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ELECTROPHILE AND SOLVENT DEPENDENT SYNTHESES OF CYCLIC ETHERS FROM (Z,Z)-CYCLOOCTA-1,5-DIENE [1]

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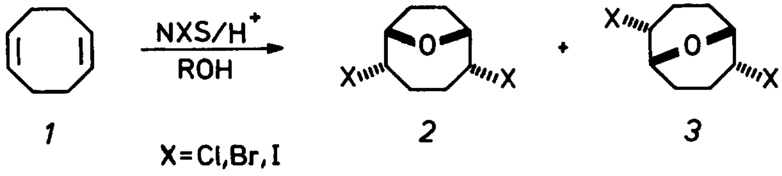
Summary: The isomer ratio in the formation of disubstituted 9-oxabicyclo[4.2.1]nonane and 9-oxabicyclo[3.3.1]nonane derivatives 2 and 3 by an oxyhalogenation procedure depends both on the electrophile and on the solvent utilized.

The formation of substituted bicyclic ethers from (Z,Z)-cycloocta-1,5-diene (1) is known by various procedures. Both BORDWELL and DOUGLASS as well as STETTER and MEISSNER obtained 9-oxabicyclo[3.3.1]nonane derivatives in oxymercuration reactions of the diene [2,3]. Iodinations in chloroform in the presence of mercuric oxide [4] and in methanol [5] as well as chlorination in methanol [6] gave dihalogen substituted 9-oxabicyclononanes in low yields. The hydroxybromination procedure of 1 with N-bromosuccinimide (NBS) in aq. dioxane or absolute methanol, respectively, gives a 4:1 ratio of endo,endo-2,5-dibromo-9-oxabicyclo[4.2.1]nonane (2b) and endo,endo-2,6-dibromo-9-oxabicyclo[3.3.1]nonane (3b) in more than 90 % isolated yield [7a], whereas otherwise the formation of 31 % 2b with NBS in water [7b] or the formation of 21 % 3b with NBS in acetone/water (4:1) [7c] was described. Recently also the formation of phenylseleno substituted 9-oxabicyclononanes using "phenylselenenylic acid" [8a], N-phenylselenophthalimide and N-phenylselenosuccinimide [8b], phenylselenenylcyanide [9] and phenylselenenylchloride [10] in the presence of water or alcohols was described. Here the reaction with PhSeCN, CuCl in ROH (R = H, alkyl) shows a strong dependence on the solvent utilized [9,11]. Because this solvent dependent heterocyclization was not achieved in the reactions of 1 with all other electrophiles it was considered to be perhaps a characteristic of organoselenium chemistry [9].

Presently, we describe the solvent and electrophile dependent rections of (Z,Z)-cycloocta-1,5-diene (1) with N-halogensuccinimides.



When an aqueous or alcoholic solution of the diene 1 containing catalytic amounts of concentrated sulfuric acid is treated successively with 2 molar equivalents of N-chloro-, N-bromo- and N-iodosuccinimide, respectively, at constant temperature between 15-20 °C a mixture of 2 and 3 was formed in excellent yield (cf. Table 1).

Table 1: Oxyhalogenation of (Z,Z)-cycloocta-1,5-diene [a]

Expt.	X	Solvent	% isolated yield 2 + 3 [e]	Isomer ratio 2 : 3 (crude mixture)
1	Cl	MeOH	86	87:13 [b]
2	Cl	Dioxane/H_2O 4:1	89	89:11 [b]
3	Br	MeOH	89	82:18 [b]
4	Br	i-PrOH	85	82:18 [b]
5	Br	Dioxane/H_2O 4:1	93	84:16 [b]
6	I	MeOH	85	1:99 [c]
7	I	EtOH	84	11:89 [c]
8	I	i-PrOH	82	43:57 [c,d]
9	I	t-BuOH	72	87:13 [c,d]
10	I	Dioxane/H_2O 4:1	91	72:28 [c]
11	I	Dioxane/H_2O 10:1	86	74:26 [c]
12	I	Acetone/H_2O 10:1	96	70:30 [c]
13	I	DMSO/H_2O 10:1	96	72:28 [c]
14	I	THF/H_2O 10:1	92	85:15 [c]
15	I	DME/H_2O 10:1	89	87:13 [c]

a) 1 (0,05 mol), NXS (0,1 mol), 100 ml solvent, 3 h room temperature

b) determined by GLC (glass capillary column, 100 m x 0,24 mm I.D., Carbowax 20 M, 180 °C)

c) determined by HPLC (Li Chrosorb Si 100, 10 µm; 250 x 4.1 mm; n-heptane, 1.6 ml/min; 30 bar; UV-detection 254 nm)

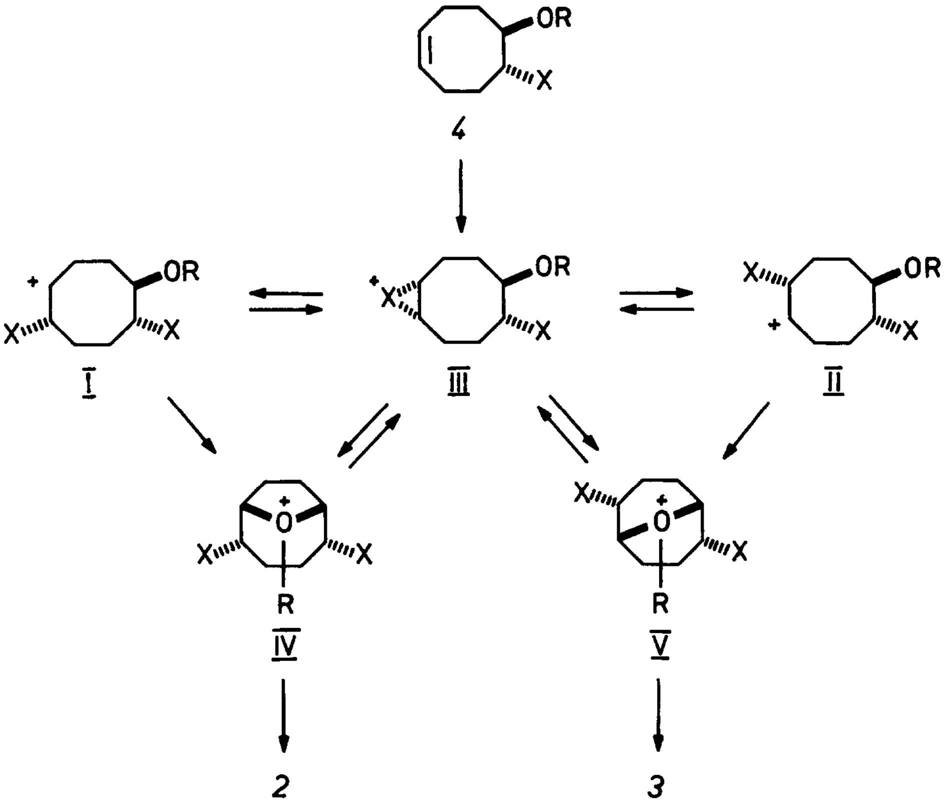
d) determined by comparison of peak heights of all related carbon atoms in the ^{13}C n.m.r. spectra

e) the products are stable under the reaction conditions for at least 72 h.

The assignment of 9-oxabicyclo[4.2.1]- and 9-oxabicyclo[3.3.1]nonane ring systems for 2 and 3 was based on their respective ^{1}H- and ^{13}C n.m.r. spectra (Table 2). Earlier it has been established that the bridgehead atoms in the [4.2.1] ring system are deshielded by 0.4 - 0.6 ppm in the ^{1}H n.m.r. spectra [5,7,12] and by about 10 ppm in the ^{13}C n.m.r. spectra compared with that in the [3.3.1] ring system [13,14].

These reactions should proceed through hydroxy- or alkoxyhalogenations of one double bond, followed by transannular attack of the oxygen function on the cationic centres which are formed on the other side of the ring by the attack of another electrophile at the second double bond [6,7a]. These reactions are not dependent on the nature of the solvent when N-chloro- or N-bromosuccinimide are used as the electrophile (cf. expt. 1-5 Table 1), but are strongly dependent in the case of N-iodosuccinimide (cf. expt. 6-10, Table 1).

The isomer ratio can be explained in terms of the different nature of the intermediates, namely the degree of bridging of the cationic species which is formed in the second step of the reactions from the initially formed 5,6-disubstituted cyclooctene derivative 4.



In the reactions with NCS, two poorly bridged isomeric chloro carbenium ions I and II are likely as intermediates. The positive charge is mainly located on the carbons. Therefore the transannular cyclization step should be irreversible independent of the leaving group R, and as a consequence of the greater tendency of formation of the five membered ring [2,5], the kinetically favoured product 2a is formed mainly.

In the NBS reactions the intermediates should be more strongly bridged and the portion of the thermodynamically more stable product 3b increases. In the case of the reactions with NIS a bridged iodonium ion III is likely and the positive charge is located mainly on the iodine. As a consequence the transannular bridging step III ⟶ IV becomes reversible. When R is not a good leaving group (R = Me, Et) IV is isomerized to the thermodynamically more stable V from which 3c is formed. In the case of a better leaving group (R = t-Bu, H) the elimination of R (IV ⟶ 2c) is faster than the isomerization IV ⟶ V and the kinetically favoured 2c becomes the main product.

The smaller influence of the cosolvents on the product ratio (cf. expt. 10 - 15, Table 1) cannot be explained in detail but seems to be caused by different stabilization of the intermediates.

Table 2: Chemical shifts in ^1H- and ^{13}C n.m.r. spectra

Compound	chemical shifts δ ($CDCl_3$, TMS)					
	C_1/C_6	C_2/C_5	C_3/C_4	C_7/C_8	H_1/H_6	H_2/H_5
2a	81.8	60.5	30.7	26.5	4.50	4.17
2b[7a,14]	81.8	53.4	32.4	27.9	4.62	4.33
2c	83.1	35.7	34.3	30.7	4.59	4.40
2(X=H)[12]	77.7	36.2	24.4	31.6	4.40[6]	
	C_1/C_5	C_2/C_6	C_3/C_7	C_4/C_8	H_1/H_5	H_2/H_6
3b[14]	71.6	51.6	27.8	23.3	4.13	4.26
3c	70.6	33.3	30.0	29.1	4.00	4.50
3(X=H)[12]	66.6	29.4	18.9	29.4	3.90[6]	

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