*Tetrahedron.* Vol. 31, pp. 2215 to 2217 Pergamon Press 1975 Printed in Great Britain

# STEREOSPECIFIC *SYN*-ADDITION OF IODINE AZIDE TO STRAINED CYCLOBUTENE MOIETY[1]

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(*Received Japan* 17 *February* 1975; *Accepted for publication* 1 *May* 1975)

**Abstract**—Addition of tricyclo[4.2.2.0$^{2,5}$]deca-3,7-diene and iodine azide was found to be *syn* on the cyclobutene moiety. Structure determination of the adducts and the formation mechanism are discussed.

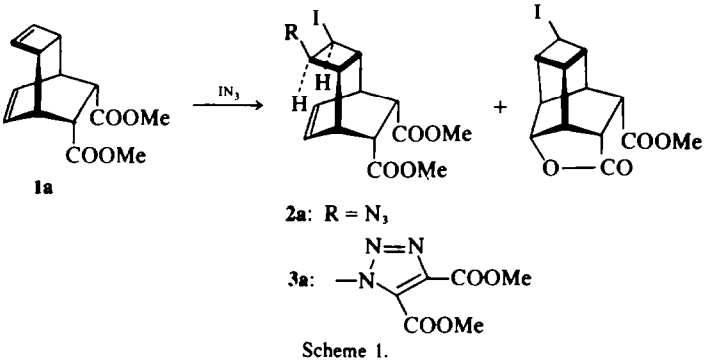
We have previously reported that the reaction of tricyclo[4.2.2.0$^{2,5}$]deca - 3,7 - diene derivatives (1:1 adducts of cyclooctatetraene with dienophiles such as dimethyl maleate and maleic anhydride) (**1a** and **1b**), some of which proceed by transannular cross bonding of the proximal $\pi$-bonds give novel caged compounds.[2] In the case of a similar reaction of **1b** with iodine azide ($IN_3$), a 1:1 adduct (**2b**) was obtained instead of the expected transannular cyclization product, however, it is difficult to determine the stereochemistry of the adduct because of the complexity of the signals of the NMR spectrum.

We have reexamined the $IN_3$ addition reactions of **1a** and **1b**, since it is necessary to show whether *syn* or *anti* addition has taken place in comparison with the results of the oxymercuration reactions of **1a** and **1b**.[3] In addition, a question whether the transannular cross-bonding of the proximal $\pi$-bonds via an intermediacy of bridged halonium ion is general or not, led us to examine the cyclization of these systems with an electrophilic reagent.

In this paper we have described the reactions of **1a** and **1b** with iodine azide and the stereochemistry of their adducts.

## RESULTS AND DISCUSSION

The reaction of the adduct (**1a**) with an $IN_3$ prepared *in situ* followed by treatment with excess dimethyl acetylene-dicarboxylate (DAC) gave a mixture of **3a** and **4** in 30 and 8·8% yields.*




Scheme 1.

The structure of **4** was easily established by comparison with an authentic sample.[2] On the other hand, elemental analysis shows the product **3a** to be $C_{20}H_{22}O_8N_3I$ indicating an initially formed 1:1 adduct (**2a**) followed by addition of one molar DAC. The NMR spectrum in the vinyl proton regions for **3a** shows two olefinic protons at $\delta$ 6·63 (2H, T) and lack of cyclobutene protons. However, the stereochemistry of **3a** could not be determined since the methine protons appear at $\delta$ 4·4–4·5 (2H) and 2·9–3·5 (6H) as complex multiplets. Thus, the structure **3a** was elucidated by the unequivocal independent synthesis as shown in Scheme 2.

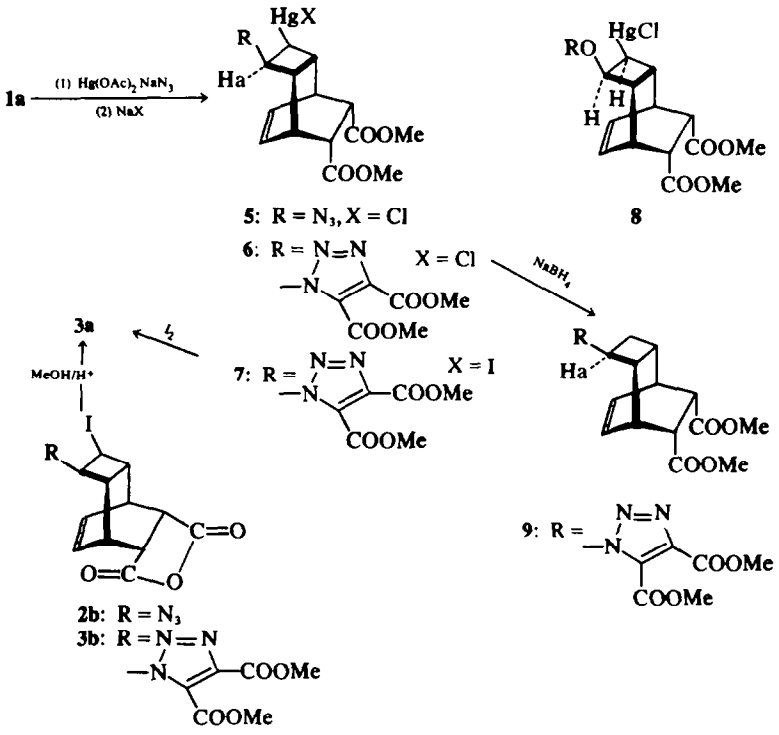
Addition of equimolar mercuric acetate to **1a** followed by treatment with aqueous sodium chloride gave a product **5**. Reaction of **5** with DAC gave **6** in almost quantitative yield (based on **1a**). When sodium iodide instead of sodium chloride was used for the reaction, **7** was obtained in 32% yield. In this connection, we have also described that the oxymercuration of **1a** in nucleophilic solvents such as methanol and acetic acid is found to proceed by *syn* attack on the cyclobtene moiety to give **8**. Thus, the structure **6** was easily determined in comparison with the NMR spectrum of **8** (Experimental). On the other hand, reduction of **6** with sodium borohydride gave **9**. Appearance of a new coupling of 8·25 Hz ($\delta$ 4·70) in the NMR of **9** was caused by replacing mercury with the proton indicating the trans coupling in the cyclobutane system since the spectrum of **6** shows Ha at $\delta$ 5·01 as a double doublet with coupling 10·5 and 3·0 Hz. Furthermore, **3a** was derived by treatment of **7** with equimolar iodine in almost quantitative yield.*

Esterification of **3b**[2] with methanol gave **3a** in quantitative yield.

From the above results, it is concluded that the $IN_3$ additions of **1a** and **1b** occurred only in the sterically unhindered olefin on the cyclobutene moiety by *syn* fashion. However, in most cases the $IN_3$ addition, observed stereospecifically is *anti*,[4] it is proposed that a 3-membered ring intermediate (iodonium ion) is initially

*Since the oxide is quite explosive at room temp., the structure determination was based on that of 1,3-dipolar cycloadduct.

*The reaction of **7** with iodine might proceed via a radical chain process[4].

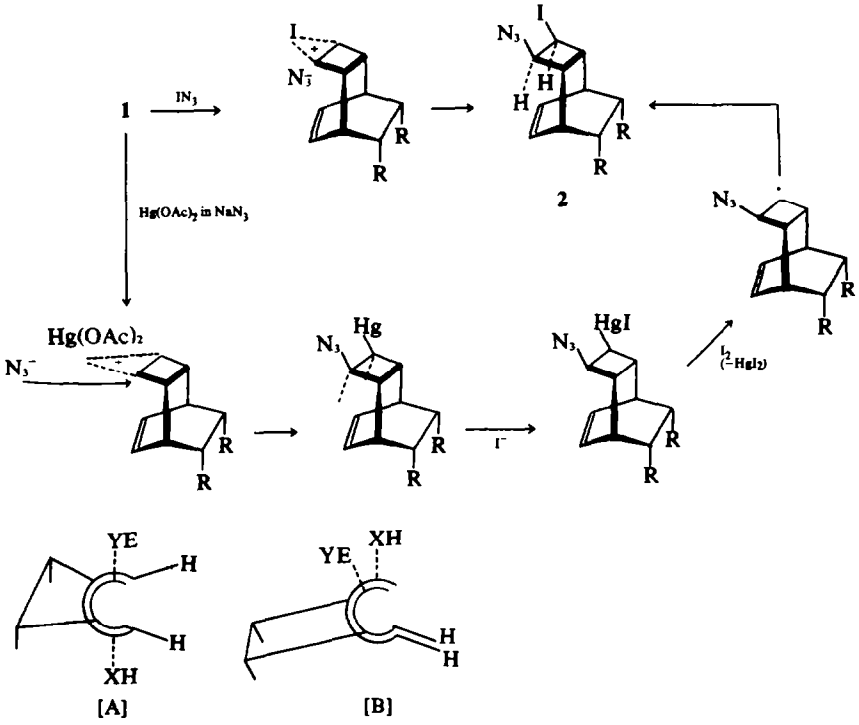



Scheme 2.

formed and then the ring opening will preferentially occur from the back side resulting in *anti* addition of the reagent.

Thus, the *syn* addition of the $IN_3$ to the cyclobutene moiety can be explained by examination of the transition state according to the twist strain theory.[6] Because of the highly strained anti coplanar transition state [A], the *syn* addition occurs preferentially *via* syn transition state [B] as shown in Scheme 3, although the steric hindrance of cyclohexene moiety can not be ignored. This formation mechanism agrees with that of oxymercuration of **1a**.

Finally, it is noteworthy from the mechanistic point of view that this is the first case where the $IN_3$ adds to strained olefins perferentially by a *syn* manner.




Scheme 3.

## EXPERIMENTAL

M.ps were measured on a Yanagimoto micro apparatus and are uncorrected. The microanalyses were performed on a Perkin-Elmer 240 elemental analyser, while the IR spectra were obtained on JASCO Model IR-S spectrometer. The NMR spectra were recorded with a JEOL Model C-60- XL spectrometer with TMS as internal standard.

*Reaction of* **1a** *with* $IN_3$. To a suspension of sodium azide (390 mg) in acetonitrile (20 ml) iodine chloride (325 mg) was added. After **1a** (500 mg) was added to the soln, the mixture was stirred for 2 days. The red-brown mixture was poured into water (50 ml), and was extracted with chloroform. To the soln an excess of dimethyl acetylendicarboxylate was added. After 2 days stirring, the solvent was evaporated under reduced pressure and the residue was subjected to silica gel chromatography using chloroform to give **3a** (330 mg) and **4** (63 mg).

**3a**: m.p. 193–195° (benzene- n-hexane), IR (KBr) 1740 and 1720 $cm^{-1}$, NMR ($CDCl_3$) $\delta_{TMS}$ 2·9–3·5 (6H, m), 3·60 (3H 2, s), 3·93 (3H, s) 3·98 (3H, s), 4·4–5·0 (2H, m), 6·63 (2H, t). (Found: C, 42·77; H, 3·98; N, 7·46. $C_{20}H_{22}O_8N_3I$ requires: C, 42·95; H, 3·97; N, 7·51%).

*Reaction of* **1a** *with mercuric acetate and sodium azide.* A mixture of **1a** in MeOH (20 ml) was stirred for 24 hr. After evaporation of the solvent under reduced pressure, the residue was treated with excess NaCl aq. The mixture was extracted with chloroform. After evaporation of the solvent, the resulting residue was dissolved in benzene (20 ml) and then was added to DAC (450 mg). After refluxing for 6 hr, followed by evaporation of the solvent, the residue was recrystallized from benzene- n-hexane to give **6** (2·03 g); m.p. 215–217°, IR (KBr) 1740 and 1730 $cm^{-1}$, NMR ($CDCl_3$) $\delta_{TMS}$ 2·7–3·3 (7H, m), 3·60 (3H 2, s), 3·95 (3H, s), 3·98 (3H, s), 5·01 (1H, dd, J = 10·5 and 3·0 Hz), 6·60 (2H, t). (Found: C, 35·84; H, 3·22; N, 6·40. $C_{20}H_{22}O_8N_3HgCl$ requires: C, 35·94; H, 3·32; N, 6·29%).

Similarly, a mixture of **1a** (500 mg), mercuric acetate (640 mg) and sodium azide (260 mg) in MeOH (20 ml) was stirred for 24 hr. Treatment with excess NaI aq, followed by extraction by chloroform, gave **7** (49 mg); m.p. 171–173° (MeOH), IR (KBr) 1740 and 1730 $cm^{-1}$, NMR ($CDCl_3$) $\delta_{TMS}$ 2·8–3·5 (7H, m), 3·58 (3H 2, s), 3·93 (3H, s), 3·98 (3H, s), 5·15 (1H, dd, J = 10·5 and 3·0 Hz), 6·60 (2H, t). (Found: C, 31·75; H, 2·88; N, 5·45. $C_{20}H_{22}O_8N_3HgI$ requires: C, 31·61; H, 2·92; N, 5·53%).

*Reduction of* **6** *with sodium borohydride.* To a soln of **6** (2·026 g) in MeOH (20 ml) $NaBH_4$ (200 mg) was added. The mixture was then added to water and extracted with chloroform. After evaporation of the solvent under reduced pressure, the residue was subjected to silica gel chromatography using chloroform to give **9** (820 mg); m.p. 75–76° (benzene- n-hexane), IR (KBr) 1740 and 1730 $cm^{-1}$, NMR ($CDCl_3$) $\delta_{TMS}$ 2·5–3·3 (8H, m), 3·53 (3H 2, s), 3·85 (3H, s), 3·90 (3H, s), 4·70 (1H, m, J = 10·5, 8·25 and 3·0 Hz), 6·50 (2H, t). (Found: C, 55·38; H, 5·39; N, 9·70. $C_{20}H_{23}O_8N_3$ requires: C, 55·42; H, 5·35; N, 9·70%).

*Reaction of* **7** *with iodine.* To a soln of **7** (350 mg) in dioxane (20 ml) a soln of $I_2$ (140 mg) in dioxane (10 ml) was added under argon at room temp. After the mixture had been stirred for 4 hr, 0·1N $Na_2S_2O_3$ was added and the soln then extracted with chloroform. The extract was evaporated under reduced pressure and the residue was subjected to silica gel chromatography using chloroform to give **3a** (260 mg).

*Methanolysis of* **3b**. A soln of **3b**[2] (200 mg), $H_2SO_4$ (2 ml) and MeOH (10 ml) was refluxed for 16 hr. After evaporation of MeOH, the mixture was added to water (50 ml) and extracted with chloroform. The solvent was evaporated under reduced pressure and the residue was subjected to silica gel chromatography using chloroform to give **3a** (210 mg).

*Acknowledgement*—We express our gratitude to Badische Anilin Soda- Fabrick (BASF) AG for a generous gift of cyclooctatetraene.

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