

NOVEL RING TRANSFER REACTION OF FURANS VIA INTRAMOLECULAR DIELS-ALDER REACTION  
OF ALLENE INTERMEDIATE: A NEW DOUBLE ANNULATION REACTION

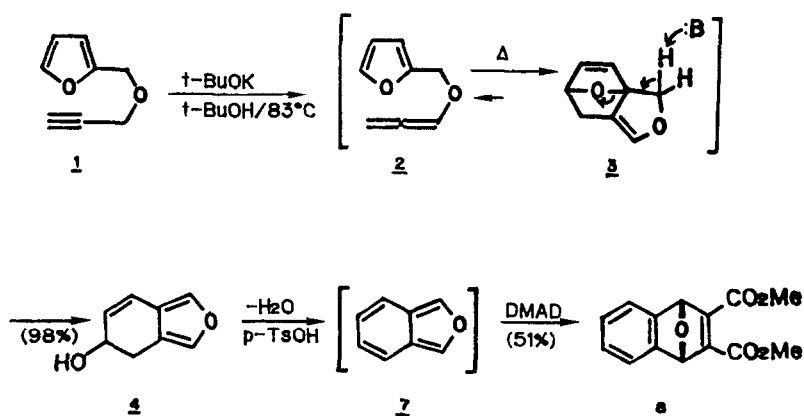
Kenji Hayakawa, Yasuchika Yamaguchi, and Ken Kanematsu\*  
Institute of Synthetic Organic Chemistry, Faculty of Pharmaceutical  
Sciences, Kyushu University 62, Higashi-ku, Fukuoka 812, Japan

Abstract: A novel ring transfer reaction of furans to fused furans by tandem intramolecular Diels-Alder reaction and base-catalyzed ring-opening of the adducts has been developed.

The intramolecular Diels-Alder reaction has been a central topic in modern organic synthesis.<sup>1</sup> The vast majority of the work reported in this area has dealt with reactions utilizing ethylenic and acetylenic dienophiles. However, in spite of its favorable geometry for  $\pi$  overlap, the intramolecular Diels-Alder reaction of allene has received less attention.<sup>2</sup> Previously, we demonstrated that the allenyl ether is a versatile synthon as the dienophile in the intramolecular cycloaddition due to the absence of unfavorable 1,3-diaxial interaction in its transition state.<sup>3</sup> Herein, we wish to report a novel ring transfer reaction of furans to fused furans by virtue of a facile intramolecular Diels-Alder reaction of allenyl ether with furan and base-catalyzed ring-opening of the resulting adduct. This general strategy may also open the way to a new generation of synthetically useful isobenzofurans.<sup>4</sup>

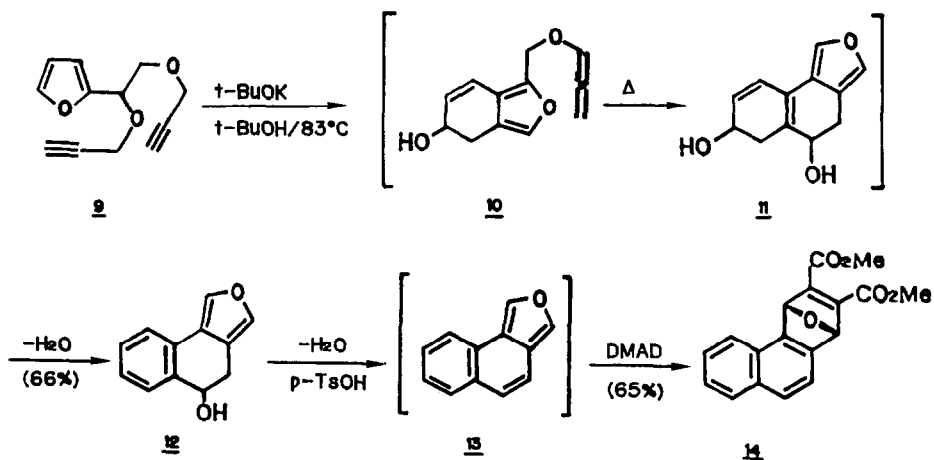
Due to the limited reactivity of furan, various devices have been made in order to facilitate the intramolecular Diels-Alder reactions of furans.<sup>5</sup> It was now found that the allenyl ether readily undergoes the intramolecular cycloaddition with furan without any activating groups. When a solution of the propargyl ether 1 (1.89 g, 13.9 mmol) and t-BuOK (3.12 g, 27.8 mmol) in t-BuOH (25 mL) was heated at 83 °C, 1 was rapidly consumed (10 min). The mixture was diluted with water (40 mL) and extracted with ether (3 x 30 mL). The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>-K<sub>2</sub>CO<sub>3</sub>, and evaporated in vacuo. The residue was chromatographed on silica gel containing 10% K<sub>2</sub>CO<sub>3</sub> with hexane-ethyl acetate (2:1) as an eluent to give 5-hydroxy-4,5-dihydroisobenzofuran (4)<sup>6,7</sup> (1.85 g, 98%) as a colorless oil, bp<sub>7</sub> 100 °C (Kugelrohr) (Scheme I). Compound 4 was confirmatively converted to the acetate 5<sup>7</sup> (Ac<sub>2</sub>O/pyridine; 95%) as well as to the tetrahydro derivative 6<sup>7</sup> (H<sub>2</sub>, 10% Pd/C, MeOH; 92%). The formation of 4 can be reasonably explained by the initial isomerization of 1 to the allenyl ether 2<sup>8</sup> which undergoes the intramolecular Diels-Alder reaction (to 3) followed by the base-catalyzed ring-opening of the strained oxa-bicyclo[2.2.1]hexene system as shown in Scheme I.

## Scheme I



Compound 4 was stable under basic to neutral conditions, but immediately polymerized by acid probably via the formation of isobenzofuran (7). This was confirmed by the trapping experiments. Thus, dropwise addition of 4 in THF to a THF solution of dimethyl acetylenedicarboxylate (DMAD) (2 equiv) and p-TsOH (1 equiv) at 25 °C led to the instantaneous formation of adduct 8<sup>9</sup> in 51% yield (Scheme I). Similarly, easy adduct formation with N-phenylmaleimide (78%) and naphthoquinone (72%) was confirmed.<sup>7</sup>

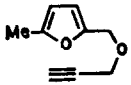
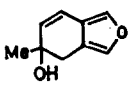
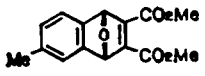
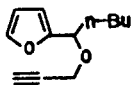
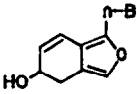
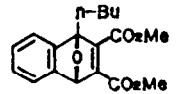
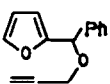
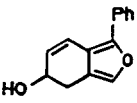
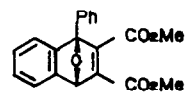
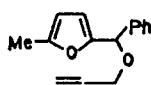
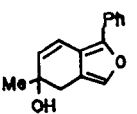
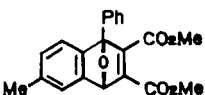
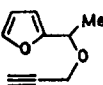
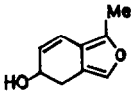
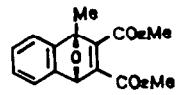
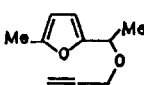
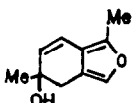
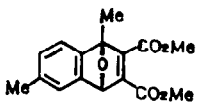
## Scheme II



As shown in Table I, the facile ring transfer reaction by tandem intramolecular Diels-Alder reaction and base-catalyzed ring-opening has been found to be general.<sup>7,10</sup> These products could serve as the good precursors of isobenzofurans as exemplified by the smooth adduct formation with DMAD on treatment with acid.

The fascinating feature of this methodology was demonstrated by the one-pot biscyclization of bispropargyl ether 9<sup>7,11</sup> (Scheme II). Treatment of 9 with t-BuOK (20 equiv) in t-BuOH at 83° C for 50 min gave 12<sup>12</sup> in 66% yield.<sup>13</sup> This

Table I. Ring Transfer Reactions of Furans and Acid-catalyzed Diels-Alder reactions with DMAD<sup>a</sup>

entry	substrate	reaction <sup>b</sup> time	product	yield <sup>c</sup> , %	Diels-Alder adduct	yield <sup>c</sup> , %
1		1.5 h		100		57
2		3 h <sup>d</sup>		93		35
3		1 h <sup>d</sup>		100		78
4		1 h		100		62
5		1 h		100		17
6		1 h		95		20

<sup>a</sup>See reference 7. <sup>b</sup>Unless otherwise noted, all reactions were carried out in *t*-BuOH at 83°C utilizing 20 equiv of *t*-BuOK. <sup>c</sup>Isolated yields. <sup>d</sup>10 equiv of *t*-BuOK was used.

can be regarded as the "double" furan ring transfer of **9** via **10** and **11** as shown in Scheme II. The acid-catalyzed reaction of **12** with DMAD afforded the adduct **14**<sup>14</sup> (65%) via the isonaphthofuran intermediate (**13**).

The facile intramolecular cycloaddition of allenyl ether with furan without any electronic activation is noteworthy and may be governed by its geometrical factors. This novel furan ring transfer reaction should find widespread use in organic synthesis, especially in the one-step construction of polycyclic carbon skeletons. Application of this methodology to the natural product synthesis is now in progress in our laboratories.

## References and Notes

- (1) For a recent review, see: Brieger, G.; Bennett, J. N. Chem. Rev., 1980, 80, 63.
- (2) For some examples of the intramolecular Diels-Alder reactions of allenic dienophiles, see: (a) Harrison, R. M.; Hobson, J. D.; Midgley, A. W. J. Chem. Soc., Perkin I, 1973, 1960. (b) Bartlett, A. J.; Laird, T.; Ollis, W. D. J. Chem. Soc., Perkin I, 1975, 1315. (c) Iwai, I.; Ide, J. Chem. Pharm. Bull., 1964, 12, 1094. (d) Himbert, G.; Diehl, K.; Maas, G. Chem. Commun., 1984, 900.
- (3) Hayakawa, K.; Yodo, M.; Ohsuki, S.; Kanematsu, K. J. Am. Chem. Soc. 1984, 106, 6735.
- (4) For recent reviews, see: (a) Wiersum, V. E. Aldrichimica Acta, 1981, 14, 53. (b) Friedrichsen, W. Advan. Heterocycl. Chem., 1980, 26, 135.
- (5) (a) Parker, K. A.; Adamchuck, M. R. Tetrahedron Lett., 1978, 1689. (b) Mukaiyama, T.; Iwasawa, N. Chem. Lett., 1981, 29. (c) Sternbach, D. D.; Rossana, D. M. J. Am. Chem. Soc. 1982, 104, 5853. (d) Van Royen, L. A.; Mijnheer, R.; Declercq, P. J. Tetrahedron Lett., 1983, 24, 3145. (e) Sternbach, D. D.; Rossana, D. M.; Onan, K. D. J. Org. Chem. 1984, 49, 3427. (f) Trost, B. M.; Lautens, M.; Hung, M.; Carmichael, C. S. J. Am. Chem. Soc. 1984, 106, 7641. (g) Jung, M. E.; Street, L. J. J. Am. Chem. Soc. 1984, 106, 8327.
- (6) Compound 4:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.31 (br s, 1H), 7.20 (br s, 1H), 6.53 (d,  $J = 10.0$  Hz, 1H), 5.92 (dd,  $J = 4.0$  and  $10.0$  Hz, 1H), 4.50 (dt,  $J = 5.5$  and  $4.0$  Hz, 1H), 2.81 (d,  $J = 5.5$  Hz, 2H), 1.62 (br s,  $\text{D}_2\text{O}$ -exchange, 1H); IR (neat)  $3340\text{ cm}^{-1}$ .
- (7) Satisfactory spectroscopic data were obtained for all new compounds.
- (8) Brandsma, L.; Verkruijsse, H. D. "Synthesis of Acetylenes, Allenes, and Cumulenes": Elsevier Scientific Publishing Co.: New York, 1981; pp 87-114.
- (9) Smith, J. G.; Dibble, P. W. J. Org. Chem. 1983, 48, 5361.
- (10) Application of this methodology to the synthesis of isobenzothiophenes and isoindoles is currently under investigation.
- (11) Compound 9 was prepared from furfural by (i) epoxy formation ( $\text{Me}_3\text{S}^+\text{I}^-$ , KOH, MeCN), (ii) diol formation (wet  $\text{SiO}_2$ ), and (iii) propargylation ( $n\text{-BuLi}$ , HMPA, THF;  $\text{HC}\equiv\text{CCH}_2\text{Br}$ ).
- (12) Compound 12:  $n_{\text{D}}^{22}$  1.6021;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.81 (br s,  $\text{D}_2\text{O}$  exchange, 1H), 2.97 (dm,  $J = 5.5$  Hz, 2H), 4.93 (t,  $J = 5.5$  Hz), 7.22-7.64 (m, 5H), 7.77 (br s, 1H); IR (neat)  $3370\text{ cm}^{-1}$ ; MS  $m/e$  186 ( $\text{M}^+$ ), 168 ( $\text{M}-18$ ).
- (13) 3-tert-Butoxy-1,3-dihydronaphtho[1,2-c]furan was also obtained as the minor product (17%).
- (14) Cornej, J. J.; Ghodsi, S.; Johnson, R. G.; Woodling, R.; Rikborn, B. J. Org. Chem. 1983, 48, 2869.

(Received in Japan 16 March 1985)