Communications to the Editor

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SYNTHESIS OF DIOXAZOLO[3.3]CYCLOPHANES BY CYCLIZATION OF BIS(2-ISOCYANO-2-TOSYLETHYL)BENZENES WITH BENZENEDICARBALDEHYDES

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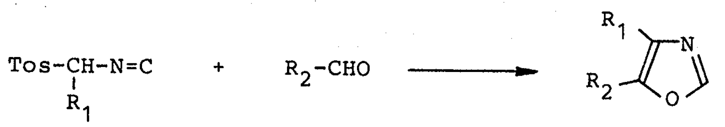
Bis(2-isocyano-2-tosylethyl)benzenes (4) reacted with benzenedicarbaldehydes (9) in the presence of sodium ethoxide as a base in refluxing ethanol to form dioxazolo[3.3]cyclophanes (10).

KEYWORDS ——— cyclophane; tosylmethyl isocyanide; isocyanide; aldehyde; oxazole; cyclization

The condensation of tosylmethyl isocyanide (TosMIC; 1a) or mono-substituted TosMIC (1b) with aldehydes (2) leading to 5-substituted or 4,5-disubstituted oxazoles (3a or 3b) has been reported in detail.[1]

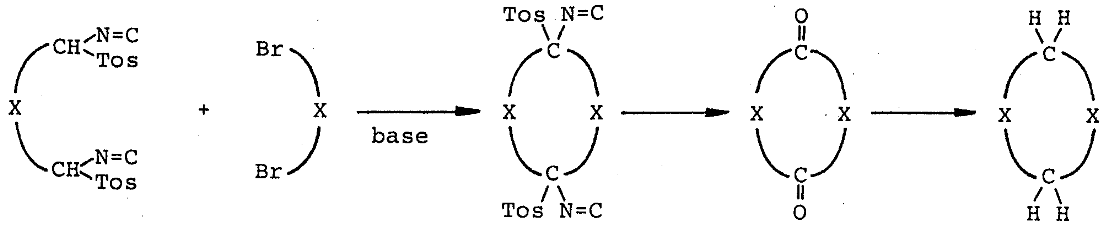


1 2 3

1a : R_1 = H
1b : R_1 = alkyl

R_2 = aryl

3a : R_1 = H, R_2 = aryl
3b : R_1 = alkyl, R_2 = aryl

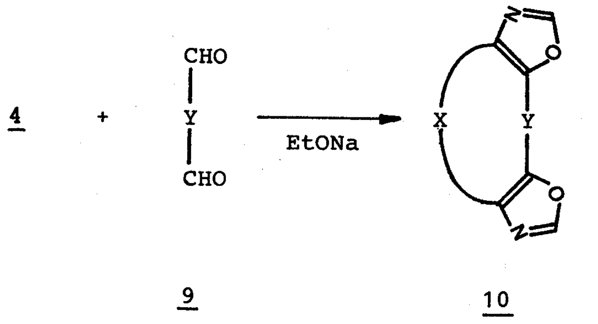


4 5 6 7 8

X : o-, m-, and p-xylylene

In continuation of our study on the preparation of [3.3]cyclophanes (8) by the reaction of bis(2-isocyano-2-tosylethyl)benzenes (4)[2] with bis(bromomethyl)benzenes (5) followed by the hydrolysis of 6 and Wolff-Kishner reduction of 7, we have effected the first preparation of dioxazolo[3.3]cyclophanes (10) from the intermolecular cyclization of 4 with benzenedicarbaldehydes (9) in the presence of sodium ethoxide as a base in refluxing ethanol.

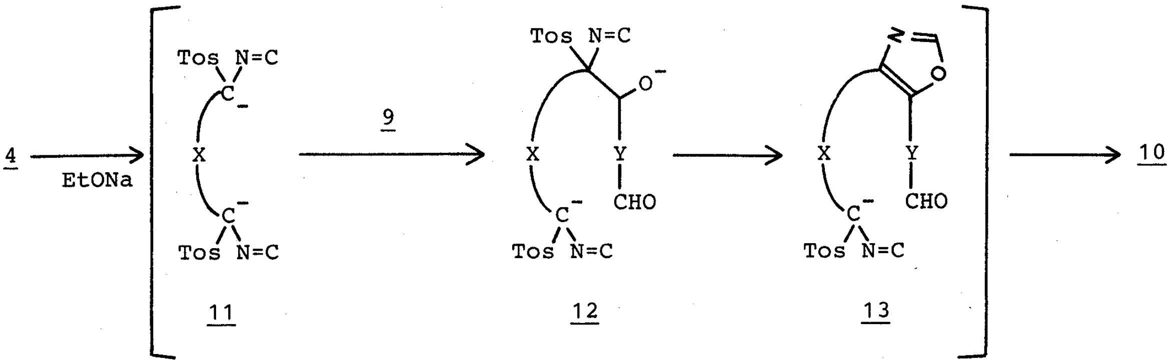
Thus, when 1,2- and 1,3-bis(2-isocyano-2-tosylethyl)benzenes (4o and 4m) were caused to react with 1,3-benzenedicarbaldehyde (9m), the corresponding dioxazolo[3.3]cyclophanes (10om and 10mm) were produced in 84% and 77% yields, respectively. Similarly, 1,4-bis(2-isocyano-2-



Y : o-, m-, and p-phenylene

tosylethyl)benzene (4p) was treated with 9m to give the corresponding cyclophane of type [3.3], 10pm, in 15% yield along with a 2:2 adduct3) in 52% yield.

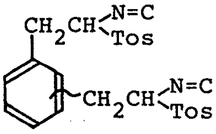
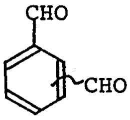
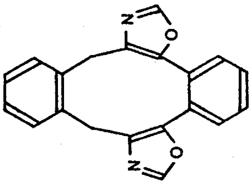
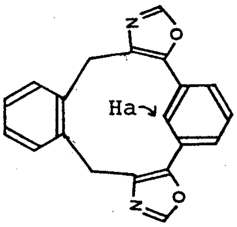
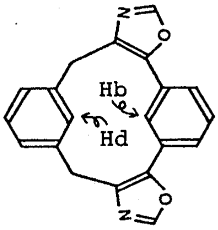
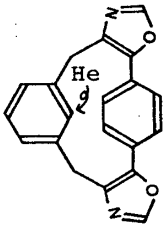
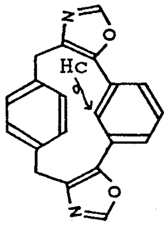
With respect to the reaction mechanism, we have rationalized as follows: the first nucleophilic addition of a bis-TosMIC derivative anion (11) to one of carbonyl carbons of 9 takes place under basic condition to provide an intermediate (12). Subsequent conversion of 12 to an oxazole (13) is induced and the following intramolecular cyclization of 13 occurs to prepare 10 as a final product.



Attempts to ascertain the sensitivity toward the structural changes of the reaction species were carried out in a practicable combination of the bis-TosMIC derivatives (4) with 1,2- or 1,4-benzenedicarbaldehydes (9o or 9p). Namely, when 9o was used as a carbonyl component, 4o led to 10oo in 2% yield along with a large amount of polymerized materials. 4m and 4p, however, did not afford the corresponding dioxazolo[3.3]cyclophanes (10mo and 10po), probably because the structure of the intermediate (13) is too strained to form a [3.3]cyclophane ring.4) In the choice of 9p as a carbonyl component, neither 4o nor 4p afforded our desired compounds (10op and 10pp) under the above-mentioned condition, whereas 4m gave the corresponding dioxazolo[3.3]metaparacyclophane (10mp) in 85% yield.

The structural assignments of the synthesized dioxazolo[3.3]cyclophanes (10oo, -om, -mm, -pm, and -mp) were achieved mainly by elemental analyses and ^{1}H-NMR(CDCl$_3$) and mass spectroscopies. The ^{1}H-NMR spectrum of each compound of type 10 exhibited a C-2 proton of each oxazole ring as a singlet at around δ 7.70-7.86. These δ values were similar to those of the 4,5-disubstituted oxazoles already reported.1a) Furthermore, the inner aryl proton (Hc) of 10pm was observed as a broad singlet at δ 5.30, whereas the corresponding protons (Ha and Hb) of 10om and 10mm were observed at δ 7.70 and δ 6.75, respectively. This up-field shift of Hc is presumably attributed

Table I

	9o	 9m	9p
4o	 10oo yield : 2 % mp : 205-6°C	 10om yield : 84 % mp : 263-4°C NMR : δ 7.70(Ha)	(10op)
4m	(10mo)$^{a)}$	 10mm yield : 77 % mp : 195-6°C NMR : δ 6.75(Hb) δ 7.50(Hd)	 10mp yield : 85 % mp : 246-8°C NMR : δ 6.10(He)
4p	(10po)$^{a)}$	 10pm yield : 15 % mp : 190-2°C NMR : δ 5.30(Hc)	(10pp)

a) see lit. 4.

to shielding of Hc by the opposite benzene ring. Incidentally, the inner aryl proton (He) of 10mp, which is isomeric with 10pm, was observed as a broad singlet at δ 6.10. The 0.80 ppm down-field shift compared with the δ value (5.30) of Hc for 10pm suggests that the meta-substituted benzene ring of 10mp stands on a site in somewhat gapped surroundings due to the greater pliability of the methylene group than that of the double bond of the oxazole ring linked up with the corresponding meta-substituted benzene ring of 10pm.

To the best of our knowledge, this facile preparation in one step provides a route to a new class of [3.3]cyclophanes, and a typical experiment for the synthesis of 10mm is described as follows: a solution of 1,3-benzenedicarbaldehyde (9m) (10 mmol) in ethanol (50 ml) was added dropwise to a suspension of 1,3-bis(2-isocyano-2-tosylethyl)benzene (4m) (10mmol) in ethanol (550 ml) containing sodium ethoxide (Na; 20 mmol) with stirring at room temperature. The resulting mixture was refluxed for 2 h, and then ethanol was removed under reduced pressure. The resulting residue was poured into water containing acetic acid (20 mmol), then extracted with ethyl acetate. After the organic solvent was removed under reduced pressure, the resultant residue was purified by recrystallization from benzene to give 10mm (mp 195-6°C) in 77% yield. 10mm showed the following spectral data; ^{1}H-NMR(CDCl$_3$) δ: 4.16(4H, br s, -CH$_2$-), 6.75(4H, m, ph-H contained Hb), 7.15(3H, m, ph-H), 7.50(1H, br s, Hd), 7.86(2H, s, oxazole C2-H); IR(KBr) ν: 3140 cm^{-1}(oxazole C2-H); MS(m/e): 314(M$^+$).

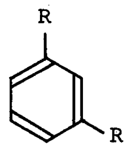
REFERENCES AND NOTES

1) a) A. M. van Leusen, B. E. Hoogenboom, and H. Siderius, Tetrahedron Lett., 1972, 2369; b) H. Saikachi, T. Kitagawa, H. Sasaki, and A. M. van Leusen, Chem. Pharm. Bull., 27, 793(1979); c) O. Possel and A. M. van Leusen, Heterocycles, 7, 77(1977).

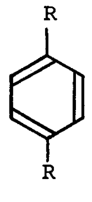
2) a) H. Sasaki and T. Kitagawa, Chem. Pharm. Bull., accepted; b) K. Kurosawa, M. Suenaga, T. Inazu, and T. Yoshino, Tetrahedron Lett., 23, 5335(1982).

3) The structure of this 2:2 adduct was assigned as tetraoxazolo[3.3.3.3]metaparametaparacyclophane, which was confirmed by elemental analysis and the following spectral data; IR(KBr) ν: 3140 cm^{-1} (oxazole C2-H) MS(m/e): 628(M$^+$).

4) Instead of 10mo and 10po, 1:2 adducts (14a and 14b) were isolated in 74% and 84% yields, which were calculated on the basis of 9. 14a and 14b were fully characterized by ^{1}H-NMR, IR, and mass spectroscopies and elemental analyses. Data for 14a; ^{1}H-NMR(CDCl$_3$) δ: 8.60-8.70 and 7.50-8.20(14H, m, aromatic-H), 8.24(2H, s, oxazole C2-H); IR(KBr) ν: 3130 cm^{-1}(oxazole C2-H); MS(m/e): 412(M$^+$). Data for 14b; ^{1}H-NMR(CDCl$_3$) δ: 7.50-8.25(14H, m, aromatic-H), 8.27(2H, s, oxazole C2-H); IR(KBr) ν: 3130 cm^{-1}(oxazole C2-H); MS(m/e): 412(M$^+$).

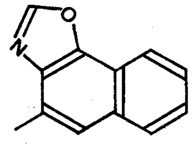


14a



14b

R;



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