Cycloaddition Reaction of Cycloheptatriene and Nitrosobenzene Derivatives

Shô Itô, Sen-ichi Narita,* and Katsuya Endo
Department of Chemistry, Tohoku University, Sendai 980

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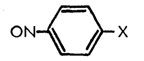
Structures of the cycloaddition products obtained from cycloheptatriene and *para*-substituted nitrosobenzene have rigorously been established by NMDR experiments and by degradation of the representative member, the cycloheptatriene-nitrosobenzene adduct, to 3-anilinocycloheptanone. All the adducts were found to be of [6+2] type. The ionic mechanism has been proposed for the cycloaddition in order to account for the substitution effect on the benzene ring.

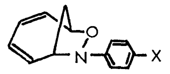
The reaction of cycloheptatriene and nitrosobenzene is known to yield a 1 : 1 cycloaddition product.[1] Structure of this compound was once assigned to be III′ in analogy with the similar reactions of the latter and various conjugated polyenes.[2] This structure was later revised to IIIa on the basis of spectroscopic and a few chemical informations.[3] However, discrimination between two structures seemed insufficient on the spectroscopic data presented and an attempted direct chemical confirmation failed.[3] This paper presents conclusive chemical as well as spectroscopic evidences, which unambiguously establish the structure IIIa for the adduct, and also deals with the discussion on the nature of the reaction.

Reaction of cycloheptatriene (I) and nitrosobenzene (IIa) at room temperature for three days yielded a colorless crystalline product IIIa in 17% yield. The melting point and all the spectroscopic properties are in agreement with the values previously reported.[1,3] Proton magnetic resonance signals (100 MHz) of IIIa appear at δ 2.01—2.60 (m, 2H, $-\mathbf{CH_2}-$), 4.22 (m, 1H, $\mathbf{H}\overset{|}{\underset{|}{C}}N-$), 4.81 (m, 1H, $\mathbf{H}\overset{|}{\underset{|}{C}}O-$), 6.03 (br.s, 4H, olefinic H) and 6.9—7.4 ppm (m, 5H, phenyl). NMDR experiment, irradiating at the methylene signals simplified both signals at 4.22 and 4.81 ppm, but caused no effect on the rest, while irradiation of both methine signals (NMTR) altered the methylene resonance to a clean AB pattern with $J=12$ Hz. These observations unambiguously establish the location of the methylene group next to both methines, and hence, combined with the informations reported before,[1,3] eliminate all possible structures but IIIa.

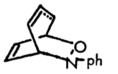
This conclusion was further confirmed by the chemical correlation. The adduct IIIa was catalytically reduced to the tetrahydro derivative IV.[1] The N–O linkage was then cleaved by zinc in acetic acid to afford an anilinocycloheptanol V, which was then oxidized with manganese dioxide to give the corresponding ketone VI. This ketone was identical (mixed mp, IR and NMR) with 3-anilinocycloheptanone prepared from 2-cycloheptenone and aniline in absolute ethanol. Sodium borohydride reduction of the ketone VI afforded another 3-anilinocycloheptanol VII in a quantitative yield. Consideration of the reaction sequence allowed assignment of *cis* and *trans* configuration for V and VII, respectively.



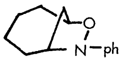
IIa X=H
b CH$_3$
c Cl
d NO$_2$
e N(CH$_3$)$_2$



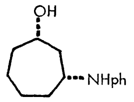
IIIa X=H
b CH$_3$
c Cl
d NO$_2$



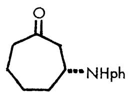
III′



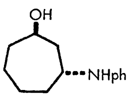
IV



V



VI



VII

Several *p*-substituted nitrosobenzene derivatives (IIb—d) also yielded the similar type of products (IIIb—d), but the rate of the reaction, therefore the yield of the product, depends very much on the *para* substituents on the benzene ring. Thus electron—withdrawing substituents such as chlorine or nitro group markedly enhanced the reactivity as well as the product yields, while strong electron donating substituents such as dimethylamino group completely inhibited the reaction, and IIe was recovered unchanged after 30 days under the reaction condition (*cf.* Table 1). These accelerating effects are in the sequence of $NO_2>Cl>H>CH_3>N(CH_3)_2$ which is parallel to Hammett's σ value.

In all the cases when the reaction was observed, the [6+2] type of structures were secured by NMR data

Table 1. The cycloaddition of cycloheptatriene and para-substituted nitrosobenzene derivatives

Substituent	Reaction condition[a)]	Product (yield %)
N(CH$_3$)$_2$	30 days at room temp.	No reaction
CH$_3$	6 days at room temp.	IIIb (5.9%)
H	3 days at room temp.	IIIa (11.6%)
Cl	3 days at toom temp.	IIIc (17.3%)
NO$_2$	5 hrs at 0 °C[b)]	IIId (6.3%)

a) The reaction was carried out in CHCl$_3$ at dark under N$_2$ atmosphere.

b) Rapid decomposition of IId takes place at room temperature even at 0 °C. No IId was detected after 5 hr.

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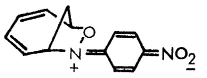
* Present address: Toa Eiyo Kagaku Kogyo, Co. Ltd., Iisaka Fukushima.

1) G. Kresze and C. Schulz, *Tetrahedron*, **12**, 7 (1961).

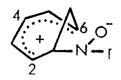
2) W. Ditney, *J. Prakt. Chem.*, **156**, 27 (1940). M. Ahmad and J. Hamer, *J. Chem. Educ.*, **41**, 249 (1964). J. Hamer, "1,4-Cycloaddition," Academic Press, New York (1969), p. 419.

3) J. Hutton and W. A. Waters, *Chem. Commun.*, **1966**, 634; P. Burns and W. A. Waters, *J. Chem. Soc. Ser., C*, **1969**, 27.

for the products. The UV spectra of these adducts having maxima at 240 and 265 nm, are also very similar to each other, except for the *p*-nitronitrosobenzene adduct; IIId, which exhibits maxima at 237 and 352 nm. Contribution of the resonance structure IIId′ may be responsible for this anomaly.



III′d



[A]

A small amount of azoxybenzenes correspond to the nitrosobenzenes employed were always formed during the reaction. Although the formation of these compounds suggests the occurrence of a hydride transfer between cycloheptatriene and nitrosobenzene derivatives resulting in the possible formation of tropylium ion, the latter is not involved in the cycloaddition reaction, since tropylium perchlorate and *p*-chloronitrosobenzene (IIc) resulted in the exclusive formation of tropone and *p,p*′-dichloroazoxybenzene (VIIIc) when reacted in aqueous dioxane (1: 2) at room temperature.

These results indicate that the reaction is the type between an electron rich triene and an electron deficient nitrosobenzene derivative, remniscent of electronic requirement in normal Diels-Alder reactions.[4]

Since the concerted thermal [6s+2s] cycloaddition is forbidden,[5] the present reaction must proceed through either concerted [6s+2a] or an ionic or a free radical mechanism. Although the experiments described above do not fully discriminate these three possibilities, the observation that the 1: 1 adduct is the only product isolated even in the presence of excess of nitrosobenzenes, which is a good radical scavenger, suggests the radical mechanism unlikely. On the other hand, the substitution effect observed would favor the ionic mechanism. Thus the electron deficient nitrogen of the nitroso group attacks the π-electron system of cycloheptatriene resulting in the dipolar intermediate [A]. This may then cyclize at either one of the cationic centers at 2, 4, and 6. Consideration of angle strain as well as the conjugation of double bond in the product leaves the 1,6-bonding most probable.

Experimental

All the melting points are uncorrected. The IR spectra were recorded on a Hitachi EPI-2 spectrophotometer, and UV spectra on a Hitachi ESP-3 spectrometer. The NMR spectra were observed with Varian HA-100 and/or A-60 spectrometer, using $CDCl_3$ as a solvent, unless otherwise stated. The chemical shifts are given in ppm relative to the internal TMS. The coupling constants are shown in Hz (s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet). The mass spectra were obtained on a Hitachi RMU-6D and RMU-7 mass spectrometer operating an ionization energy of 70 eV.

9-Phenyl-8-oxa-9-azabicyclo[4,2,1]nona-2,4-diene (IIIa). A solution of nitrosobenzene (IIa, 987 mg) and cycloheptatriene (I, 5 g) in chloroform (30 ml) was allowed to stand for 3 day under nitrogen. The solution was then concentrated under a reduced pressure, and the residue chromatographed on a silica gel column. Petroleum ether–benzene eluted a colorless compound, which was identified as azoxybenzene (VIIIa) by its IR spectra. Further chromatography with benzene–chloroform eluted a colorless compound (IIIa, 285 mg, 11.6%), mp 108—109°C (from cyclohexane); *m/e* 156, 107, 92, 91; λ_{max}^{MeOH} 238 nm (ε 12300), 264 nm (ε 6300); δ 2.01—2.60 (m, 2H), 4.22 (m, 1H), 4.81 (m, 1H), 6.03 (br. s, 4H), 6.9—7.4 (m, 5H). These spectroscopic data agreed well with those reported for IIIa.[1,3]

A similar reaction in benzene at 0—5 °C for 16 day resulted in somewhat better yield (17.5%).

Reaction of Cycloheptatriene and para-*Substituted Nitrosobenzene Derivatives.* The reaction and work up followed the procedure described above. The reaction conditions were listed in Table 1. Dimethylaminonitrosobenzene (IIe) was recovered unchanged after 30 days under the reaction condition. IIIb: mp 99—100 °C (from petroleum ether); Found: C, 79.74; H, 7.16%. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09%. *m/e* 213 (M^+); λ_{max}^{MeOH} 238 nm (ε 13300), 265 nm (ε 8300); δ 2.18 (s, 3H), 2.30 (m, 2H), 4.21 (m, 1H), 4.84 (m, 1H), 6.09 (m, 4H), 7.01 and 7.07 (q, AB type, J=9.0, 4H); ν_{max}^{KBr} 1615, 1505, 1301, 1167. *p,p*′-Dimethylazoxybenzene (VIIIb) mp 69—71 °C. IIIc: mp 101—102 °C (from cyclohexane); Found: C, 66.11; H, 5.23%. Calcd for $C_{13}H_{12}NOCl$: C, 66.81; H, 5.18%. *m/e* 235 and 233 (M^+); λ_{max}^{MeOH} 246 nm broad (ε 17600); δ 2.33 (m, 2H), 4.20 (m, 1H), 4.81 (m, 1H), 6.05 (m, 4H), 7.20 and 7.35 (q, AB type J= 9.0, 4H); ν_{max}^{KBr} 1590, 1448, 1291, 1169, 1086. *p,p*′-Dichloroazoxybenzene (VIIIc) mp 156—157 °C. IIId: mp 107—108° (from benzene–cyclohexane); Found: C, 63.98; H, 4.99%. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.92; H, 5.39%. *m/e* 244 (M^+); λ_{max}^{MeOH} 237 nm (ε 9600), 352 nm (ε 11000); δ 2.51 (m, 2H), 4.45 (m, 1H), 4.90 (m, 1H), 6.14 (m, 4H), 7.06 and 8.22 (q, AB type, J=9.5, 4H); ν_{max}^{KBr} 1592, 1505, 1338, 1242, 1175, 1112, 1089.

Catalytic Hydrogenation of IIIa. A solution of IIIa (140 mg) in methanol was hydrogenated for 4 hr in the presence of PtO_2 (15 mg). Concentrate of the mixture, after the removal of the catalyst, was chromatographed on a silica gel column. Elution with chloroform yielded pale yellow oil (IV, 80 mg), which crystallized on standing. Mp 27—28 °C, *m/e* 203 (M^+); λ_{max}^{MeOH} 239 nm (ε 9400); $\nu_{max}^{liq.}$ 2920, 1600, 1490, 1198, 1008, 762, 696; δ 1.20—2.06 (m, 6H), 4.03 (m, 1H), 4.86 (m, 1H), 7.33 (m, 5H).

cis-*3-*N-*Phenylaminocycloheptanol (V).* The hydrogenation product IV (70 mg) and HCl-activated zinc powder (200 mg) was stirred in acetic acid (10 ml) under nitrogen for 30 min. The mixture was partly neutralized (pH—5) with 2M aqueous sodium hydroxide and then made alkaline with sodium carbonate. The chloroform extract of the resulting solution was worked up as usual to afford a pale yellow oil (V, 62 mg) which was purified further by chromatography. $\nu_{max}^{liq.}$ 3350, 1605, 1506, 1302, 1028, 750, 698; δ ~1.8 (m, 10H), 3.43 (m, 1H), 3.93 (m, 1H), 6.47—7.32 (m, 5H). V crystallizes with a mole of ether of crystallization, mp 48—51 °C.[1)]

*3-*N-*Phenylaminocycloheptanone (VI).* A chloroform solution (5 ml) of V (110 mg) was added to a suspension of active manganese dioxide (600 mg) in the same solvent (15 ml) and the mixture was stirred at room temperature for 18 hr under nitrogen. The reaction mixture was filtered and the filtrate chromatographed on silica gel. Elution

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4) R. Huisgen, R. Grashey, and J. Sauer, "The Chemistry of Alkenes," ed. by S. Patai, Interscience Publishers, New York (1964), pp. 919—922. and references therein.

5) R. B. Woodward and R. Hoffmann, *Angew. Chem. Internat. Edit.*, **8**, 781 (1969).

with chloroform afforded a crystalline product (IV, 21 mg), mp 63—64 °C (from *n*-hexane); Found: C, 76.78; H, 8.73; N, 6.14%. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.86%. *m/e* 203 (M^+); λ_{max}^{MeOH} 249 nm (ε 14600), 296 nm (ε 2500); ν_{max}^{KBr} 3350, 1692, 1602, 1506, 1315, 1280, 991, 745, 694; δ 1.80 (m, 8H), 2.65 (m, 2H), 3.61 (br. 2H), 6.90—7.40 (5H).

Michael Addition of Aniline to 2-Cycloheptenone. 2-Cycloheptenone (301 mg), prepared from 2-bromocycloheptanone and quinoline, was allowed to react with aniline (5 ml) in absolute ethanol (5 ml) at room temperature for 20 hr. The reaction mixture was worked up normally to yield a colorless crystalline compound, mp 62—63 °C (from *n*-hexane); mixed mp with VI 62—63 °C. All the spectroscopic properties were identical with those of VI.

$NaBH_4$ Reduction of VI. The reduction of VI (55 mg) with $NaBH_4$ (50 mg) in methanol (7 ml) at room temperature for 1 hr followed by usual work up yielded an isomeric alcohol VII, mp 86—87 °C (from cyclohexane); *m/e* 205 (M^+); ν_{max}^{KBr} 3350, 1601, 1494, 1035, 760, 700.

Reaction of p-*Chloronitrosobenzene with Tropylium Perchlorate.* Tropylium perchlorate (764 mg) and *p*-chloronitrosobenzene (IIc) (471 mg) was stirred in dioxane-water (2:1, 40 ml) for 2 hr under nitrogen. Along the reaction proceeded, the green solution turned to yellow and crystalline particles precipitated. The crystals were collected and recrystallized to give 334 mg (78%) of *p,p′*-dichloroazoxybenzene (VIIIc), mp 156—157 °C. The filtrate was worked up normally, followed by silica gel chromatography to yield 22 mg of tropone, which was identified by its IR spectra.

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