Pergamon

Tetrahedron Letters 39 (1998) 5375–5376

TETRAHEDRON
LETTERS

Novel Heteroaromatic C-H Insertion of Alkylidenecarbenes. A New Entry to Furopyridine Synthesis

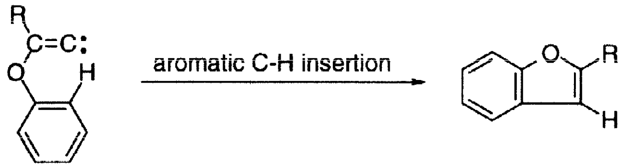
Tsugio Kitamura,* Kuniyuki Tsuda, and Yuzo Fujiwara

Department of Chemistry and Biochemistry, Graduate School of Engineering,
Kyushu University, Hakozaki, Fukuoka 812-8581, Japan

Received 18 April 1998; revised 14 May 1998; accepted 15 May 1998

Abstract: Reaction of alkynyl(phenyl)iodonium tosylates with 4-hydroxypyridine and 3-hydroxypyridine in the presence of potassium *tert*-butoxide undergoes a novel heteroaromatic C-H insertion of alkylidenecarbenes generated *in situ* to give the corresponding furopyridine derivatives. The heteroaromatic C-H insertion shows an extremely high selectivity compared with the possible aliphatic C-H insertion. This process is also applied to furoquinoline synthesis. © 1998 Elsevier Science Ltd. All rights reserved.

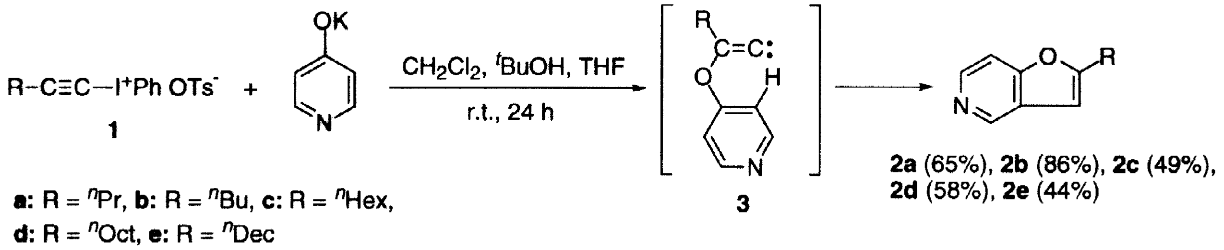
In gas phase reactions at a high temperature, aromatic C-H insertion of alkylidenecarbenes takes place to construct fused aromatic compounds.[1] But, very little is known about the aromatic C-H insertion of alkylidenecarbenes in the solution phase.[2] Very recently, we have found that 2-phenoxyalkylidenecarbenes generated by reaction of alkynyliodonium salts with phenoxide ion undergo the aromatic C-H insertion to give benzofuran derivatives.[3] The high selectivity of the aromatic C-H insertion and the deuterium incorporation have been observed in the reaction of the 2-phenoxyalkylidenecarbenes. This aromatic C-H insertion process using alkynyliodonium salts takes place under very mild conditions and has a great potential for synthetic use.



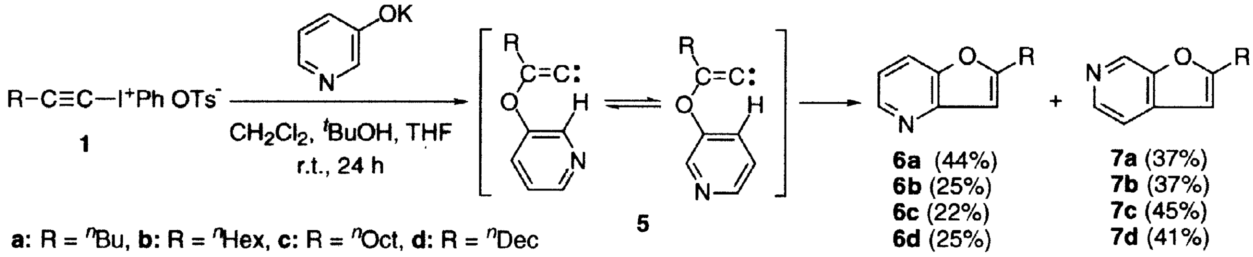
The aromatic C-H insertion reaction has been limited only to the phenyl ring. If the C-H insertion takes place even in heteroaromatic rings, this process will have a wide range of application to synthesis of heterocyclic compounds. In this paper, we wish to report a novel heteroaromatic C-H insertion of alkylidenecarbenes applicable to a new furopyridine synthesis.

Reaction of alkynyl(phenyl)iodonium tosylates (**1**)[4] with 4-hydroxypyridine was conducted in the presence of *t*-BuOK. First, the potassium salt of 4-hydroxypyridine was prepared by mixing of *t*-BuOK (1.1 mmol) and 4-hydroxypyridine (1.2 mmol) in *t*-BuOH and THF. Then, the solution of the potassium salt was added to a stirred solution of alkynyliodonium tosylates **1** (1.0 mmol) in CH_2Cl_2 and the mixture was stirred for 24 h at room temperature. The product was extracted with ether and separated purely by column chromatography on silica gel. The identified product was 2-substituted furo[3,2-*c*]pyridine (**2**). The furopyridines **2** were formed in good yields. The formation of furopyridines **2** demonstrates that 2-(4-pyridyloxy)alkylidenecarbenes (**3**) are generated by the reaction of alkynyliodonium tosylates **1** with the potassium salt of 4-hydroxypyridine and undergo the heteroaromatic C-H insertion. No (4-pyridyloxy)cyclopentenes (**4**) derived from the aliphatic C-H insertion were observed despite the existence of linear alkyl substituents such as *n*-propyl, *n*-butyl, *n*-hexyl, *n*-octyl and *n*-decyl groups. This means that the C-H insertion at the heteroaromatic ring precedes the aliphatic C-H insertion at the alkyl group.

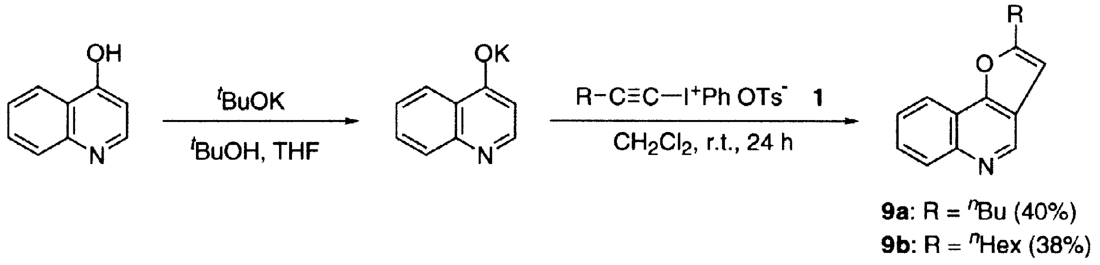
0040-4039/98/$19.00 © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)01034-X



Similarly, the reaction of alkynyliodonium tosylates **1** with 3-hydroxypyridine in the presence of *t*-BuOK was conducted. There are two kinds of C-H bonds available for the heteroaromatic C-H insertion since two conformers exist in the 2-(3-pyridyloxy)alkylidenecarbenes (**5**). Accordingly, the two kinds of products, 2-substituted furo[3,2-*b*]pyridines (**6**) and 2-substituted furo[2,3-*c*]pyridines (**7**), were obtained. These products were easily separated by column chromatography on silica gel. Again, no aliphatic C-H insertion giving (3-pyridyloxy)cyclopentenes (**8**) was observed.



Since the high selectivity is very useful for heterocycle synthesis, we have applied this method to the quinoline system. Treatment of the potassium salt of 4-hydroxyquinoline with alkynyliodonium tosylates **1b** and **1c** provides the corresponding furo[3,2-*c*]quinolines (**9a** and **9b**) in 40 and 38% yields, respectively. Therefore, the method developed in this study based on the heteroaromatic C-H insertion of alkylidenecarbenes has a wide range of application to synthesis of furopyridines and furoquinolines.



Acknowledgments This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan.

References

1. For a review on the gas phase reactions, see Brown, R. C. C.; Eastwood, F. W. *Synlett* **1993**, 9-19.
2. Kirmse, *Carbene Chemistry*, Academic Press: New York, 1971; Jones, M.; Moss, R. A. *Carbenes*, Wiley-Interscience: New York, 1973; Stang, P. J. *Chem. Rev.* **1978**, *78*, 383-405.
3. Kitamura, T.; Zheng, L.; Taniguchi, H.; Sakurai, M.; Tanaka, R. *Tetrahedron Lett.* **1993**, *34*, 4055-408; Kitamura, T.; Zheng, L.; Fukuoka, T.; Fujiwara, Y.; Taniguchi, H.; Sakurai, M.; Tanaka, R. *J. Chem. Soc. Perkin Trans. 2* **1997**, 1511-1515.
4. Kitamura, T.; Stang, P. J. *J. Org. Chem.* **1988**, *53*, 4105-4106.