1,3-DIPOLAR CYCLOADDITION REACTIONS OF *N*-ARYL-2,4,6-CYCLOHEPTATRIEN-1-IMINES WITH *p*-SUBSTITUTED BENZONITRILE OXIDES: FORMATIONS OF 1,2,4-OXADIAZASPIRO[4.6]UNDECA-6,8,10-TRIENES

Kazuaki Ito, Katsuhiro Saito,* and Kensuke Takahashi

Department of Applied Chemistry, Nagoya Institute of Technology,
Gokiso-cho, Showa-ku, Nagoya 466, Japan

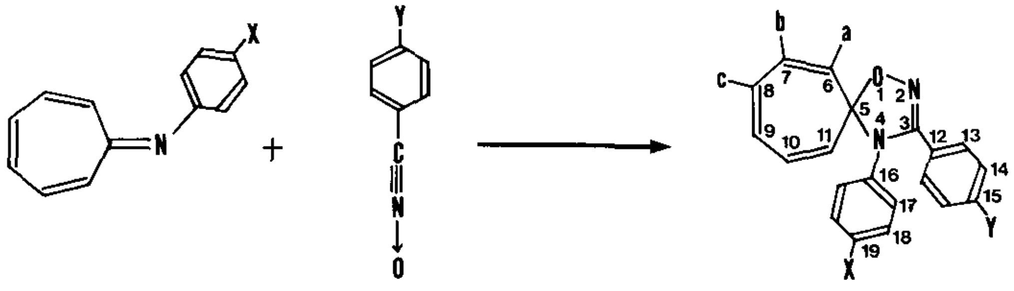
Abstract ———— Reactions of *N*-aryl-2,4,6-cycloheptatrien-1-imines with *p*-substitutied benzonitrile oxides afforded 1,2,4-oxadiazaspiro[4.6]undeca-6,8,10-trienes *via* [2+4] type cycloadditions. The study of substituent effects on the reaction rates suggested the nucleophilic attacks of the imines to the nitrile oxides.

Nitrile oxides are known to be active 1,3-dipoles in 1,3-dipolar cycloaddition reactions and have been extensively investigated from viewpoints of their utility for synthesis of five membered heterocyclic compounds and of the elucidation of the reaction mechanism in 1,3-dipolar cycloaddition reactions.[1] However we were unaware of any reactions of nitrile oxides with troponoid compounds, except for the reaction with 2,4,6-cycloheptatrien-1-one.[1a]

2,4,6-Cycloheptatrien-1-imines possess large dipole momenta due to contributions of 6π-aromatic structures.[2] Despite their aromaticities, 2,4,6-cycloheptatrien-1-imines are fairly active in cycloaddition reactions and are known to react only as 8π-components.[4] Previously, Gandolfi *et al.* reported an exceptional case; the reactions of 2,4,6-cycloheptatrien-1-imines with diphenyl nitrile imine afforded [8+4] type adducts *via* [2+4] type cycloaddition reactions, where the imine acted as 2π-components. But they did not succeed in the isolation of the [2+4] type cycloadducts.[3,4]

We report here the first example of the isolation of the [2+4] type cycloadducts in the reactions of *N*-aryl-2,4,6-cycloheptatrien-1-imines with *p*-substituted benzonitrile oxides.

A mixture of *N*-aryl-2,4,6-cycloheptatrien-1-imine (1) and two equimolar amounts of *p*-substituted benzonitrile oxide (2) was stirred at room temperature for 30 min to give [2+4] type adducts, 1,2,4-oxadiazaspiro[4.6]undeca-6,8,10-trienes, in 77–98 % yields.[5,6] The results of the reactions were summarized in Table 1.



1 2 3

a:X=OMe, c:X=Cl, a:Y=H, c:Y=Me,
b:X=Me, d:X=Br b:Y=OMe, d:Y=Cl

Talbe 1. Results of The Reactions of *N*-Aryl-2,4,6-cycloheptatrien-1-imines (1) with *p*-Substituted Benzonitrile Oxides (2)

cycloheptatriene -1-imines (1)	nitrile oxides (2)	adducts (3)	yields/%
1a	2a	3a	90
1b	2a	3b	86
1c	2a	3c	92
1d	2a	3d	98
1b	2b	3e	77
1b	2c	3f	89
1b	2d	3g	95

The structural elucidation of 3 was accomplished on the basis of the spectral data. ^1H and ^{13}C Nmr spectra showed the existences of 7,7-disubstituted 2,4,6-cycloheptatriene and two aryl moieties. The chemical shifts of the signals of C_5 (*ca.* 100 ppm) on oxadiazoline skeltons of 3 well resembled to those of the anologous compound.[7] NOE experiments clarified the neighboring configuration of two aryl groups, supporting the structures of 3. The relative rate ratios (k_X/k_H) of the reactions of 1b with *p*-substituted benzo-

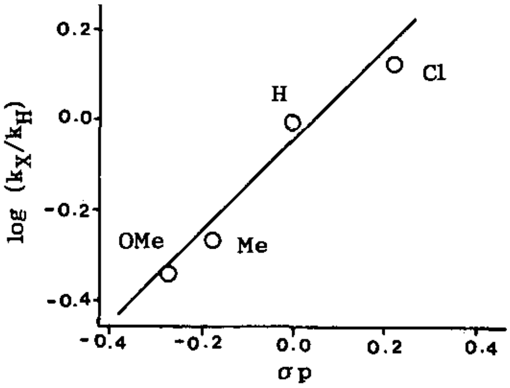


Figure 1. Correlation of Relative Rate Ratio with Hammett's σp

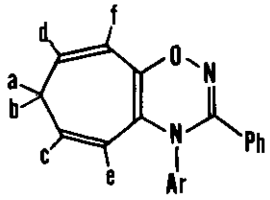
nitrile oxides (2a–d) were measured in a similar way to our previous method.[8] The ratio of 1.00 : 0.46 : 0.54 : 1.35 for 2a : 2b : 2c : 2d was obtained. There is a good linear relation between their logarisms (log k_X/k_H) and Hammett's sigma values (σp). The positive ρ–value (+0.99) suggests the nucleophilic attack of 1 to 2.

REFERENCES

1. a) C. De Michele, R. Gandolfi, and D. Gruenager, *Tetrahedron*, 1974, 30, 3765. b) K. Bast, M. Christl, R. Huisgen, and W. Mack, *Chem. Ber.*, 1973, 106, 3312; K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Strozier, and J. K. George, *J. Am. Chem. Soc.*, 1973, 95, 7287; K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *ibid.*, 1973, 95, 7301; R. Huisgen, *J. Org. Chem.*, 1976, 41, 403; R. A. Firestone, *Tetrahedron*, 1977, 33, 3009; D. P. Curran, "Advances in Cycloaddition", Vol. 1, JAI Press Inc., London, 1988.
2. Y. Kitahara, T. Asao, and M. Oda, "New Aromatic Chemistry", Kagaku Sosetsu, No 15, Gakujutsu Center, Tokyo, 1977.
3. a) G. Gandolfi and L. Toma, *Tetrahedron*, 1980, 36, 935. b) K. Ito, K. Saito, and K. Takahashi, *Heterocycles*, 1991, 32, 1117; *idem*, *Bull. Chem. Soc. Jpn.*, 1992, 65, 812; K. Ito, K. Saito, S. Takeuchi, and K. Takahashi, *Heterocycles*, 1992, 34, 1415.
4. Gandolfi *et al.* reported that the [2+4] type adducts could be isolated in the reactions of tricarbonyl(*N*–aryl–2,4,6–cycloheptatriene–1–imines)iron complex with diphenyl nitrile imine.[4a]
5. Physical data of 3a–g are as follows. 3a: mp 118–119°C (from toluene). Hrms: m/z 330.1343. Calcd for $C_{21}H_{18}N_2O_2$: m/z 330.1367. Ms m/z (rel intensity): 330 (M^+, 19), 149 (100). ^{1}H Nmr ($CDCl_3$) δ 3.71 (s, 3H, Me), 6.04 (m, 2H, H_a), 6.42 (m, 4H, H_b and H_c), 6.65–6.95 (m, 4H, aryl protons), 7.20–7.60 (m, 5H, phenyl protons). ^{13}C Nmr ($CDCl_3$) δ 55.3 (OMe), 99.6 (C_5), 114.0 (C_{18}), 125.8 (C_{12}), 127.3 (C_6, C_{11}, and C_{17}), 128.2 (C_7 and C_{10}), 128.4 (C_{13} or C_{14}), 129.0 (C_{14} or C_{13}), 129.7 (C_8 and C_9), 130.1 (C_{15}), 130.9 (C_{16}), 153.9 (C_3), 157.8 (C_{19}). 3b: mp 92–94°C (from benzene). Hrms: m/z 314.1410. Calcd for $C_{21}H_{18}N_2O$: m/z 314.1417. Ms m/z (rel intensity): 314 (M^+, 19), 149 (100). ^{1}H Nmr ($CDCl_3$) δ 2.26 (s, 3H, Me), 6.04 (m, 2H, H_a), 6.42 (m, 4H, H_b and H_c), 6.70–7.05 (m, 4H, aryl protons), 7.15–7.65 (m, 5H, phenyl protons). ^{13}C Nmr ($CDCl_3$) δ 20.9 (Me), 99.6 (C_5), 125.8 (C_{12}), 126.9 (C_6 and C_{11}), 127.4 (C_{17}), 127.5 (C_7 and C_{10}), 128.3 (C_{13} or C_{14}), 128.4 (C_{14} or C_{13}), 129.1 (C_{19}), 129.4 (C_{18}), 129.8 (C_8 and C_9), 130.1 (C_{15}), 135.6 (C_{16}), 153.7 (C_3). 3c: mp 91–92°C (from benzene). Hrms: m/z 334.0893. Calcd for $C_{20}H_{15}N_2OCl$: m/z 334.0872. Ms m/z (rel intensity): 336 (M^+, 5), 153 (100). ^{1}H Nmr ($CDCl_3$) δ 6.02 (m, 2H, H_a), 6.45 (m, 4H, H_b and H_c), 6.74–7.22 (m, 4H, aryl protons), 7.25–7.70 (m, 5H, phenyl protons). ^{13}C Nmr ($CDCl_3$) δ 100.2 (C_5), 125.4 (C_{12}), 127.1 (C_6

and C_{11}), 127.7 (C_7 and C_{10}), 128.0 (C_{17}), 128.1 (C_{13} or C_{14}), 128.6 (C_{14} or C_{13}), 128.8 (C_{18}), 129.9 (C_8 and C_9), 130.5 (C_{15}), 131.3 (C_{19}), 136.9 (C_{16}), 153.3 (C_3). 3d: mp 120–121°C (from toluene). Hrms: m/z 378.0354. Calcd for $C_{20}H_{15}N_2OBr$: m/z 378.0367. Ms m/z (rel intensity): 380 (M^+, 13), 378 (M^+, 14), 103 (100). ^1H Nmr ($CDCl_3$) δ 6.06 (d, 2H, H_a), 6.50 (m, 4H, H_b and H_c), 6.68–7.70 (m, 9H, aromatic protons). ^{13}C Nmr ($CDCl_3$) δ 100.2 (C_5), 119.1 (C_{19}), 125.4 (C_{12}), 127.1 (C_6 and C_{11}), 127.7 (C_7 and C_{10}), 128.2 (C_{13} or C_{14}), 128.2 (C_{17}), 128.6 (C_{14} or C_{13}), 129.9 (C_8 and C_9), 130.5 (C_{15}), 131.8 (C_{18}), 137.4 (C_{16}), 153.2 (C_3). 3e: mp 131–132°C (from benzene). Hrms: m/z 344.1522. Calcd for $C_{22}H_{20}N_2O_2$: m/z 344.1522. Ms m/z (rel intensity): 344 (M^+, 12), 328 (100). ^1H Nmr ($CDCl_3$) δ 2.20 (s, 3H, Me), 3.70 (s, 3H, OMe), 5.92 (m, 2H, H_a), 6.30 (m, 4H, H_b and H_c), 6.50–7.50 (m, aromatic protons, 8H). ^{13}C Nmr ($CDCl_3$) δ 20.9 (Me), 55.2 (OMe), 99.3 (C_5), 113.8 (C_{14}), 117.9 (C_{12}), 127.0 (C_6 and C_{11}), 127.3 (C_{17}), 127.6 (C_7 and C_{10}), 129.3 (C_{18}), 129.8 (C_8, C_9 and C_{13}), 130.0 (C_{19}), 135.7 (C_{16}), 153.5 (C_3), 161.0 (C_{15}). 3f: mp 142–143°C (from benzene). Hrms: m/z 328.1583. Calcd for $C_{22}H_{20}N_2O$: m/z 328.1575. Ms m/z (rel intensity): 328 (M^+,4), 117 (100), 78 (100). ^1H Nmr ($CDCl_3$) δ 2.27 (s, 3H, Me), 2.32 (s, 3H, Me), 6.04 (m, 2H, H_a), 6.42 (m, 4H, H_b and H_c), 6.72–7.44 (m, 8H, aromatic protons). ^{13}C Nmr ($CDCl_3$) δ 20.9 (Me), 21.4 (Me), 99.4 (C_5), 122.8 (C_{12}), 126.9 (C_6 and C_{11}), 127.3 (C_{17}), 127.6 (C_7 and C_{10}), 128.1 (C_{13} or C_{14}), 129.1 (C_{14} or C_{13}), 129.3 (C_{18}), 129.7 (C_8 and C_9), 135.5 (C_{16} or C_{19}), 135.7 (C_{19} or C_{16}), 140.3 (C_{15}), 153.7 (C_3). 3g: mp 90–92°C (from benzene). Hrms: m/z 350.0978. Calcd for $C_{21}H_{17}N_2OCl$: m/z 350.0998. Ms m/z (rel intensity) : 348 (M^+, 2), 133 (100). ^1H Nmr ($CDCl_3$) δ 2.20 (s, 3H, Me), 5.90 (m, 2H, H_a), 6.40 (m, 4H, H_b and H_c), 6.60–7.50 (m, 8H, aromatic protons). ^{13}C Nmr ($CDCl_3$) δ 21.0 (Me), 99.9 (C_5), 124.4 (C_{12} or C_{15}), 127.1 (C_6 and C_{11}), 127.3 (C_{17}), 127.5 (C_7 and C_{10}), 128.7 (C_{13} or C_{14}), 129.5 (C_{14} or C_{13} and C_{18}), 129.8 (C_8 and C_9), 130.0 (C_{19}), 135.3 (C_{16}), 136.1 (C_{15} or C_{12}), 152.9 (C_3).

6. Upon heating at 60°C for 50 h 3c gave an isomer (4) whose structure was tentatively specurated to be shown in the figure according to the following spectral data: Ms m/z (rel intensity): 334 (M^+, 8), 180 (100). ^1H Nmr ($CDCl_3$) δ 2.55 (dd, 2H, H_a and H_b), 5.30–5.55 (m, 2H, H_c and H_d), 6.15 (d, H_e), 6.87 (d, H_f), 7.10–7.50 (m, 9H, aromatic protons). The detailed investigation on this reaction is now in progress.



4

7. H. Suga and T. Ibata, *Chem. Lett.*, 1991, 1221.
8. K. Saito, S. Isobe, K. Ito, S. Kagabu, and K. Takahashi, *Chem. Lett.*, 1989, 1541.

Received, 27th July, 1992