YLIDE-INDUCED YLIDE FORMATION: A NOVEL DOUBLE CYCLOADDITION REACTION OF A [1,2,4]TRIAZOLO[1,5-a]PYRIMIDINIUM YLIDES

Mikio Hori,* Tadashi Kataoka, Hiroshi Shimizu, Eiji Imai

Gifu Pharmaceutical University, 5-6-1, Mitahora-higashi, Gifu 502,

Kiyomi Tanaka, Kazuhiko Kimura, Yoshinobu Hashimoto

Kaken Pharmaceutical Co., Ltd., 2-28-8, Honkomagome, Bunkyo-ku, Tokyo 113,

Masaru Kido

Otsuka Pharmaceutical Co., Ltd., Kawauchi-cho, Tokushima 771-01, Japan

Abstract: Treatment of 5,7-dimethyl-3-phenacyl[1,2,4]triazolo[1,5-<u>a</u>]pyrimidinium ylide (<u>2</u>) with methyl propiolate leads to a novel double cycloaddition and resulted in the formation of 3,9-dihydropyrazolo[1,5-<u>c</u>]pyrimidine derivative (<u>4</u>).

We recently reported the generation of 5,7-dimethyl-3-phenacyl[1,2,4]triazolo[1,5-<u>a</u>]pyrimidinium ylides and their thermal reactions¹ as a part of a systematic investigation of [1,2,4]triazolo[1,5-<u>a</u>]pyrimidinium ylides. We now report the double 1,3-dipolar cycloaddition reaction of the ylides with methyl propiolate (MP). This reaction is the first example of the double 1,3-dipolar cycloaddition reaction with dipolarophiles.



Iminium salt $(\underline{1})^1$ was treated with triethylamine in the presence of MP in dry acetonitrile at 0°C for 1.5 h. We isolated two products; pyrimidine deriva-tive $(\underline{3})$ (18,5 %) and pyrazolo $[1,5-\underline{c}]$ pyrimidine $(\underline{4})$ (26.6 %).

The product <u>3</u> was identical with authentic sample.¹ The new product <u>4</u> was 1:2 adduct of the ylide <u>2</u> and MP from mass spectrum. No 1:1 adduct was obtained from the reaction. ¹H-NMR spectrum of <u>4</u> showed a mixture of the two diastereoisomers (<u>4a</u>,<u>b</u>) in the ratio of 5:4. The major isomer (<u>4a</u>) was separated by fractional recrystallization from ether as colorless needles (mp 150-152°C). The ¹³C-NMR of <u>4a</u> showed a singlet for C(9) and a quartet for C(9)-Me at δ 63.8 and 22.2, respectively. The ¹H-NMR of <u>4a</u>² indicated the existence of allylic protons [δ 5.13 (1H, q, J=1.4 Hz), 6.56 (1H, d, J=1.4 Hz)] and a shielded methyl group [δ 1.37 (s, 3H)]. Moreover, when the C(9)-Me (δ 1.37) was irradiated, 20 % of nuclear Overhauser effect (NOE) was observed at C(3)-H (δ 3.65). These results are in good accordance with the structure of <u>4a</u>, and the structure was further confirmed by X-ray analysis.³

The plausible formation mechanism of $\underline{4}$ involves the addition of the ylide (<u>2B</u>), which is one of resonance structures of azomethine ylide (<u>2A</u>), with 2 eq. of MP to give tetracyclic compound (<u>5</u>). The intermediate (<u>5</u>) readily affords ring-opened product (<u>4</u>). This novel reaction provides a new synthetic route to 3,9-dihydropyrazolo[1,5-c]pyrimidine derivatives.

Cycloaddition reaction of [1,2,4]triazolo $[1,5-\underline{a}]$ pyrimidine itself did not proceed, indicating no ylidic nature of the triazolopyrimidine ring. However, the ylidic nature was induced by construction of the exo-ylide (<u>2A</u>). We would like to name such ylide (<u>2B</u>) the "ylide-induced ylide" and further investigation in this area is under way.

References and Notes

- M. Hori, K. Tanaka, T. Kataoka, H. Shimizu, E. Imai, K. Kimura, and Y. Hashimoto, <u>Tetrahedron Lett.</u>, 1985, <u>26</u>, 1320; <u>J. Chem. Soc. Perkin Trans</u> <u>1</u>, in the press.
- 1, in the press.
 2 IH-NMR data of <u>4a</u> (CDCl₃, 400 MHz). 67.98 (lH, d, J=1.9 Hz), 7.89-7.45
 (m, 5H), 7.12 (lH, d, J=1.9 Hz), 6.56 (lH, d, J=1.4 Hz), 5.13 (lH, q, J=1.4
 Hz), 3.82 (s, 3H), 3.72 (s, 3H), 3.65 (lH, d, J=1.4 Hz), 1.96 (3H, d, J=1.4
 Hz), 1.37 (s, 3H).
- 3 The details of the X-ray structure analysis will be published in a full paper. (Received in Japan 26 October 1985)

718