R = C(O) (57%)

In summary, β-functionalized ethynyl(phenyl)iodonium triflates readily undergo 1,3-dipolar[3+2]-cycloadditions with ethyl diazoacetate, nitrones and nitrile oxides resulting in functionalized pyrroles, dihydroisoxazoles and isoxazoles, respectively in moderate isolated yields. In all three types of cycloadditions only a single regioisomer was observed in each reaction in accord with both steric and electronic expectations. As the iodonium moiety is readily displaced[12] by a wide variety of nucleophiles, the iodonium substituted heterocycles **3** and **5** may serve as useful precursors to a wide variety of hitherto unknown[6] functionalized heterocyclic systems.

Acknowledgements. Financial support by the NIH (CA16903) is gratefully acknowledged as are the Lady Davis Foundation and the hospitality of Professor Y. Apeloig during the writing of this ms. in Israel.

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(*Received in USA* 22 *July* 1997; *revised* 6 *October* 1997; *accepted* 9 *October* 1997)