Tetrahedron Vol 23, pp. 4549 to 4555 Pergamon Press Ltd 1967 Printed in Great Britain

THE STEREOCHEMISTRY OF BICYCLO[3.2.1]-OCTANE—XII

THE PHOTOHALOGENATION OF BICYCLO[3.2.1]OCTENE-2 DERIVATIVES[1]

C. W. JEFFORD and E. HUANG YEN[2]
Chemistry Department, Temple University, Philadelphia, Pa. 19122

(*Received in USA 26 January 1967; accepted for publication 28 March 1967*)

Abstract The light-initiated halogenation of bicyclo[3.2.1]octene-2, its 3-phenyl and 3-bromo derivatives with N-bromosuccinimide and t-butyl hypochlorite resulted in the exclusive formation of the *exo*-4-halobicyclo[3.2.1]octene-2 derivatives.

INTRODUCTION

THE bicyclo[3.2.1]octene-2 skeleton (I) can be considered as a model for a static cyclohexenyl system.[3] However, from an examination of a Dreiding model[4] of I, it appears that the cyclohexene moiety may be flattened by the ethane bridge to make the $C_1C_2C_3C_4C_5$ atoms coplanar (cf. XIV). A possible stereoelectronic consequence of this flattening is that both the *exo* and *endo* C_4 allylic bonds, in the absence of steric hindrance, could display the same chemical reactivity.[5] On the other hand, the C_1-H bond, as it lies in the plane of the C_2-C_3 double bond, should be an unreactive allylic bond.

However, spectral evidence[6, 7] is best accommodated by a conformation of the cyclohexene moiety which is somewhere between the flat chair found in the model and the half-chair encountered in mobile cyclohexenyl systems.[5] Further, despite an apparently unfavorable geometry, the bridgehead proton in I may well be reactive, in view of the fact that bromination of isokaurene with N-bromosuccinimide gave 13-bromokaurene-15 in low yield.[8]

Accordingly, it was decided, for the above considerations, to test the reactivity of the bicyclo[3.2.1]octene-2 skeleton under unambiguous, radical generating con-

---

[1] For a preliminary account see C. W. Jefford and E. Huang Yen, *Tetrahedron Letters* No. 37, 4477 (1966). For Part XI see C. W. Jefford and R. T. Medary, *Tetrahedron* **23**, 4023 (1967).

[2] This paper describes work submitted by E.H.Y. in partial fulfilment of the requirements for the M.A. degree at Temple University.

[3] C. W. Jefford, S. Mahajan, J. Gunsher and B. Waegell, *Tetrahedron Letters* No. 28, 2333 (1965).

[4] W. Büchi, Glasapparatefabrik, Flawil, Switzerland.

[5] In undistorted cyclohexenyl systems the breaking or formation of an allylic bond occurs more easily when it is *quasi-axial* than *quasi-equatorial* (third paragraph, p. 6273 to first column p. 6274, E. J. Corey and R. A. Sneen, *J. Am. Chem. Soc.* **78**, 6269 (1956); R. E. Ireland, T. I. Wrigley and W. G. Young, *Ibid.* **80**, 4604 (1958); H. L. Goering and R. R. Josephson, *Ibid.* **84**, 2779 (1962)).

[6] G. A. Russell, K. Y. Chang and C. W. Jefford, *J. Am. Chem. Soc.* **87**, 4384 (1965).

[7] C. W. Jefford, J. Gunsher and K. C. Ramey, *J. Am. Chem. Soc.* **87**, 4385 (1965).

[8] L. H. Briggs, R. C. Cambie, P. S. Rutledge and D. W. Stanton, *J. Chem. Soc.* 6212 (1965).

ditions.[9] Two reagents were used for allylic halogenation; (i) N-bromosuccinimide (NBS) in carbon tetrachloride with irradiation by UV light, and (ii) t-butyl hypochlorite under the same conditions as in (i).

RESULTS AND DISCUSSION

It is known that photolysis of t-butyl hypochlorite in the absence of oxygen and in the presence of a suitable hydrocarbon results in the formation of the hydrocarbon radical which then reacts with more hypochlorite in a chain process.[10]

Similarly, allylic bromination with NBS is also a free radical chain process.[11] However, it is not entirely clear[12] whether succinimidyl radicals[13] or molecular bromine[14] are responsible for chain propagation. Nevertheless, there is no doubt that the photobromination of alkenes with NBS in the heterogeneous phase proceeds through the intermediacy of the free alkenyl radical.[15]

It was found in the present work that bicyclo[3.2.1]octene-2 (I), its 3-bromo (II) and 3-phenyl (III) derivatives, on photoinitiated chlorination and bromination with t-butyl hypochlorite and NBS underwent exclusive substitution by halogen at the *exo* C_4 position (IV IX). Yields were variable, ranging from 34% to 42% for bromination and 20–60% for chlorination. Reaction mixtures were carefully monitored by TLC. In all cases, a single reaction product was formed.[16]

The identification of the halogenated products was chiefly accomplished by analysis of their NMR spectra. Free radical bromination of 3-bromobicyclo[3.2.1]octene-2 (II) gave a product which was identical to that obtained by the addition of dibromocarbene to norbornene, namely *exo*-3,4-dibromobicyclo[3.2.1]octene-2 (V).[17] As the structure of V has been elucidated previously by nuclear magnetic double resonance spectroscopy,[18] the *exo* disposition of the bromine on C_4 in similar compounds can be assigned safely from the magnitude of the vicinal coupling between the allylic C_4 and the bridgehead hydrogen atoms (i.e. $^3J \sim 2{\cdot}8$ Hz). Accordingly, the structures of *exo*-3-phenyl-4-bromo- (VI), *exo*-3-bromo-4-chloro- (VIII) and *exo*-3-phenyl-4-chlorobicyclo[3.2.1]octene-2 (IX) all follow from their NMR spectra, which display a downfield doublet ($^3J \sim 7{\cdot}0$ Hz) due to a cyclohexenyl vinyl proton and more

---

[9] [a] The copper salt catalysed reaction of t-butyl perbenzoate with bicyclo[3.2.1]octene has been studied (H. L. Goering and U. Mayer, *J. Am. Chem. Soc.* **86**, 3753 (1964)). However, reaction could have proceeded through the octenyl radical or the cation. Moreover, it was tacitly assumed, without grounds save the results themselves, that the cyclohexenyl part of the bicyclo[3.2.1]octene skeleton was geometrically similar to that in a free cyclohexenyl system; [b] cf. D. B. Denney, D. Z. Denney and G. Feig, *Tetrahedron Letters* No 15, 19 (1959); [c] cf. B. Cross and G. H. Whitham, *J. Chem. Soc.* 1650 (1961).

[10] C. Walling and B. B. Jacknow, *J. Am. Chem. Soc.* **82**, 6108, 6113 (1960).

[11] [a] C. Djerassi, *Chem. Rev.* **43**, 271 (1948); [b] L. Horner and E. H. Winkelmann, *Angew. Chem.* **71**, 349 (1959).

[12] cf [a] C. Walling, A. L. Riefer and D. D. Tanner, *J. Am. Chem. Soc.* **85**, 3129 (1963); [b] G. A. Russell and K. M. Desmond, *Ibid.* **85**, 3139 (1963) and the view of L. Horner and E. Winkelmann (Ref. 11*b*).

[13] C. Walling, *Free Radicals in Solution* p. 383. Wiley, New York (1957).

[14] [a] J. Adam, P. A. Gosselain and P. Goldfinger, *Bull. Soc. Chim. Belge* **65**, 533 (1956); [b] F. L. J. Sixma and R. H. Riem, *Koninkl. Ned. Akad. Wetenschap. Proc.* **61B**, 183 (1958).

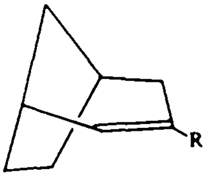
[15] G. F. Bloomfield, *J. Chem. Soc.* 114 (1944).

[16] A brief note, without details of the stereochemistry, has described the allylic bromination of several methylcyclohexenes with NBS (M. Mousseron, F. Winternitz and R. Jacquier, *C.R. Acad. sci. Paris* **224**, 1062 (1947).

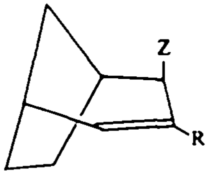
[17] C. W. Jefford, S. Mahajan, J. Waslyn and B. Waegell, *J. Am. Chem. Soc.* **87**, 2183 (1965).

[18] C. W. Jefford, B. Waegell and K. Ramey, *J. Am. Chem. Soc.* **87**, 2191 (1965).

importantly, a doublet (${}^3J \sim 2{\cdot}8$ Hz) characteristic of an allylic proton geminal to an *exo* disposed halogen atom.



I: R = H
II: R = Br
III: R = Ph



IV: R = H, Z = Br
V: R = Z = Br
VI: R = Ph, Z = Br
VII: R = H, Z = Cl
VIII: R = Br, Z = Cl
IX: R = Z = Cl
X: R = H, Z = OH
XI: R = Br, Z = OH
XII: R = Ph, Z = OH

The products obtained by free radical halogenation of bicyclo[3.2.1]octene-2 (I) were difficult to obtain analytically pure since they decomposed progressively during the purification process.[19] Fortunately, both *exp*-4-bromo- (IV) and *exo*-4-chlorobicyclo[3.2.1]octene-2 (VII) furnished characteristic, NMR spectra.[20] The chloro compound VII, which is typical, showed a doublet of doublets at 6·15 ppm due to the C_2 proton (${}^3J_{\text{large}} = 9{\cdot}6$, ${}^3J_{\text{medium}} = 6{\cdot}3$ Hz) and a doublet of doubled doublets at 5·61 ppm (${}^3J_{\text{large}} = 9{\cdot}6$, ${}^3J_{\text{medium}} = 4{\cdot}0$ and $J_{\text{small}} = 1{\cdot}9$ Hz) due to the C_3 proton. At 4·32 ppm appeared a merged doublet of doublets (triplet) (${}^3J_{\text{large}} = 4{\cdot}0$ and ${}^3J_{\text{small}} = 2{\cdot}6$ Hz) arising from the *endo* C_4 proton. The vicinal couplings of 9·6, 6·3, 4·0 and 2·6 Hz are completely in accord with the geometries of the C_2-C_3, C_1-C_2, C_3-C_4 and C_4-C_5 proton pairs in the *exo*-4-halobicyclo[3.2.1]octene-2 skeleton.[7, 18, 20]

It has been mentioned elsewhere[17] that mild hydrolysis of *exo*-3,4-dibromobicyclo[3.2.1]octene-2 (V) afforded the 4-hydroxy derivative of *exo* configuration (XI). Similar hydrolysis of *exo*-4-bromo- (VI) and *exo*-4-chloro-3-phenylbicyclo[3.2.1]octene-2 (IX) gave *exo*-3-phenyl-4-hydroxybicyclo[3.2.1]octene-2 (XII). Moreover, by the same procedure both the unstable *exo*-4-halobicyclo[3.2.1]octenes-2 (IV and VII) were converted to stable *exo*-4-hydroxybicyclo[3.2.1]octene-2 which was identical to an authentic sample. V was also converted by the action of aqueous hydrogen chloride to *exo*-3-bromo-4-chlorobicyclo[3.2.1]octene-2 (VIII). Once again, the magnitude of the coupling constants of the C_4 allylic resonances (2·8 Hz) corroborated the *exo* configuration of the C_4 substituents.

All these 4-hydroxy derivatives and VIII arise by stereospecific attack of water (or chloride in the latter case) on the *exo* face of the appropriate bicyclo[3.2.1]octenyl cation.[17, 3]

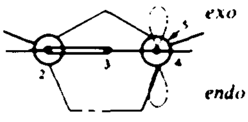
The free radical process of halogenation can be interpreted in terms of the initial

---

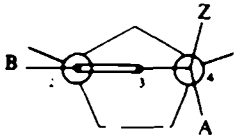
[19] The same products were formed by the stereospecific rearrangement of *exo-syn*-3-chloro-(and bromo-)-tricyclo[3.2.1.$0^{2,4}$]octanes (Ref. 1).

[20] For the detailed NMR analysis of compounds IV and VII see C. W. Jefford and K. C. Ramey, *Tetrahedron* to be published.

generation of a bicyclo[3.2.1]octenyl radical which subsequently undergoes stereospecific attack by halogen on the *exo* side of the C_4 atom. Such stereospecificity could spring from three different effects: torsional,[21] steric or stereoelectronic.



XIII



XIVa: Z = H, A = substituent
XIVb: Z = substituent, A = H

The intermediate bicyclo[3.2.1]octenyl radical may be depicted by the Newman projection (XIII). Consequently, a new bond can be formed by attack on the *exo* or *endo* lobe of the orbital on C_4 to form XIV. If bond eclipsing strain between the C_4 and C_5 peripheral bonds is going to be dominant in the two transition states possible for the change in hybridization at C_4, then *exo* attack will be favored. However, the expected difference in energy between these two processes should be at the most about one kilocalorie,[22] a difference which in itself does not sufficiently account for the high stereoselectivity of the reaction.

A similar conclusion can be drawn from a consideration of steric effects. Generally, the *endo* side of bridged bicyclic molecules is thought to be more hindered than the *exo* side. Nevertheless, the reaction of the norbornyl radical with non-bulky molecules gives rise to an appreciable amount (about 20–30%) of *endo* products despite apparent *endo* hindrance.[23] Furthermore, acetolysis of *exo*-3-bicyclo[3.2.1]-octyl tosylate yields exclusively the *endo* acetate.[24] Therefore, the non-appearance of *endo* C_4 products of bicyclo[3.2.1]octene on free radical halogenation is adequately explained by the operation of stereoelectronic control. If torsional or steric contributions are neglected, then the transition states for *exo* and *endo* attack on the octenyl radical (XI) will be equally delocalized *provided* that the developing products have the geometries reflected by their Dreiding models (XIVb and XIVa). However, there is strong evidence that the cyclohexene moiety of bicyclo[3.2.1]octene-2 derivatives is twisted (XV). The electronic paramagnetic resonance spectrum[6] of the bicyclo[3.2.1]octa-2,3-dione radical anion reveals that the optical electron (which spends some of its time on C_3 (cf. XV) interacts *unequally* with the C_4 allylic C-H bonds (hyperfine splitting constants of 13·5 and 8·7 gauss) thereby implying greater hyperconjugation with the C_4 *exo* bond (C_4-Z) than the *endo* bond (C_4-A).

Additional corroboration for the twisted bicyclo[3.2.1]octene-2 skeleton (XV) is provided by the unequal vinyl allylic proton couplings (J_{BZ} = 2·0 Hz and J_{BA} = 1·0 Hz cf. XVb) which are observed in the nuclear magnetic resonance spectra of derivatives of I.[7] Therefore, the C_4 *exo* and *endo* allylic bonds of I retain *quasi-axial* and *quasi-equatorial* character despite the constraint of the ethane bridge. Accordingly,

---

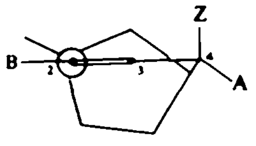
[21] P. v R. Schleyer, *J. Am. Chem. Soc.* 701 (1967).

[22] D. R. Lide, *J. Chem. Phys.* **29**, 1426 (1958); K. S. Pitzer, *Discuss. Faraday Soc.* **10**, 66 (1951).

[23] [a] E. C. Kooyman and G. C. Vegter, *Tetrahedron* **4**, 382 (1958); [b] H. Kwart and J. L. Nyce, *J. Am. Chem. Soc.* **86**, 2601 (1964).

[24] C. W. Jefford, J. Gunsher and B. Waegell, *Tetrahedron Letters* No. 38, 3405 (1965).

preferential attack occurs at the *quasi-axial* or *exo* position of the radical XIII owing to better orbital overlap. In the bicyclo[3.2.1]octane system there is reason to believe that such stereoelectronic control is paramount. For example, ionic bromination of bicyclo[3.2.1]octanone-3, under conditions of kinetic control, resulted in *axial* insertion of the *second* bromine as well as the first, despite the setting up of an unfavorable 1,3 diaxial interaction.[25]



XVa: Z = substituent
A = B = H
XVb: Z = A = B = H

EXPERIMENTAL*

NMR spectra were measured at 60 Hz on a model A-60-A spectrometer (Varian Associates, Palo, Alto, Calif) using 10% CCl_4 or $CDCl_3$ solns containing TMS as a standard. Characteristic data are entered in Table 1. Data for compounds II, V, X, XI is omitted as it has been described previously. The detailed NMR analysis of compounds IV and VII together with a correlation of their molecular geometry will be found elsewhere.[20]

Preparation of bicyclo[3.2.1]*octene-2 derivatives.* Compounds I and II were prepared by previously described procedures.[25b,26]

3-*Phenylbicyclo*[3.2.1]*octene*-2 (III). A dry ethereal soln of Grignard reagent was prepared from Mg turnings (1·2 g) and bromobenzene (8·6 g, 0·055 M). The soln was cooled to 0° and an ethereal soln of bicyclo[3.2.1]octanone-3 (3·1 g, 0·025 M) was added. The mixture was stirred overnight and then poured onto ice. $Mg(OH)_2$ was dissolved with cold dil H_2SO_4. After work-up an oil was obtained. Chromatography over silica followed by distillation (b.p. 80° at 0·5 mm) gave an oil (1·5 g, 25%) which showed as a single spot on TLC. (Found: C, 90·89; H, 8·84. $C_{14}H_{16}$ requires: C, 91·30; H, 8·70%.)

Photocatalytic bromination. N-Bromosuccinimide (NBS) was purified by rapid recrystallization from 10 times its wt of hot water, and dried in air for 3 days. The general procedure is typified by the bromination of II.

exo-3,4-*Dibromobicyclo*[3.2.1]*octene*-2 (V). Compd II (18·7 g, 0·1 M) in CCl_4 (25 ml) was placed in a 50 ml 3-neck flask, fitted with a reflux condenser and a $CaCl_2$ drying tube. NBS (8·9 g, 0·05 M) was added to the soln and the resulting suspension was heated to boiling while being irradiated with an UV light lamp ("Mineralight", Model No. R-51, Ultraviolet Products Inc., San Gabriel, Calif.). Heating and irradiation were continued for 20 hr. The resulting brown colored soln was cooled at 0° overnight. The deposited crystals of succinimide were removed by filtration. The solvent was removed and the residual oil was fractionally distilled; the fraction boiling at 90–91° at 0·25 mm (4·5 g) was collected. It showed as one spot on TLC (silica gel G, E. Merck, Darmstadt, W. Germany) and 80% cyclohexane, 20% AcOEt as solvent). The product was identical with *exo*-3,4-dibromobicyclo[3.2.1]octene-2 prepared by the addition of dibromocarbene to norbornene.[17] The yield was 34% based on NBS.

exo-3-*Phenyl-4-bromobicyclo*[3.2.1]*octene*-2 (VI). Bromination of III (2 g, 0·0076 M) with NBS (0·9 g, 0·005 M) afforded the product (0·57 g, 42% yield), b.p. 125° at 1 mm, one spot on TLC (Found: C, 64·00; H, 5·69; Br, 30·85. $C_{14}H_{15}Br$ requires: C, 63·88; H, 5·70; Br, 30·42%.)

---

* Elemental analyses were performed by Dr G. Robertson, West End Avenue, Florham Park, N.J.

[25] [a] C. W. Jefford and B. Waegell, *Tetrahedron Letters* No. 28, 1981 (1963); [b] B. Waegell and C. W. Jefford, *Bull Soc Chim Fr.* 844 (1964).

[26] K. Alder, H. Krieger and H. Weiss, *Chem. Ber* **88**, 144 (1955).

exo-4-*Bromobicyclo*[3.2.1]*octene*-2 (IV). Bromination of I (2·0 g. 0·02 M) NBS (2·5 g. 0·014 M) gave the product (b.p. 90° at 13 mm, 0·9 g, 35% yield). All attempts to obtain an acceptable analysis failed. Chromatography over silica and alumina, as well as repeated distillation, resulted in decomposition. However, the skeleton of IV was confirmed by hydrolysis with an aqueous acetone soln of $AgNO_3$ to X which was identical to an authentic sample.[27] Fortunately, one distillation was enough to purify the product so that an impeccable NMR spectrum could be obtained. The stereochemistry of IV was confirmed by double resonance NMR spectroscopy.[20]

TABLE 1. CHEMICAL SHIFTS[a] AND VICINAL[b] COUPLING CONSTANTS[c] OF THE PHENYL (P), VINYL (B) AND ALLYL (A) RESONANCES OF SOME BICYCLO[3.2.1]OCTENE-2 DERIVATIVES

	P	B	A
III[e]	7·21	6·32	-
	m	d 7·00	
VI[e]	7·21	6·19	4·93
	m	d 6·90	d 2·80
VII[g]	C_2-H 6·15	C_3-H 5·61	4·32
	d of d	d of d.d	d of d
VIII[e]		6·36	4·23
		d 7·0	d 2·8
IX[e]	7·25	6·22	4·68
	m	d 6·90	d 2·8
XII[f]	7·32	6·38	4·31
	m	d 6·8	d 2·9

[a] In ppm. [b] Both vinyl and allylic signals display additional splitting due to remote coupling cf. refs 7 and 18. [c] In Hz. [d] Doublet. [e] In CCl_4 as solvent. [f] $CDCl_3$ as solvent. [g] See text for further description. m, multiplet.

Photocatalytic chlorination

exo-3-*Bromo-4-chlorobicyclo*[3.2.1]*octene*-2 (VIII). Compd II (6·2 g. 0·033 M) and CCl_4 (25 ml) was placed in a 50 ml 3-neck flask equipped with a magnetic stirrer, reflux condenser, gas inlet and outlet tubes, and an addition funnel. The apparatus and soln were flushed initially for 30 min with CO_2 and a current of gas was maintained over the surface of the soln during the reaction. While the soln was stirred and irradiated with UV light, t-butyl hypochlorite[28] (3·6 g. 0·033 M) in CCl_4 (10 ml) was added gradually. The reaction was judged to be complete when the color and smell of the t-butyl hypochlorite had disappeared, which usually required 2 days. Solvent and t-butanol were removed by distillation. The fraction boiling at 112–114° at 2·2 mm was collected (1·5 g. 20% yield); TLC of the product showed a single spot (Found: C, 43·36; H, 4·52; Br + Cl, 51·91. $C_8H_{10}BrCl$ requires: C, 43·34; H, 4·51; Br + Cl, 52·12%.) Compound VIII was identical with that obtained by treating *exo*-3,4-dibromobicyclo[3.2.1]octene-2 with an aqueous-acetone soln of HCl.

exo-3-*Phenyl-4-chlorobicyclo*[3.2.1]*octene*-2 (IX). Compd III (1·61 g. 0·0087 M) was chlorinated with t-butyl hypochlorite (1·65 g. 0·015 M) according to the above procedure. The crude product was purified by column chromatography over silica gel (85 g. 28–200 mesh) using pentane as eluant (0·98 g. 51% yield) (Found: C, 77·08; H, 7·11; Cl, 16·10. $C_{14}H_{15}Cl$ requires: C, 76·90; H, 6·87; Cl, 16·23%.)

exo-4-*Chlorobicyclo*[3.2.1]*octene*-2 (VII). Compd I (1·45 g. 0·013 M) on chlorination with t-butyl hypochlorite (0·99 g. 0·009 M) yielded 0·78 g of product (60%). Attempted purification resulted in decomposition. It was found that a single distillation afforded the product in its purest possible state (as judged

---

[27] H. L. Goering, R. W. Greiner and M. F. Sloan, *J. Am. Chem. Soc.* **83**, 1391 (1961).

[28] H. M. Teeter and E. W. Bell, *Org. Syn.* Coll. Vol. **4**, 125 (1963).

by its NMR spectrum). Its structure was confirmed by hydrolysis to X[27] and by double resonance NMR spectroscopy.[20]

exo-3-*Phenyl-4-hydroxybicyclo*[3.2.1]*octene*-2 (XII). A mixture of *exo*-3-phenyl-4-bromobicyclo[3.2.1]-octene-2 (2·65 g, 0·01 M) in acetone (30 ml) and $AgNO_3$ (2·0 g, 0·012 M) in water (30 ml) was gently boiled under reflux for 30 min. AgBr was removed and the resulting soln was worked up to yield a colorless solid. Recrystallization from ether cyclohexane afforded 0·76 g (38% yield) of product, m.p. 82–83. The IR spectrum showed maxima at 3250 and 1625 cm^{-1} (Found: C, 83·90; H, 7·92. $C_{14}H_{16}O$ requires: C, 83·95; H, 8·05%.) Treatment of compound IV under the same conditions also gave XII.

Acknowledgements. We thank the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation for financial support of this research.