

Received: May 5, 1981

Synthesis of Aromatic Trifluoromethyl Compounds by Ring
Expansion of Cycloienes*

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SUMMARY

Chlorotrifluoromethyl-1-diazirine was used for a source of chlorotrifluoromethyl carbene. The carbene added to cyclic dienes to give trifluoromethylated six-membered aromatic compounds. Thus, pyrrole gave 3-(trifluoromethyl)pyridine and cyclopentadiene gave benzotrifluoride.

In the course of our research to develop a new synthetic method for aromatic trifluoromethyl compounds [1], we planned to use the reaction of chlorotrifluoromethyl carbene ($\underline{1}$) with a five-membered cyclic diene. The reaction of pyrrole with dichlorocarbene was reported to give 3-chloropyridine [2]. Therefore, we expected that the similar type of reaction of $\underline{1}$ with a five-membered cyclic diene would provide a new method for the syntheses of aromatic trifluoromethyl compounds. We chose chlorotrifluoromethyl-1-diazirine ($\underline{2}$) [3] as the precursor of $\underline{1}$.

* Part of this work was presented at the 98th Annual Meeting of the Pharmaceutical Society of Japan, Okayama, March, 1978.

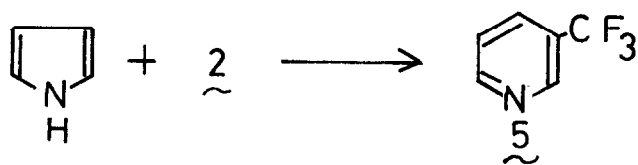
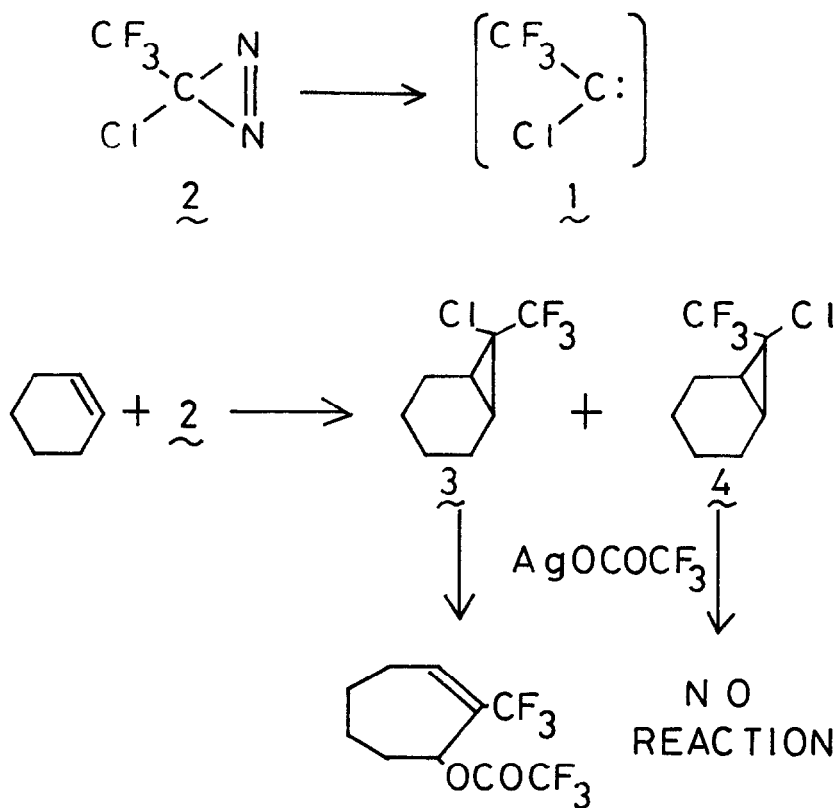


Chart 1

First, we examined the reaction of 2 with cyclohexene to learn the reactivity of 1. Heating the solution of 2 in cyclohexene at 120° for 3 h gave two adducts (3 and 4). Both products were separated by the preparative g.l.c. using a DEGS column of 7 m at 60°C. 3: 36%; m/e 198 (M⁺); ¹H-NMR δ(CDCl₃) 0.88-2.60 (m); ¹⁹F-NMR δ [4] 10.2. 4: 10% m/e 198; ¹H-NMR δ(CDCl₃) 0.80-2.60; ¹⁹F-NMR δ -1.2. Compound 3 reacted with silver trifluoroacetate to give 2-(trifluoromethyl)cyclohepten-3-yl trifluoroacetate, while 4 did not. This result established the Stereochemistry of both products as shown in Chart 1. This reaction showed that 2 was a good precursor of 1 and that 1 had a high reactivity to a double bond.

To utilize this reaction for the synthesis of an aromatic trifluoromethyl compound, thermolysis of 2 with five-membered cyclic dienes was investigated. A solution of 2 (230 mg) in pyrrole (500 mg) was sealed in a Pyrex tube under vacuum and heated at 120°C for 2 h. The reaction mixture was purified by a trap-to-trap distillation. Analysis of the distillate by g.l.c. showed that 3-(trifluoromethyl)pyridine (5) was obtained in 35% yield based on 2. The g.l.c.-mass spectrum and ¹⁹F-NMR of 5 were identical with those of the authentic sample [5]. Similar thermolysis and work-up of a solution of 2 (160 mg) in cyclopentadiene (550 mg) at 140°C for 3 h gave benzo-trifluoride in 23% yield. All the results are summarized in Chart 1.

The characteristic point of this procedure is that a trifluoromethyl group was introduced to a five membered ring with one carbon atom under ring expansion. Yields shown above were not optimized and this method can be used for synthesis of some aromatic trifluoromethyl compounds, which are difficult to synthesize by the usual methods.

REFERENCES

- 1 See Y. Kobayashi, K. Yamamoto, J. Chem. Soc., Perkin Trans. I. (1980), , and references therein.
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- 3 M. W. Grayston, and D. M. Lemal, *J. Am. Chem. Soc.*, 98 (1976) 1278.
- 4 Benzotrifluoride was used as an internal standard.
- 5 M. S. Raasch, *J. Org. Chem.*, 27 (1962) 1406.