NUCLEOPHILIC SUBSTITUTION REACTIONS OF THE 2- AND 3-HALOBICYCLO[3.2.1]-

OCT-2-ENES WITH POTASSIUM t-BUTOXIDE AND WITH SODIUM PYRROLIDIDE

A. T. Bottini and Bruce Anderson

Department of Chemistry, University of California, Davis, California 95616

In 1961, Wolinsky[1] described the conversion of ω-bromocamphene to a mixture of 2- and 3-t-butoxy-4,4-dimethylbicyclo[3.2.1]oct-2-ene effected by potassium t-butoxide (t-BuOK), and he rationalized the reaction on the basis of a bicyclo[3.2.1]oct-2-yne intermediate (1) that adds t-BuO⁻ at the 2- and 3-positions in a ratio of 2:1. Recently, Mohanakrishnan et al. reported that the reaction of t-BuOK with 3-bromobicyclo[3.2.1]oct-2-ene (3b) in dimethylsulfoxide (DMSO) gave only the corresponding 3-t-butyl ether 3d and, by analogy with the behavior of 1,2-cyclohexadiene,[3] concluded that the reaction leading to the ether occurs exclusively via the corresponding cyclic allene. As a continuation of our studies of reactions of 1-halocyclo-alkenes with strong base,[3-5] we have investigated reactions of the 2- and 3-halobicyclo[3.2.1]-oct-2-enes (2a, 2c, 3a-c) with t-BuOK and with sodium pyrrolidide (NaNC₄H₈). Our results, which contradict in part the conclusion of Mohanakrishnan et al., are described here.
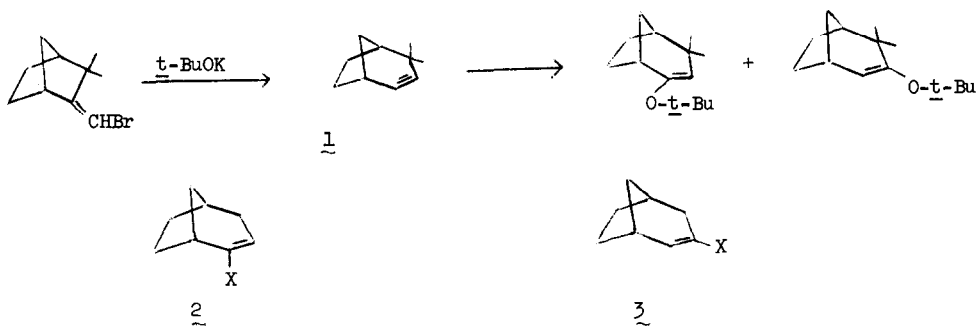
a: X = Cl;   b: X = Br;   c: X = I;   d: X = t-BuO;   e: X = NC₄H₈

2-Chlorobicyclo[3.2.1]oct-2-ene (2a),[6] bp 100-102°/65 mm, was prepared in 60% yield[7] by treatment of 2-bicyclo[3.2.1]octanone[8] with phosphorous pentachloride, and 2a was converted to 2c,[6] bp 74-75°/2.8 mm, in 62% yield via the lithium derivative (cf. ref. 3 and 5). Literature

procedures[9] were used to prepare 3-chloro- and 3-bromobicyclo[3.2.1]oct-2-ene (3a and 3b); and

3c,[6] bp 83-84° (3.2 mm), was prepared in 73% yield from 3b via the lithium derivative.

The 2- and 3-halobicyclo[3.2.1]oct-2-enes were treated with t-BuOK in DMSO and in tetra-

hydrofuran (THF) as well as with NaNC₄H₈ in THF. The product fractions containing the vinyl

ethers 2d[6b] and 3d[6] or enamines 2e[6,12] and 3e[6,12] were separated by distillation, a portion of

each mixture was converted to the corresponding ketones by acid hydrolysis (cf. ref. 3 and 5),

and the ketones were analyzed by vpc on 5% FFAP/60-80 chromosorb W-HMDS. (The vinyl ethers

were also analyzed directly but less precisely by means of their nmr spectra: 2d, δ 1.28; 3d,

δ 1.24 ppm.) As the reaction of 2a with t-BuOK in THF at 65° was very slow, 2a was also

treated with t-BuOK in diglyme (DG) at 130°. The yields and compositions of vinyl ethers and

enamines obtained from these reactions are summarized in Table I.

The essentially identical compositions of the ethers 2d and 3d obtained from the 2- and 3-

halobicyclo[3.2.1]oct-2-enes in THF indicate that all of these nucleophilic substitution

reactions with t-BuOK take place via a common intermediate, and bicyclo[3.2.1]oct-2-yne (8) is

clearly the most likely intermediate. The results in DMSO indicate that the 2-iodo compound

2c also gives vinyl ether exclusively via 8, and, by analogy with the halocyclohexenes,[3] that

the 3-chloro compound 3a gives vinyl ether exclusively via the strained allene 9. On the other

hand, the vinyl-ether forming reactions of the 3-bromo and 3-iodo compounds (3b and 3c) in DMSO

occur by a mixture of mechanisms, with the cycloalkyne 8 being the more important intermediate.

Conceivably, some of the 3-ether 3d could have been formed from the 2-halobicyclo[3.2.1]oct-2-

enes (2) via the allene 9, which could have been formed by prototropic rearrangement of 2 to

the corresponding 4-halobicyclo[3.2.1]oct-2-ene (10), followed by dehydrohalogenation. This

possibility was ruled out by examining the reaction of exo-4-bromobicyclo[3.2.1]oct-2-ene (10:

X = Br)[11] with t-BuOK in DMSO, which gave a 28% yield of 4-t-butoxybicyclo[3.2.1]oct-2-ene (4),[6]
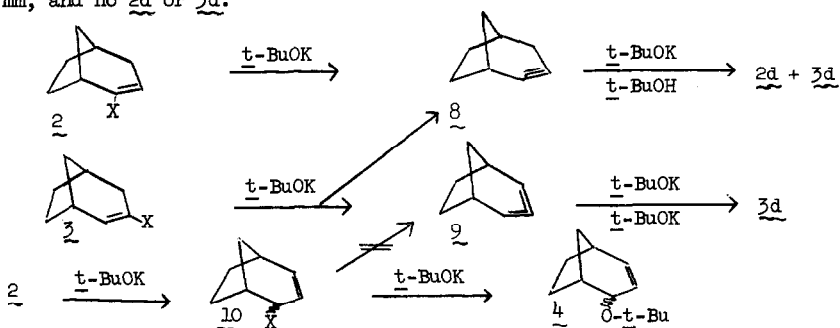
bp 92-95°/17 mm, and no 2d or 3d.

TABLE I. Yields and Compositions of Vinyl Ethers and Enamines from Reactions

of 2- and 3-Halobicyclo[3.2.1]oct-2-enes with t-BuOK and NaNC$_4$H$_8$[a]

Halo-cycloalkene	Base and Solvent	% Yield 2d + 3d (2e + 3e)	% Composition[b] 2d (2e)	3d (3e)
2a	t-BuOK/DMSO	0[c]	-	-
2c	t-BuOK/DMSO	15[d]	9.9	90.1
3a	t-BuOK/DMSO[e]	12	0	100
3b	t-BuOK/DMSO	28	6.5	93.5
3c	t-BuOK/DMSO	27	7.4	92.6
2a	t-BuOK/THF	23[f]	9.7	90.3
2a	t-BuOK/DG	10[g]	13.6	86.4
2c	t-BuOK/THF	49[h]	9.9	90.1
3a	t-BuOK/THF	47[i]	9.0	91.0
3b	t-BuOK/THF	62	8.5	91.5
3c	t-BuOK/THF	63	9.3	90.7
2a	NaNC$_4$H$_8$/THF	(40)	(11.9)	(88.1)
2c	NaNC$_4$H$_8$/THF	(26)	(12.4)	(87.6)
3a	NaNC$_4$H$_8$/THF	(38)	(9.8)	(90.2)
3b	NaNC$_4$H$_8$/THF	(22)	(9.5)	(90.5)
3c	NaNC$_4$H$_8$/THF	(20)	(6.9)	(93.1)

[a] Reactions in DMSO were conducted with 1.1 equiv t-BuOK·t-BuOH per 2 or 3; in THF or DG, t-BuOK:2 (or 3) and NaNC$_4$H$_8$:2 (or 3) mol ratio = 2.2. Reaction temperature = 65° in DMSO and THF, 130° in DG. [b] Analyzed as the corresponding ketones; average of at least 4 determinations, ada = 0.2 - 1.4%. [c] A 14% yield of 4-t-butoxybicyclo[3.2.1]oct-2-ene (4)[6] was obtained. When 2.2 equiv of t-BuOK was used, identifiable amounts of 4-methylene-bicyclo[3.2.1]oct-2-ene (5)[10], 3-methyl-4-methylenebicyclo[3.2.1]oct-2-ene (6)[6b], and 2,3-dimethylenebicyclo[3.2.1]octane (7)[6b] were obtained. [d] A 2% yield of 4 was also obtained. [e] Reactions with 2.2 equiv t-BuOK and 2.5 equiv t-BuOK·t-BuOH gave, respectively, 0.6 and 25% yields of 100% 3d. 5, 6, and 7 were also identified as products (yields ca. 2-3%) from the former reaction. [f] 17% conversion; reaction time, 30 days; a 16% yield of 4 was also obtained. [g] An 18% yield of 4 was also obtained. [h] A 6% yield of 4 was also obtained. [i] 32% conversion; reaction time, 30 days.

Comparison of the above results with those obtained for similar reactions of the halocyclo-hexenes[3] with t-BuOK shows that the corresponding cycloalkyne is significantly more important as an intermediate in the nucleophilic substitution reactions of the 3-halobicyclo[3.2.1]octenes.

The most straightforward interpretation of the results of the reactions with NaNC$_4$H$_8$ is that the enamines are formed from 2a and 2c exclusively via the yne 8, and that the enamines

from the 3-halobicyclo[3.2.1]oct-2-enes are formed _via_ both 8 and the cyclic allene 9. Significantly, and in contrast to the reactions of the 1-halocyclohexenes[3] and the 3-halobicyclo-[3.2.1]oct-2-enes with t-BuOK, the pathway _via_ the cyclic allene (or some other nonrearranging mechanism) is most important for the iodo compound.

With the obvious exception of the reaction of 3-chlorobicyclo[3.2.1]oct-2-ene (3a) with t-BuOK in DMSO, nucleophilic substitution reactions of 3a, 3b, and 3c with t-BuOK and NaNC$_4$H$_8$ occur mainly _via_ the cycloalkyne 8. As was shown in the study of reactions of the halocyclohexenes with t-BuOK,[3] this does not necessarily give a clear picture of the relative amounts of yne (8) and cyclic allene (9) formed from the 3-halobicyclo[3.2.1]oct-2-enes in these reactions Such a picture could possibly result from further study of these reactions carried out in the presence of trapping reagents specific for strained cyclic allenes[2,3,13] or cycloalkynes.[14]

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6. a. A satisfactory elemental analysis was obtained. b. The mass, ir, 100-MHz nmr, and, for 6 and 7, UV spectra were consistent with the assigned structure. (Details will be published in B.A.'s forthcoming Ph.D. Dissertation.)

7. An isomeric impurity, separable by fractional distillation, was also obtained.

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