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# The Cycloaddition Reaction of Isobenzofuran with Fulvenes: The Formation of an *endo*-(6+4)$\pi$ Adduct

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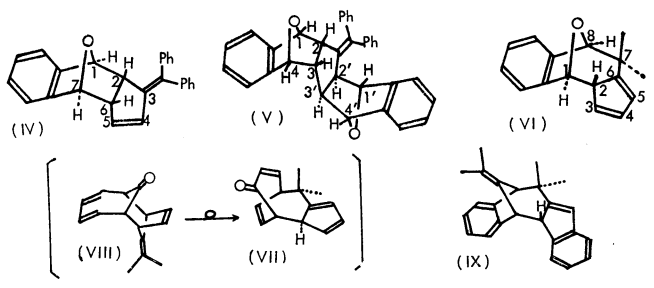
**Synopsis.** Isobenzofuran (I) was shown to react at 160 °C with 6,6-diphenylfulvene to give two *endo*-(2+4)$\pi$ cycloadducts, an *endo*-1: 1-adduct and an *endo-anti-endo*-1: 2-adduct. On the other hand, I and 6,6-dimethylfulvene gave an *endo*-(6+4)$\pi$ cycloadduct at room temperature.

Recently, we have reported the results on the cycloaddition reaction of isobenzofuran (I) with some typical tropones.[1] To extend the study to the reaction of I with other possible 6$\pi$-dienophiles, we have now carried out experiments with fulvenes, 6,6-diphenylfulvene (II), and 6,6-dimethylfulvene (III).

When II was placed to react with I, which has been generated at room temperature, it caused no change and resulted in the quantitative recovery of II. At higher temperatures (160—165 °C), however, a smooth reaction occurred to give two crystalline products, IV (48.1%) and V (14.9%). The structure of IV was, on the basis of the NMDR [$\delta$: 3.77 ($H_6$, ddd, $J$=7.5, 5.5, 2.5 Hz), 4.19 ($H_2$, dd, $J$=7.5, 5.5 Hz), 4.83 ($H_1$, d, $J$=5.5 Hz), 5.38 ($H_7$, d, $J$=5.5 Hz), 5.63 ($H_5$, dd, $J$=6.0, 2.5 Hz), 5.79 ($H_4$, d, $J$=6.0 Hz) and 6.65—7.4 (14H, m)] spectral evidence, identified as an *endo*-(2+4)-$\pi$ cycloadduct. The other compound, V, was shown to be a 1: 2-cycloadduct, and was independently proven to be formed from I and IV, having at least one *endo*-configuration. Furthermore, its NMR [$\delta$: 2.43 (2H, dd, $J$=9.0, 5.3 Hz), 2.93 (2H, dd, $J$=9.0, 5.3 Hz), 4.35 (2H, d, $J$=5.3 Hz), 5.23 (2H, d, $J$=5.3 Hz) and 6.8—7.4 (18H, m)] spectrum indicated the presence of an element of symmetry, ruling out two isomers of the *endo-anti-exo*- and *endo-syn-exo*-configurations. From the remaining two isomers (*endo-anti-endo*- and *endo-syn-endo*-adducts), the former must represent the structure, since it is impossible to construct the molecular frame with the latter. Accordingly, the observed chemical shifts of the methine protons are interpreted in terms of an up-field shift caused by the induced ring current from the aryl group of the other half of the molecule.[2] Obviously, the absence of the (6+4) $\pi$ cycloaddition process to give a *gem*-diphenyl derivative may be a result of the steric hindrance.




Chart

On the other hand, when III was treated with I at room temperature, a 1: 1-adduct (VI), a colorles liquid, was formed in a 25.0% yield. The NMR spectrum of VI showed the presence of a *gem*-dimethyl group and three olefinic protons [$\delta$: 1.22 (3H, s), 1.50 (3H, s), 5.56 ($H_5$, dddd, $J$=1.9, 1.4, 0.6, 0.5 Hz), 6.14 ($H_3$, ddd, $J$=5.5, 1.4, 1.0 Hz) and 6.20 ($H_4$, dd, $J$=5.5, 1.9Hz)], together with three methine protons and aromatic protons [$\delta$: 3.46 ($H_2$, ddd, $J$=5.2, 1.0, 0.5 Hz), 4.59 ($H_8$, br. s), 5.48 ($H_1$, d, $J$=5.2 Hz), and 6.7—7.2 (4H, m)], indicating it to be a (6+4) $\pi$ cycloadduct. Interstingly, the vicinal coupling constant between the two methine protons ($H_1$ and $H_2$), measured as 5.2 Hz, was in the range for the magnitude of the *endo*-adduct, while the *exo*-adduct was estimated to have a smaller coupling constant.[3] No other product was detected in the reaction of I with III.

The occurrence of this rather rare *endo*-(6+4)$\pi$ cycloaddition is neteworthy. The cross-conjugated 6$\pi$-arrangement of the fulvene ring might be less effective in determing the stereospecificity than the linearly oriented 6$\pi$-dienophiles because of orbital overlapping, and, according to a molecular model, the *exo*- and *endo*-(6+4) $\pi$ adducts show no significant difference in steric hindrance, yet the results show a throughly inverted stereospecificity. As we have shown in the cycloaddition of tropones with I,[1] the *exo*-(6+4)$\pi$ adducts are derived from the *endo*-(2+4)$\pi$ adduct; one should consider the possibility that VI is also formed from a thermodynamically less stable adduct, for which, only the *exo*-(2+4)$\pi$ adduct can be taken into account in this case. However, (2+4)$\pi$ adducts were obtained under more severe conditions, and their structures were unrelated *endo*-(2+4)$\pi$ as can be seen in the formation of IV and V. Therefore, VI is probably not a secondary cycloadduct. In this regard, Paddon-Row and Warrener[4] have recently suggested that the *exo*-(6+4)$\pi$ cycloadduct[5] obtained from the reaction of III with tropone could be formed afterwards by a [3,3]-sigmatropy of another initially formed *exo*-(4+6)$\pi$ adduct (VIII), which was regarded as thermodynamically unstable. Thus, the stereospecificity of the formation of VII should be inherited after that of a linearly arranged (4+6)$\pi$ adduct. Interestingly, dimethylisobenzofulvene has been shown to form an *endo*-(6+4)$\pi$ cyclodimer (IX)[6] which, like VI, includes a non-linear 6$\pi$ component; it could not be derived from a (4+2)$\pi$ precursor.

## Experimental

*Reaction of Isobenzofuran (I) and 6,6-Diphenylfulvene (II) at a Higher Temperature.* The adduct (1.24 g)[1] obtained

from tetracyclone and 7-oxabenzonorbornadiene was dissolved in cellosolv acetate (15 ml), together with II (566 mg), and the mixture was heated at 160—165 °C for 4 hr. The mixture was then poured into ice water and extracted with benzene. After the removal of the solvent, the residual mass was separated by silica gel column chromatography; from the less polar fraction eluted with benzene, recovered II (217 mg) and tetraphenylbenzene were isolated, and subsequently, from a benzene–ether (1: 1) mixture, colorless crystals (IV), (mp 160—161 °C; 254 mg (Found: C, 89.16; H, 5.79%. Calcd for $C_{26}H_{22}O$: C, 89.62; H, 5.79%. $\lambda_{max}^{MeOH}$: 295 nm ($\varepsilon$: 27300)), and colorless crystals (V) (mp 250—251 °C, 106 mg (Found: C, 87.81; H, 5.82%. Calcd for $C_{34}H_{26}O_2$: C, 87.52; H, 5.62%)) were obtained.

*Reaction of IV and I: Formation of V.* IV (50 mg) was similarly allowed to react with I at 160—165 °C for 2 hr. Then, a similar work-up afforded colorless crystals (30 mg) (mp 250—251.5 °C), which were identical with the authentic V obtained from the preceeding experiment (IR and NMR spectral and mixed mp comparisons).

*Reaction of I and 6,6-Dimethylfulvene (III) at Room Temperature.* 3,6-Diphenyltetrazine (1.13 g) and III (500 mg) were dissolved in dichloromethane (60 ml), to which a dichloromethane (10 ml) solution of 7-oxabenzonorbornadiene (677 mg) was then added, drop by drop; the mixture was then kept 3.5 hr at room temperature with stirring. Then, the solvent was removed *in vacuo*, and the residue was fractionated by silica gel column chromatography. The first few fractions (from *n*-hexane) gave the recovered III (145 mg). The next few fractions, eluted by benzene, afforded an oily adduct VI (188 mg (*m/e*: 224 ($M^+$). $\lambda_{max}^{MeOH}$: 256 nm ($\varepsilon$: 3100), 264 (2600), 270.5 (2000). IR 1340, 1160, 755, 725 $cm^{-1}$). The more polar fraction gave two crystalline compounds, the *exo-exo*-adduct of 7-oxabenzonorbornadiene with I (mp 262—264 °C (lit,[7] 264—265 °C)) and the *exo-endo*-isomer (mp 174—175 °C (lit,[7] 175—176 °C)).

## References and Notes

1) H. Takeshita, Y. Wada, A. Mori, and T. Hastui, *Chem. Lett.*, **1973**, 355.

2) Thus, $\Delta\delta$ ($H_2$ of IV and $H_2$ of V) is 1.76. Similarly, $\Delta\delta$ ($H_6$ of IV and $H_3$ of V) = 0.84, $\Delta\delta$ ($H_1$ of IV and $H_1$ of V) = 0.48 and $\Delta\delta$ ($H_7$ of IV and $H_4$ of V) = 0.15 are obtained.

3) The dihedral angles for *exo*- and *endo*-adducts were deduced to be *ca.* 100 and 50 °C respectively; these figures should show the *vic*-coupling constants as 0.5 Hz and 4.0 Hz according to the Williamson-Johnson modified version (*cf. J. Amer. Chem. Soc.*, **83**, 4623 (1961)), or 0.4 Hz and 5.1 Hz according to the Abraham-Holker version (*cf. J. Chem. Soc.*, **1963**, 803), of the original Karplus equation.

4) M. N. Paddon-Row and R. N. Warrenner, *Tetrahedron Lett.*, **1974**, 3797.

5) K. N. Houk, L. J. Luskus, and N. S. Bhacca, *ibid.*, **1972**, 2297.

6) H. Tanida, T. Irie, and K. Tori, This Bulletin, **45**, 1999 (1972).

7) R. N. Warrener, *J. Amer. Chem. Soc.*, **93**, 2346 (1971).