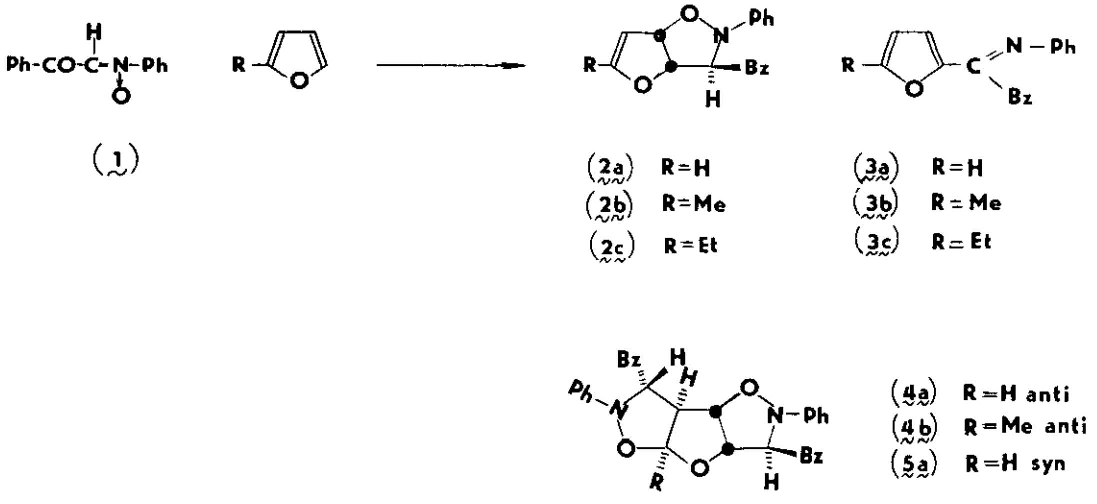
A 1,3-DIPOLAR CYCLOADDITION AND 1,3-ADDITION OF 2-METHYLFURAN.

Ľubor Fišera,*[1] Jaroslav Kováč and Jaroslava Poliačiková

Department of Organic Chemistry, Slovak Technical University,
Jánska 1, 880 37 Bratislava, Czechoslovakia

Abstract - A 1,3-dipolar cycloaddition reaction of 2-methyl- and 2-ethylfurans with C-benzoyl-N-phenylnitron has been carried out. A 1,3-dipolar cycloaddition product and a non-cyclic addition product were obtained, under the different molar ratio of the starting components.

On the basis of the perturbation interaction diagram for 1,3-dipolar cycloaddition reactions of nitrones with furan we have found [2] that the reaction rate is controlled by the LU$_{1,3\text{-dipole}}$-HO$_{\text{furan}}$ interaction. Through the reaction of C-benzoyl-N-phenylnitrone (1) with furan at 60° the monocycloadduct (2a) and two biscycloadducts (4a) and (5a) [3] have been isolated. No 1,3-addition product (3a) (non cyclic addition product) has been found. Now, we would like to report the reaction of 1 with 2-methyl and 2-ethylfurans where, beside the 1,3-dipolar cycloaddition, there has also occured a 1,3-addition.



(1)

(2a) R=H
(2b) R=Me
(2c) R=Et

(3a) R=H
(3b) R=Me
(3c) R=Et

(4a) R=H anti
(4b) R=Me anti
(5a) R=H syn

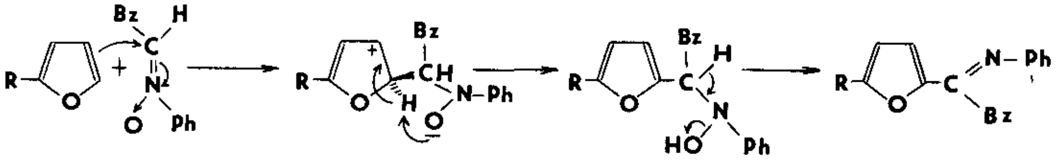
Scheme 1

Caramella [4] is reported to have found in the reaction of benzennitrile oxide (BNO) with furan a 1,3-addition product, beside two monocycloadducts. Firestone [5] has explained the origin of the 1,3-addition product as the hydrogen shift from the appropriate biradical intermediate, in this way he explained the course of all the 1,3-dipolar cycloaddition reactions on heterocyclic compounds.

It is obvious from the perturbation interaction diagram [2] that the electron-releasing substituents on the furan ring will increase the reactivity, because they increase the HOMO energy and thus lower the difference on the frontier orbitals of the $LU_{\mathbf{1}}$-HO_{furan} [6] interaction. Besides decreasing the IP value the methyl group in the 2-methylfuran may stabilise the biradical or zwitterionic intermediates eventually formed.

After the reaction of **1** at 60° under N_2 with the exclusion of light in excess of 2-methylfuran and after removal of the solvent in vacuo, the reaction products of the cycloaddition (**2b**) (37 %) and (**4b**) (14 %), as well as the 1,3-addition products (**3b**) (9 %) were separated on preparative silica gel TLC plates (thickness 2 mm, eluant chloroform - n-heptane 8:2). Through the reaction of **1** with 2-ethylfuran we were able to isolate the monocycloadduts (**2c**) (47 %) and the 1,3-addition product (**3c**) (11 %). **2b**, **2c**, **3b**, **3c** and **4b** structures have been assigned on the basis of the following spectroscopic evidence [7]. Structure **2b** was established according to the ^{1}H-NMR and UV spectra with the monocycloadduct **2a** [2]. The attribution of structure **3b** to the 2,5-disubstituted furan derivate followed the value of interaction constant J_{3-4} = 3.5 Hz, typical for furan derivatives, mainly the value λ_{max}^{MeOH} = 293 nm, which has proved the restoration of the heterocyclic furan system. Further, the value of the valence vibration ν (CO) 1665 cm^{-1} for **3b** compared with the value of 1681 cm^{-1} for **2b**, testifies an α, β -unsaturated system. The transiently formed 1,3-addition product (**7**) spontaneously released H_2O as it is obvious from the value of the molecular peak 289 (**2b** - 18) and from the absence of valence vibration of the OH-groups in the IR spectrum.

The origin of the 1,3-addition products **3b** and **3c** may be accounted for the attack of the electrophilic terminal carbon in the 1,3-dipole **1** through the zwitterionic intermediate (**6**) (Scheme 2).



(**6**) (**7**) (**3b**), (**3c**)

Scheme 2

If **1** reacted under similar conditions in large excess of 2-methylfuran, the 1,3-dipolar cycloaddition product only was formed with the high yield of 88 %. The presence of **3b** was determined neither by ^{1}H-NMR spectroscopy nor in the reaction mixture without isolation.

Thus, in the reaction of **1** with 2-methylfuran there must be two competitive reactions next to each other; the one to form **2b** by 1,3-dipolar cycloaddition and the stepwise one to form **3b** by the 1,3-addition through zwitterion **6**. With a large excess of the dipolarophile, only the 1,3-dipolar cycloaddition took place. The formation of the cycloadduct **2b** could apparently be also explained through the zwitterion **6**; in this case, howewer, the substitution product **3b** would exclusively, be formed, due to the restoration of the heterocyclic system. The present day knowledge of cycloadditions with nitrones makes the concerted mechanism for the 1,3-dipolar cycloaddition of nitrones to be the most probable [8].

In our case the portion of the 1,3-addition product **3b** was surprisingly high, in relation to the product of the 1,3-dipolar cycloaddition (1:4), (equally as with **3c** to **2c**). In the cycloaddition of BNO with furan the ratio was 1:91 (determined by GLC without isolation) and for 2-methylfuran the formation of the 1,3-addition product was not even described [4]. We have determined the ratio of the cycloaddition and that of the 1,3-addition directly from the reaction mixture without isolation, from the integrated intensites of the methyl group signals in **2b** and **3b**. The investigation of the reaction mixture by GLC was not possible, in our case, as **2b** undergoes a cycloreversion at the temperature of 130°C, according to DTA values.

Acknowledgement. We are grateful to Professors R. Huisgen, E. Meyers and Elguerro for helpful discussions.

References and Notes

1. Part 138 in the series Furan Derivatives, Part 2 in 1,3-Dipolar Cycloadditions of Heterocycles.
2. Ľ. Fišera, J. Kováč, J. Poliačiková and J. Leško, Monatsh. Chem. (in press).
3. Futher reaction product of **1** such as azoxybenzene, benzanilide, phenyl glyoxylicanilide, benzoic acid and phenyl glyoxylic acid were obtained.
4. P. Caramella, G. Cellerino, A. Corsico Coda, A. Gamba Invernizzi, P. Grünanger, K. N. Houk and F. Marinone Albini, J. Org. Chem., 1976, **41**, 3349.
5. R. A. Firestone, Tetrahedron, 1977, **33**, 3009.
6. Dr. H.-J. Timpe from Merseburg has determined for us the IP values for 2-methylfuran (IP = 8.25 eV) and for 2-ethylfuran (IP = 8.22 eV) from their CT-Complex with TCNE. For furan the value is IP = 8.81 eV.
7. All new compounds have been crystallized from CH_2Cl_2 - n-hexane and give correct analytical values.

   Compound **3b**, m.p. 120-122°, uv$_{max}$ (MeOH) 246 nm (4.43); ir ν_{max} (CCl_4) 1681 cm^{-1} (C=O); mass m/e 307 (M^{+}) and nmr δ ($CDCl_3$) 1.31 (3H, s, CH_3),

4.72 (1H, d, *J* 0.5 Hz, C_6-H), 5.52 (1H, d-d, *J* 6.5 Hz, *J* 0.5 Hz, C_5-H), 5.72 (1H, s, C_3-H), 5.87 (1H, d, *J* 6.5 Hz, C_4-H) and 6.82-8.12 (10H, m, aromatic-H). Compound **3b**, m.p. 117°, uv_{max} (MeOH) 293 nm (4.27); ir ν_{max} (CCl_4) 1665 cm^{-1} (C=O); mass m/e 289 ($M^{+\cdot}$) and nmr δ ($CDCl_3$) 2.41 (3H, s, CH_3), 6.12 (1H, d, *J* 3.5 Hz, C_4-H), 6.67 (1H, d, *J* 3.5 Hz, C_3-H) and 6.83-7.82 (10H, m, aromatic-H). Compound **4b**, m p. 180-182°, uv_{max} (MeOH) 248 nm (4.65); ir ν_{max} (KBr) 1695 cm^{-1} (C=O) and nmr δ ($CDCl_3$) 1.41 (3H, s, CH_3), 3.97 (1H, s C_4'-H), 4.43 (1H, d, *J* 5.6 Hz, C_4-H), 5.18 and 5.41 (2H, each s, C_3-H and C_3'-H) and 6.75-8.01 (20H, m, aromatic-H). Compound **2c**, m.p. 91-93°, uv_{max} (MeOH) 248 nm (4.37); ir ν_{max} (KBr) 1683 cm^{-1} (C=O); mass m/e 225 and 96 (cycloreversion fragments), 105 (base peak) and nmr δ ($CDCl_3$) 0.68 (3H, t, *J* 7.0 Hz, CH_3), 1.62 (2H, q, *J* 7.0 Hz, CH_2), 4.70 (1H, d, *J* 1.0 Hz, C_6-H), 5.51 (1H, d-d, *J* 6.7 Hz, *J* 1,0 Hz, C_5-H), 5.67 (1H, s, C_3-H), 5.87 (1H, d, *J* 6.7 Hz, C_4-H) and 6.80--8.10 (10H, m, aromatic-H). Compound **3c**, m.p. 123-125°, uv_{max} (MeOH) 298 nm (4.14); ir ν_{max} (KBr) 1668 cm^{-1} (C=O); mass m/e 303 ($M^{+\cdot}$) and nmr δ ($CDCl_3$) 1.28 (3H, t, *J* 7.5 Hz, CH_3), 2.80 (2H, q, *J* 7.5 Hz, CH_2), 6.15 (1H, d, *J* 3.2 Hz, C_4-H), 6.68 (1H, d, *J* 3.2 Hz, C_3-H) and 6.82-7.82 (10H, m, aromatic-H).

8. For excellent source of references, see: R. Huisgen, *J. Org. Chem.*, 1976, **41**, 403.

Received, 19th April, 1979