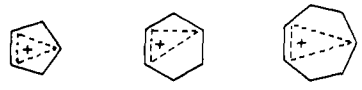
A Novel $C_7H_{11}^+$ Cation

Wolfgang Kirmse,* Rainer Siegfried, and Joachim Streu

Abteilung für Chemie der Ruhr-Universität
D-4630 Bochum, FRG

Received December 19, 1983
Revised Manuscript Received February 27, 1984

Winstein's concept of homoaromaticity[1] proved to be most useful in the field of carbocations.[2] π-Delocalization is expected to decrease as the number of saturated, interrupting centers increases.[2] However, the limits of "bridge extension" are not obvious. The bishomocyclopropenyl cations **1** and **2** intervene in solvolyses of cyclopent-3-enyl and cyclohex-3-enyl tosylates, respectively.[3,4] Cation **1** has also been generated by protonation of 3-cyclo-



1 **2** **3**

pentenylidene,[5] and **2** was found to arise from bicyclo[2.2.0]-hex-*exo*-2-yl tosylate.[6] The homologous ion **3** has not been accessible from cyclohept-4-enyl precursors.[7] We report here on a σ route to **3**.

Acetolyses of the epimeric bicyclo[3.2.0]hept-2-yl brosylates (**4**-OBs, **6**-OBs) afforded bicyclo[3.2.0]hept-*exo*-2-yl acetate (**4**-OAc) and 7-norbornyl acetate (**5**-OAc).[8,9] The higher **4**/**5** ratio observed with **6**-OBs may be attributed to ion pairing and/or k_s processes. The nitrous acid deamination of the *exo*-amine **4**-NH_2[10] gave a product distribution closely resembling that obtained from **4**-OBs (Table I). In contrast, the *endo*-amine **6**-NH_2[10] produced a substantial fraction of *endo*-alcohol **6**-OH and small amounts of cyclohept-4-enol (**7**-OH). Fragmentation was greatly enhanced with 5-methylbicyclo[3.2.0]hept-*endo*-2-ylamine (**8**),[10] which gave 1-methylcyclohept-4-enol (**9**) as the major product (66%). Only traces of **9** (≤0.2%) were formed from the *exo*-amine **10** (Scheme I).

Obviously, bicyclo[3.2.0]heptane-*exo*-2-diazonium and -*endo*-2-diazonium ions decompose, at least in part, by different reaction paths. Participation of the C-1–C-5 bond in **6**-N_2^+, with consequent intervention of **3**, is a suggestive route to **6**-OH and **7**-OH. In accordance with these ideas, diazotization of [2-^{2}H]**6**-NH_2 produced **6**-OH with an even distribution of the deuterium among C-1 and C-2 (Scheme II). In contrast, **4**-OH was formed without scrambling of the label (^{2}H NMR, ±2%). Not surprisingly, the deuterium was located at C-1 of **5**-OH and at C-4,5 of **7**-OH. Complementary evidence came from the diazotization of optically active **6**-NH_2.[12] We obtained racemic **6**-OH whereas **4**-OH was enantiomerically pure.[13]

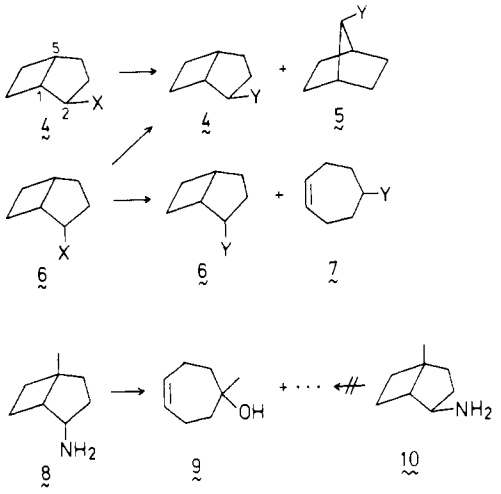
Our results strongly support **3** as the immediate precursor to **6**-OH. Rapid equilibration of open ions, **11** ⇄ **11′**, is incompatible

Table I. Product Distributions (%)

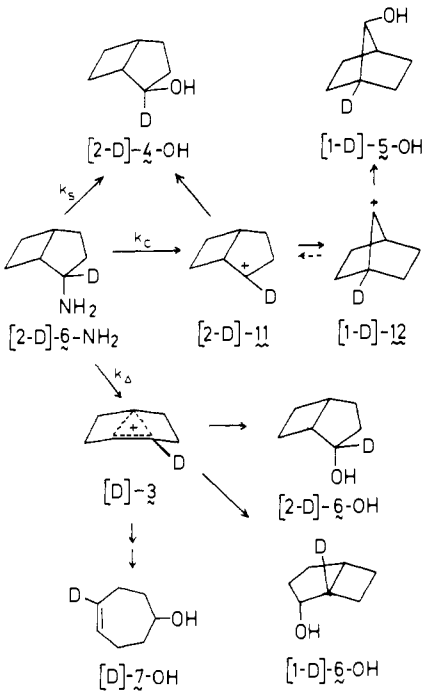
reaction	4-OR	5-OR	6-OR	7-OR
4-OBs, HOAc[8,9]	5	94		
6-OBs, HOAc[9]	26	73		
4-NH_2, HNO_2, H_2O[a]	8.1	91.0	0.8	0.1
6-NH_2, HNO_2, H_2O[a]	15.0	47.6	30.6	6.8

[a] $NaNO_2$, aqueous perchloric acid, pH 3.5.

Scheme I



Scheme II



(1) Winstein, S. *J. Am. Chem. Soc.* **1959**, *81*, 6524.
(2) For reviews, see: (a) Winstein, S. *Q. Rev. Chem. Soc.* **1969**, *23*, 141. (b) Warner, P. M. *Top. Nonbenzenoid Aromat. Chem.* **1976**, 2. (c) Paquette, L. A. *Angew. Chem.* **1978**, *90*, 114; *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 106.
(3) Lambert, J. B.; Finzel, R. B.; Belec, C. A. *J. Am. Chem. Soc.* **1980**, *102*, 3281.
(4) Lambert, J. B.; Featherman, S. I. *J. Am. Chem. Soc.* **1977**, *99*, 1542.
(5) Kirmse, W.; Pham, V. C.; Henning, P. G. *J. Am. Chem. Soc.* **1983**, *105*, 1695.
(6) McDonald, R. N.; Curi, C. A. *J. Am. Chem. Soc.* **1979**, *101*, 7116.
(7) (a) Cope, A. C.; Park, C. H.; Scheiner, P. *J. Am. Chem. Soc.* **1962**, *84*, 4862. (b) Capellini, C.; Corbella, A.; Gariboldi, P. *Gazz. Chim. Ital.* **1977**, *107*, 171. (c) Streu, J., Unpublished results.
(8) Winstein, S.; Gadient, F.; Stafford, E. T.; Klinedinst, P. E. *J. Am. Chem. Soc.* **1958**, *80*, 5895.
(9) Svensson, T. *Chem. Scripta* **1974**, *5*, 20.
(10) *exo*-Amine **4**-NH_2 was prepared from **6**-OTs by azide displacement (NaN_3, Me_2SO, 80 °C, 24 h, 86%) followed by $LiAlH_4$ reduction of **4**-N_3 (64%). *endo*-Amine **6**-NH_2 was obtained by hydrogenation (PtO_2, HOAc) of bicyclo[3.2.0]heptan-2-one oxime (76%). Analogous procedures were applied to 5-methylbicyclo[3.2.0]heptan-2-one,[11] yielding **8** and **10**, respectively.
(11) Cargill, R. L.; Wright, B. A. *J. Org. Chem.* **1975**, *40*, 120.
(12) Fermenting yeast reduction of bicyclo[3.2.0]heptan-2-one afforded (1*R*,5*R*)-**6**-OH (e.e. 80%) whereas diisopinocampheylborane and bicyclo-[3.2.0]hept-2-ene gave (1*S*,5*S*)-**4**-OH (ee 82%; configuration assigned by CD of the ketone). The alcohols were processed as above[10] to **6**-NH_2 whose enantiomeric excess (82%) was confirmed by GC of the *N*-(trifluoroacetyl)-(*S*)-prolylamide.
(13) Base-line separation of the enantiomers of **6**-OH was achieved by GC on glass capillaries coated with optically active polypropylene glycol.[14] The enantiomers of **4**-OH gave overlapping peaks. Therefore, **4**-OH was isolated by preparative GC and converted into **6**-OH (PCC oxidation followed by $LiAlH_4$ reduction) for analysis.
(14) Kirmse, W.; Siegfried, R. *J. Am. Chem. Soc.* **1983**, *105*, 950.

0002-7863/84/1506-2465$01.50/0

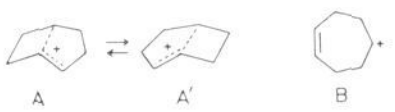
with the absence of deuterium scrambling (racemization) in **4**-OH. These data also exclude significant "leakage" from **3** to **11**. The structure(s) of the intermediate(s) en route to **4** and **5** will be discussed in a forthcoming full paper.[15] The **4**-OH/**6**-OH ratios of **4**-NH_2 and **6**-NH_2 (Table I) indicate that solvolytic displacement (k_s) contributes to the formation of **4**-OH from **6**-N_2^+.

The generation of **3** from **6**-N_2^+, but not from **6**-OBs, deserves comment. The small activation energy of nitrogen extrusion from diazonium ions brings the rates of several competing processes (k_s, k_c, k_Δ) closer together.[16] As a rule, k_Δ processes provide low-energy reaction paths and are therefore more prominent in solvolysis than in deamination. The present case is thought to be exceptional because bridging is associated with increased strain energy. Thus k_Δ is accentuated by the better leaving group. Our observations with **6**-NH_2 parallel previous reports on *endo*-2-norbornylamine[14] and add a new species to the $C_7H_{11}^+$ manifold.[17]

(15) The symmetrical 7-norbornyl cation (**12**), drawn here for the sake of simplicity, is not an adequate representation; see: Sunko, D. E.; Vancik, H.; Deljac, V.; Milun, M. *J. Am. Chem. Soc.* **1983**, *105*, 5364 and references cited therein.

(16) Streitwieser, A. *J. Org. Chem.* **1957**, *22*, 861.

(17) A referee has pointed out that our data do not distinguish the bishomocyclopropenyl cation **3** from a pair of rapidly equilibrating homoallylic ions, A ⇄ A′. The open 4-cycloheptenyl cation (**B**), although not a precursor



to the bicyclo[3.2.0]heptan-2-ols,[7] may intervene on the reaction path from **3** to **7**.

Photoactivated Stereospecific Cleavage of Double-Helical DNA by Cobalt(III) Complexes

Jacqueline K. Barton* and Adrienne L. Raphael

Department of Chemistry, Columbia University
New York, New York 10027

Received November 28, 1983

There has been considerable interest in DNA endonucleolytic cleavage reactions that are activated by metal ions,[1,2] both for the preparation of "footprinting" reagents[3] and as models for the reactivity of some antitumor antibiotics, notably bleomycin[4] and streptonigrin.[5] The features common to these complexes are that the molecule has a high affinity for double-stranded DNA and that the molecule binds a redox-active metal ion cofactor. The delivery of high concentrations of metal ion to the helix, in locally

(1) (a) Hertzberg, R. P.; Dervan, P. B. *J. Am. Chem. Soc.* **1982**, *104*, 313. (b) Schultz, P. G.; Taylor, J. S.; Dervan, P. B. *Ibid.* **1982**, *104*, 6861. (c) Schultz, P. G.; Dervan, P. B. *Proc. Natl. Acad. Sci. U.S.A.* **1983**, *80*, 6834. (d) Taylor, J. S.; Schultz, P. G.; Dervan, P. B. *Tetrahedron* **1984**, *40*, 457.

(2) (a) Sigman, D. S.; Graham, D. R.; Marshall, L. E.; Reich, K. A. *J. Am. Chem. Soc.* **1980**, *102*, 5419; (b) *Biochemistry* **1981**, *20*, 244. (c) Que, B. G.; Downey, K. M.; So, A. G. *Ibid.* **1980**, *19*, 5987. (d) Recently a phenanthroline–copper complex was shown to cleave right-handed DNA conformations preferentially. See: Pope, L. A.; Sigman, D. S. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 3.

(3) (a) Van Dyke, M. W.; Hertzberg, R. P.; Dervan, P. B. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 5470. (b) Cartwright, I. L.; Hertzberg, R. P.; Dervan, P. B.; Elgin, S. C. R. *Proc. Natl. Acad. Sci. U.S.A.* **1983**, *80*, 3213. (c) Cartwright, I. L.; Elgin, S. C. R. *Nucleic Acids Res.* **1982**, *10*, 5835. (d) Jessee, B.; Gargiulo, G.; Razvi, R.; Woral, A. *Ibid.* **1982**, *10*, 5823. (e) Van Dyke, M. W.; Dervan, P. B. *Biochemistry* **1983**, *22*, 2372. (f) Lane, M. J.; Dabrowiak, J. C.; Vournakis, J. N. *Proc. Natl. Acad. Sci. U.S.A.* **1983**, *80*, 3260.

(4) (a) "Bleomycin: Chemical, Biochemical, and Biological Aspects"; Hecht, S. M., Ed.; Springer-Verlag: New York, 1979. (b) Sausville, E. A.; Peisach, J.; Horwitz, S. B. *Biochemistry* **1978**, *17*, 2740. (c) Burger, R. M.; Peisach, J.; Horwitz, S. B. *Life Sci.* **1981**, *28*, 715. (d) Dabrowiak, J. C. *J. Inorg. Biochem.* **1980**, *13*, 317. (e) Lown, J. W.; Sim, S. K. *Biochem. Biophys. Res. Commun.* **1977**, *77*, 1150.

(5) Cone, R.; Hasan, S. K.; Lown, J. W.; Morgan, A. R. *Can. J. Biochem.* **1976**, *54*, 219.

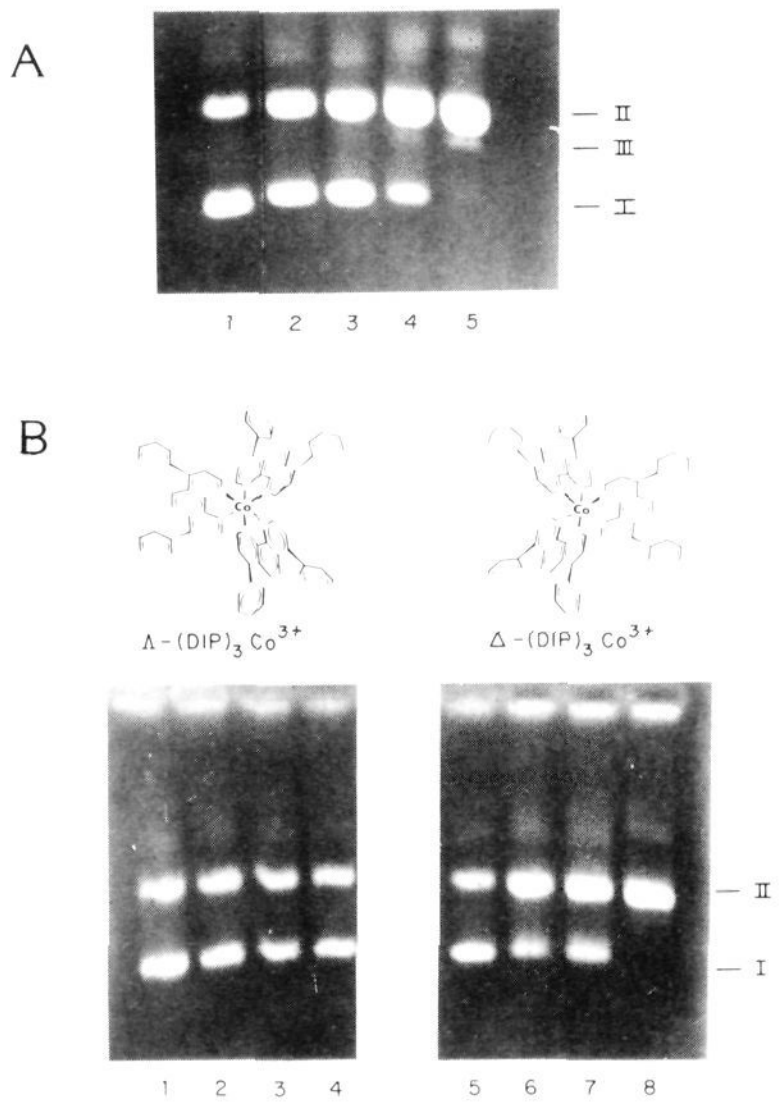


Figure 1. (A) Cleavage of plasmid ColE1 DNA in the presence of $(phen)_3Co^{3+}$ and light. The 1% agarose gel shows the distribution of DNA forms (100 μM nucleotide) initially without cobalt (lane 1) and after irradiation at 254 nm (4-W mercury lamp) in the presence of 10 μM $Co(phen)_3^{3+}$ *for 0, 20, 40, and 60 min (lanes 2–5, left to right). The* samples were incubated in 50 mM Tris acetate buffer, pH 7.0, and 18 mM NaCl and then electrophoresed for 1 h at 60 V and stained with ethidium. (B) The cleavage is also stereoselective. Plasmid ColE1 DNA (100 μM) was incubated with Λ- (left) or Δ-$Co(DIP)_3^{3+}$ (right) (5 μM) and irradiated for 0, 0.5, 1.0, or 1.5 h (lanes 1–4 and 5–8 for the Λ and Δ isomers, respectively). Incubation of this DNA with Λ-$Co(DIP)_3^{3+}$ in light has no effect, while incubation with Δ-$Co(DIP)_3^{3+}$ in light causes complete conversion of form I to form II.

generating oxygen or hydroxide radicals, yields an efficient DNA cleavage reaction. We have demonstrated[6] that tris(phenanthroline) complexes of zinc(II) and ruthenium(II) display enantiomeric selectivity in binding to DNA. This chiral discrimination is enhanced markedly in the case of tris(diphenylphenanthroline)ruthenium(II) isomers, which serve as spectroscopic probes in solution to distinguish right- and left-handed DNA helices.[7] It occurred to us that a *stereospecific* DNA nicking agent might be prepared by using tris(diphenylphenanthroline) complexes with the suitable choice of a redox-active metal; metallointercalation reagents[8] offer that flexibility. Our work has been prompted also by the finding[9] that cobalt(III) bleomycins cleave DNA in the presence of light.[10] We report here that tris(phenanthroline)cobalt(III)[11] at low concentrations cleaves

(6) (a) Barton, J. K.; Dannenberg, J. J.; Raphael, A. L. *J. Am. Chem. Soc.* **1982**, *104*, 4967. (b) Barton, J. K.; Danishefsky, A.; Goldberg, J. *Ibid.*, in press.

(7) (a) Barton, J. K.; Basile, L. A.; Danishefsky, A.; Alexandrescu, A. *Proc. Natl. Acad. Sci. U.S.A.*, in press. (b) Barton, J. K. *J. Biomol. Struct. Dyn.* **1983**, *1*, 621.

(8) (a) Lippard, S. J. *Acc. Chem. Res.* **1978**, *11*, 211. (b) Lippard, S. J.; Bond, P. J.; Wu, K. C.; Bauer, W. R. *Science (Washington, D.C.)* **1976**, *194*, 726. (c) Bond, P. J.; Langridge, R.; Jennette, K. W.; Lippard, S. J. *Proc. Natl. Acad. Sci. U.S.A.* **1975**, *72*, 4285. (d) Jennette, K. W.; Lippard, S. J.; Vassiliades, G. A.; Bauer, W. R. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 3839.

(9) Chang, C. H.; Meares, C. F. *Biochemistry* **1982**, *21*, 6332.

(10) Cobalt(III) polyamine complexes generally undergo photoreduction reactions. See: (a) Adamson, A. W. *Coord. Chem. Rev.* **1968**, *3*, 169. (b) Balzani, V.; Maggi, L.; Manfrin, M. F.; Bolletta, F. *Ibid.* **1975**, *15*, 321. (c) Adamson, A. W. *Pure Appl. Chem.* **1979**, *51*, 313.

0002-7863/84/1506-2466$01.50/0