hydrogen was irradiated, causing an enhancement of the signal at δ 2.25 and not the hydrogens at δ 3.30; ^{13}C NMR δ 210.11, 167.84, 132.79, 118.55, 44.29, 43.71, 33.50, 31.29, 24.39, 20.68.

Acknowledgment. We are grateful to Dr. M. J. Shapiro of Sandoz, Inc., for kindly providing the ^{13}C NMR and 200-MHz ^1H NMR spectra.

Registry No. **3a** (*n* = 3), 1121-64-8; **3c** (*n* = 3), 42205-56-1; **3c** (*n* = 4), 17606-95-0; **3c** (*n* = 5), 42205-59-4; (*E*)-**3c** (*n* = 6), 42205-61-8; **3d** (*n* = 3), 90743-12-7; **3d** (*n* = 4), 90743-15-0; **3d** (*n* = 5), 90743-18-3; (*E*)-**3d** (*n* = 6), 90743-22-9; (*Z*)-**3d** (*n* = 6), 90762-82-6; **3e** (*n* = 3), 90743-13-8; **3e** (*n* = 4), 90743-16-1; **3e** (*n* = 5), 90743-19-4; (*E*)-**3e** (*n* = 6), 90743-21-8; **3f** (*n* = 3), 90743-14-9; **3f** (*n* = 4), 90743-17-2; **3f** (*n* = 5), 90743-20-7; (*E*)-**3f** (*n* = 6), 90743-23-0; **4a** (*n* = 3), 1121-66-0; **4c** (*n* = 3), 42205-57-2; **4c** (*n* = 4), 90743-28-5; **4d** (*n* = 3), 90743-25-2; **4d** (*n* = 4), 90743-29-6; **4d** (*n* = 5), 90743-32-1; **4d** (*n* = 6), 90743-24-1; **4e** (*n* = 3), 90743-26-3; **4e** (*n* = 4), 90743-30-9; **4f** (*n* = 3), 90743-27-4; **4f** (*n* = 4), 90743-31-0; **5** (*n* = 3), 90743-33-2; Δ²-**5** (*n* = 3), 90743-37-6; **5** (*n* = 4), 90743-34-3; **5** (*n* = 5), 90743-35-4; (*E*)-**5** (*n* = 6), 90743-36-5; (*Z*)-**5** (*n* = 6), 90743-38-7; **6** (*n* = 3), 90743-40-1; **6** (*n* = 4), 90743-39-8; **6** (*n* = 5), 90743-41-2; **6** (*n* = 6), 90743-42-3; **7** (*n* = 3), 90743-43-4; **7** (*n* = 4), 90743-45-6; **7** (*n* = 5), 90743-46-7; **7** (*n* = 6), 90743-47-8; **8** (*n* = 3), 90743-48-9; **8** (*n* = 4), 90743-49-0; **8** (*n* = 5), 90743-50-3; **8** (*n* = 6), 90743-51-4; **9** (*n* = 3), 90743-53-6; **9** (*n* = 4), 90743-52-5; **9** (*n* = 5), 90743-54-7; (*E*)-**9** (*n* = 6), 90743-55-8; (*Z*)-**9** (*n* = 6), 90743-56-9; **10** (*n* = 3), 90743-57-0; **10** (*n* = 4), 90743-58-1; **10** (*n* = 5), 90743-59-2; **10** (*n* = 6), 90743-60-5; **11** (*n* = 3), 90743-61-6; **11** (*n* = 4), 90743-62-7; **11** (*n* = 5), 90743-63-8; **11** (*n* = 6), 90743-64-9; **12** (*n* = 3), 90743-65-0; **12** (*n* = 4), 90743-66-1; **12** (*n* = 5), 90743-72-9; (*E*)-**12** (*n* = 6), 90743-67-2; (*Z*)-**12** (*n* = 6), 90743-68-3; **13**, 90743-71-8; **14**, 90743-69-4; **15**, 90743-70-7; DBN, 3001-72-7; dimethylaluminum amide, 24758-44-9; trimethylaluminum, 75-24-1; ammonia, 7664-41-7; 2-methyl-6-oxo-1-cyanocycloheptane ethylene ketal, 90743-44-5.

The Search for Long Range Aryl Migration in the Solvolysis of Suitably Positioned Monoaryl Derivatives in the Tricyclo[3.2.1.0^{2,4}]octane and Bicyclo[3.2.1]octane Skeletal Systems[1,2]

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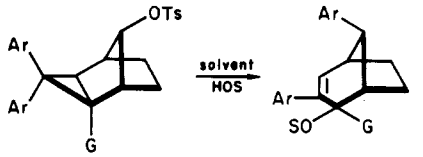
Received February 7, 1984

Previous work has established that long range aryl migration (LRAM) and electrocyclic ring opening (ERO) combine (LRAMERO) to rearrange the *exo*-3,3-diaryltricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl system in solvolysis. Left uninvestigated in the earlier work were the necessity of the second ("stationary") aryl group and the extent and need that ERO contribute to the process. The present study involved the synthesis, characterization, and solvolytic behavior of substrates designed to investigate these aspects of reaction. It has been determined that a second aryl group is not necessary in order to observe LRAMERO, although the proximate positioning of the migrating aryl group and the leaving group center remains critical. The *syn*-3-phenyl and *syn*-3-*p*-tolyl (note *mono*aryl) analogues of the previously studied *di*aryl systems exhibit undiminished LRAMERO, whereas the *anti*-3-phenyl epimer is inert. The kinetics exhibited by the syn compounds, coupled with the rearranged products observed, additionally support the view that ERO occurs in concert with LRAM. Regretably, the question of the necessity of ERO remains unanswered. The bicyclo[3.2.1]octane substrate chosen to decide the question eschewed LRAM, presumably because of a conformational bias, and instead underwent solvolysis via σ-participation in exactly the same manner as its parent, the solvolysis of which was reported some time ago.

Introduction

Rearrangement via long range aryl migration (LRAM) coupled with electrocyclic ring opening (ERO) characterizes the solvolysis of certain substrates, as shown in eq 1.[5]

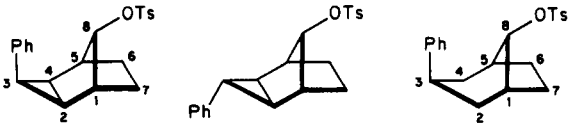


(1)

In spite of the considerable information gained in earlier studies, two items of mechanistic interest remained. First, what role in the solvolysis, if any, is played by the stationary aryl group? Second, is ERO necessary, so that the rare transannular aryl migration observed is restricted to tricyclics as in eq 1 or might other substrates with suitable geometry but lacking the possibility of ERO nonetheless exhibit LRAM? The present study investigated these aspects of the reaction.

Results

Tosylates *syn*-1-OTs, its *p*-tolyl analogue, *anti*-1-OTs, and 2-OTs have been synthesized.[6]



syn-1-OTs *anti*-1-OTs 2-OTs

(1) Electrocyclic Effects in Solvolysis. 6. Part 5. Wilt, J. W.; Curtis, V. A.; O-Yang, C. *J. Org. Chem.* **1982**, *47*, 3721.

(2) Taken in part from the M.S. Thesis of L.N.C., Loyola University of Chicago, June, 1983.

(3) Present address: Department of Chemistry, Northeastern Illinois State University, Chicago, IL.

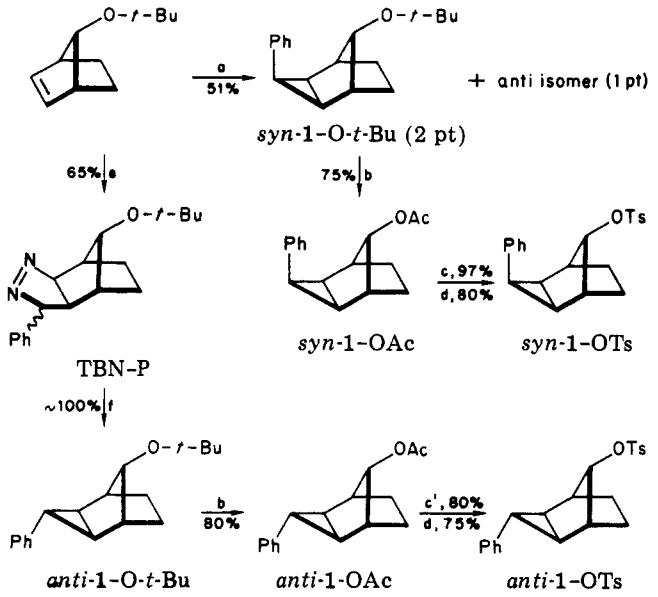
(4) Undergraduate Research Scholar, 1983.

(5) A summary of earlier work may be found in Part 5 of this series (ref 1).

(6) Our use of syn and anti corresponds, respectively, to the endo and exo prefixes occasionally employed for such substituents. The former terms (to us) better convey the stereochemical relationship of the phenyl group to its migration terminus in LRAM observed in some of these substances.

0022-3263/84/1949-2937$01.50/0

Scheme I[a]



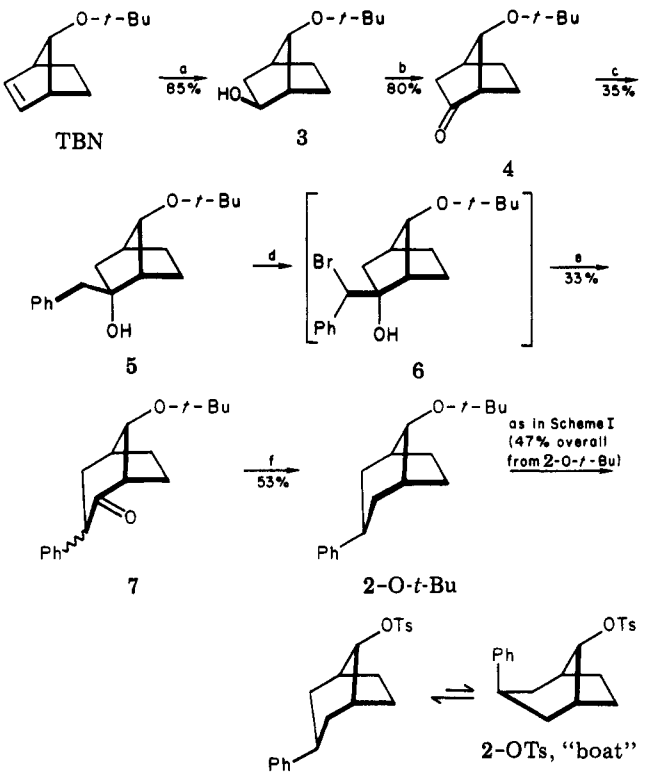
[a] (a) $PhCH_2Cl$, LiTMP, ether, 25 °C; (b) Ac_2O, HOAc, $HClO_4$, 0 °C; (c) $LiAlH_4$, ether (c' THF), Δ; (d) TsCl, pyr, 25 °C; (e) $PhCHN_2$, pentane, 25 °C; (f) *hν*, acetone.

The routes to *syn*- and *anti*-1-OTs used the reactions recently described by Creary[7-9] for the preparation of the corresponding hydrocarbons. The route to the *p*-tolyl analogue mirrored that for *syn*-1-OTs and is not shown. See Scheme I.

The addition of phenylcarbene (carbenoid) to *anti*-7-*tert*-butoxynorbornene (TBN), carried out by using benzyl chloride and lithium 2,2,6,6-tetramethylpiperidide (LiTMP) under Creary's conditions,[7] afforded a reasonable yield of the tricyclic ethers *syn*- and *anti*-1-O-*t*-Bu. As with norbornene,[7] the former was preferred. Separation of the epimeric ethers was accomplished by chromatography to afford the pure solid *syn* isomer (mp 50–51 °C). The oily anti isomer was preferably prepared in an alternative manner (see below). Although a number of spectral differences were apparent, the shielding caused by the proximate phenyl ring caused the H-8 resonance in the syn isomer to occur at δ 2.93, compared to δ 3.63 in the anti analogue, thereby allowing a ready differentiation between the two. The transformation of the syn ether to the tosylate followed the same route used previously in the diaryl studies.[10]

For the synthesis of the anti system, phenyldiazomethane (distilled[11]) was allowed to stand with excess TBN in a small volume of pentane at room temperature. Eventually the red solution turned yellow from which the pyrazoline adduct TBN-P was isolated in 60% yield. Its stereoisomeric composition was not determined. Upon photolysis in quartz at 300 nm in acetone (both solvent and photosensitizer) the pyrazoline was quantitatively converted to the anti tricyclic ether. Benzophenone (used by Creary[8] in a similar study) was a more effective photosensitizer (shorter reaction time at 366 nm) but its removal from the product was difficult. The subsequent conversions of the ether to *anti*-1-OTs again were routine.

Scheme II[a]



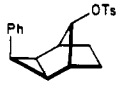
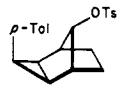
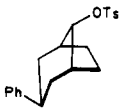
[a] (a) $Hg(OAc)_2$, H_2O-THF, NaOH, $NaBH_4$; (b) $pyrH^+$, CrO_3Cl^-, CH_2Cl_2; (c) $PhCH_2MgCl$, ether, Δ; (d) NBS, $(PhCO_2)_2$, CCl_4, Δ; (e) *i*-PrMgBr, ether, 0–25 °C, Δ; (f) N_2H_4, KOH, TEG, Δ.

The selected preparation of 2-OTs involved the ring expansion of a 2-norbornanone and followed the sequence developed by Sisti[12] for the synthesis of 3-phenylbicyclo-[3.2.1]octan-2-one. As applied to the present system, the sequence is given in Scheme II.

Sisti[12] employed hydrogen–deuterium exchange studies on the ketone product to establish the course of the skeletal rearrangement of the bromohydrin to the ring-enlarged bicyclo[3.2.1]octane system. Our evidence for the course of the skeletal rearrangement of **6** to **7** ultimately rests upon the ^{13}C NMR spectra of the subsequent 2-O-*t*-Bu and 2-OH. The symmetry plane present in the **2** system was manifested by the reduced number of resonances observed, and by the correspondence of the spectra to that of the non-phenyl analogue,[13] confirming that the skeletal rearrangement of **6** involved methylene rather than methine migration. Of equal importance to the site of phenyl group is its epimeric configuration in 2-O-*t*-Bu and subsequent derivatives. For possible LRAM the phenyl group must be positioned proximally to C-8, as shown in Scheme II as the "boat" conformer. Unfortunately for this purpose, the chair conformer in bicyclo[3.2.1]octane is more stable than the boat by molecular mechanics calculations.[14] The calculated energy difference between the

(7) Creary, X.; Keller, M.; Dinnocenzo, J. P. *J. Org. Chem.* **1978**, *43*, 3874.
(8) Creary, X. *J. Org. Chem.* **1980**, *45*, 4653.
(9) We are indebted to Professor Creary (University of Notre Dame) for correspondence and explicit directions for certain of these reactions. For some time we had been thwarted in our desired study of monoaryl substrates by synthetic difficulties too numerous to mention here, so the effective approaches developed by Creary were really the well-spring of this work.
(10) Wilt, J. W.; Malloy, T. P.; Mookerjee, P. K.; Sullivan, D. R. *J. Org. Chem.* **1974**, *39*, 1327.
(11) Creary, X. *Org. Synth.*, submitted for publication. We thank Professor Creary for a copy of his procedure.
(12) Sisti, A. J. *Tetrahedron Lett.* **1967**, 5327. Cf. also: Sisti, A. J. *J. Org. Chem.* **1968**, *33*, 453. Sisti, A. J. *J. Org. Chem.* **1970**, *35*, 2670. Sisti, A. J.; Rusch, G. M. *J. Org. Chem.* **1974**, *39*, 1182.
(13) Stothers, J. B.; Tan, C. T. *Can. J. Chem.* **1977**, *55*, 841.
(14) Allinger, N. L.; Hickey, M. J. *J. Am. Chem. Soc.* **1975**, *97*, 5167.

Table I. Kinetic Data in TFE:H_2O (97:3 v/v)[a]

tosylate	temp, °C[b]	$10^5 k$, s^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
	85.1	3.17 ± 0.03		
	90.5	4.72 ± 0.06		
	99.1	12.06 ± 0.23		
syn-1-OTs	(25)[c]	(2.18×10^{-8})[d]	24.9 ± 1.98	−10.1 ± 1.5
	85.5	9.24 ± 0.38		
	84.2	inert (24 h)		
	119-120	inert (1 week)[e]		
anti-1-OTs				
	39.5	0.233 ± 0.014		
	55.0	1.48 ± 0.03		
	85.4	22.4 ± 0.9		
	(25)[c]	(4.73×10^{-7})[d]	21.3 ± 0.8	−16.0 ± 0.6
2-OTs				

[a] For details, see ref 1 and the Experimental Section. [b] <100 ± 0.2 °C; >100 ± 0.5 °C. [c] Extrapolated value. [d] Value is k, not $10^5 k$. [e] With the assumption that 1% reaction could have been missed, the calculated $k = 1.66 \times 10^{-8}$ s^{-1} at 120 °C.

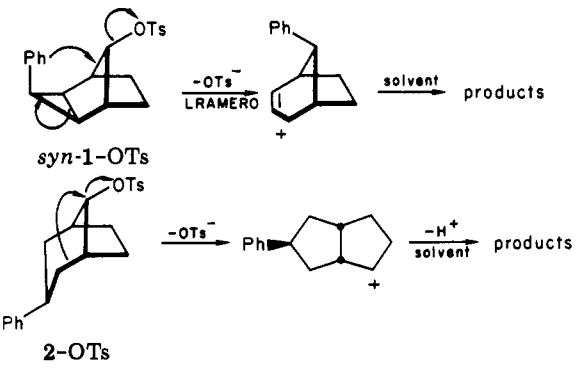
two is somewhat smaller, however, than in cyclohexane (6.43 kcal mol^{-1} vs. 7.1 kcal mol^{-1}) and the ring flip must be fairly facile, as evidenced by the well-known N ⇌ O migrations in tropine alkaloids.[15] On this basis it was hoped that the conformational bias against the possibility of LRAM might be small in 2-OTs and allow the aryl migration to be seen. In addition to the "boat" requirement, the phenyl group must be equatorial (in the chair). Because the Huang–Minlon reduction of 7 involved strong base at elevated temperature, it is therefore probable that 7 was converted via its enolate to the requisite equatorially positioned phenyl isomer,[16] the reduction of which then led to 2-O-*t*-Bu as a conformationally mobile mixture, as shown in Scheme II for the subsequently formed tosylate. It may be seen clearly that in the boat conformer the now axial-like phenyl group is properly positioned for LRAM in 2-OTs.

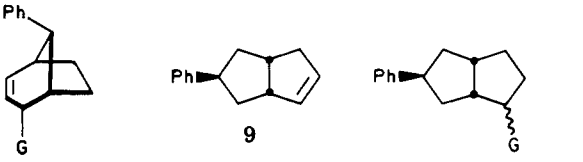
The solvolysis of the four tosylates was carried out in trifluoroethanol–H_2O (97:3 v/v) in the presence of excess 2,6-lutidine, as described in an earlier study.[1] The titrimetric rate constants and activation parameters are collected in Table I.

The tosylates exhibited well-behaved kinetics past 80–85% completion, except for *anti*-1-OTs which was inert under the conditions used. The *p*-tolyl substrate was studied at only one temperature simply to determine its rate relative to the phenyl analogue. This rate ratio was used earlier[1] to measure the contribution of ERO to LRAM in the combined processes.

The solvolysis products (~90% yield) were investigated for the cases of *syn*-1-OTs and 2-OTs. From *syn*-1-OTs rearranged products 8-OH (86%) and 8-TFE (14%) were detected.[17] Tosylate 2-OTs formed predominantly bicycloalkene 9 (this was essentially the only product in dioxane–water, 80:20 v/v, at 110 °C for 70 h), along with minor amounts of 9-OH and 9-TFE.

Scheme III





8-OH, G = OH
8-TFE, G = OCH_2CF_3

9-OH, G = OH
9-TFE, G = OCH_2CF_3

Discussion

The course of the solvolyses studied can be most economically[18] described as shown in Scheme III.

From the rate and product data, *syn*-1-OTs follows the same pathway as did its diphenyl analogue.[10] Combined LRAMERO is undoubtedly again involved, *and* to the same extent in the mono- and diaryl systems, a point substantiated by the *p*-tolyl:phenyl rate ratio (2.9) which is comparable to that calculated from rate data[1] for the diaryl cases at the same temperature (3.1). So it can be concluded that the *stationary aryl group present in the earlier systems studied plays no significant role.* Such was the expectation, first conjectured some years ago,[10] because this aryl group is located at the node of the molecular orbital (LUMO) of the allylic ion intermediate predicted to react with the solvent to form the products.

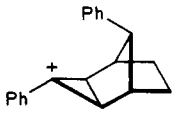
(15) Fodor, G.; Nador, K. *J. Chem. Soc.* **1953**, 721. Fodor, G; Kovacs, O. *J. Chem. Soc.* **1953**, 724.

(16) This view is based upon the assumption that the equatorial epimer is the more stable and that thermodynamic control was developed in the Huang–Minlon reduction.

(17) The ratio of alcohol to ether (6:1) is uncharacteristically large. Normally water is two to three times more effective (on a molar basis) as a nucleophile than is TFE. Cf. Shiner, V. J., Jr.; Dowd, W.; Fisher, R. D.; Hartshorn, S. R.; Kessick, M. A.; Milakovsky, L.; Rapp, M. W. *J. Am. Chem. Soc.* **1969**, *91*, 4838. Our earlier studies[1] had ratios ranging from 1:1 to 4:1. These ratios differ for each system and also reflect experimental error in the quantitative analysis of complex product mixtures formed in small amounts.

(18) Though both *syn*-1-OTs and 2-OTs are achiral, their various products are chiral. Only one enantiomeric ion is shown for the intermediate leading to racemic products. The transition state descriptions are omitted because they have been discussed in ref 1 and 10.

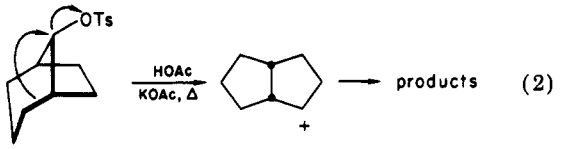
As an additional point of interest, the absence of any significant stationary aryl group effect *substantiates the view that ERO is concomitant with LRAM.* This follows because such a combined rearrangement pathway avoids the cyclopropyl cation intermediate shown. This inter-



mediate would be anticipated were ERO to *follow* LRAM rather than being *simultaneous* with it. Such ions are known to be stabilized by aryl substituents,[19] and a significant effect due to the stationary aryl group should therefore have been manifested. This cyclopropyl cationic species had earlier eluded detection when the solvolysis was conducted in the presence of sodium borohydride.[20]

The lack of reactivity evident in *anti*-1-OTs was not unexpected. Clearly LRAM is impossible for geometric reasons. Moreover, the parent tricyclic analogue is some 7000-fold slower in solvolysis than its 3,3-diphenyl derivative.[10] The absence of any effective π- or σ-participation pathway simply deadens *anti*-1-OTs under the conditions used.

At the very outset of the study of 2-OTs it was feared that σ-participation rather than LRAM would occur. Such a result would thereby render 2-OTs an inappropriate model to test the necessity of ERO in these rearrangements. The σ-participation pathway in fact was proposed some time ago in a study of the acetolysis of the parent tosylate,[21] as shown in eq 2. The earlier study found that



(2)

products containing the bicyclo[3.3.0]octane skeleton comprised 93% of the product. Anchimeric participation was suggested, although the kinetics of the acetolysis were complicated by internal return to rearranged tosylate. With 2-OTs being studied in TFE–H_2O, a far superior medium for observing participation than is acetic acid,[22] the likelihood of internal return is much reduced and the clean kinetic behavior of 2-OTs is understandable. Because the relative reactivities of *syn*-1-OTs (via LRAM) and 2-OTs are comparable (~20-fold greater reactivity for the latter at 25 °C), the kinetic results themselves did not indicate whether 2-OTs followed σ- or π(LRAM)-participation. The matter could be resolved only by the nature of the products. This turned out to be a difficult task chemically and the decision that 2-OTs involved σ-participation was made solely on the basis of ^{13}C NMR spectroscopy.[23] In Table II are collected the relevant data with **9** shown as its deduced structure.

The agreement between **9** and bicyclo[3.3.0]oct-2-ene is clearly better than that between **9** and bicyclo[3.2.1]oct-2-ene.[24] A similar correspondence held for the C-2 reso-

Table II. ^{13}C NMR Chemical Shifts (δ_c)

C no.	9		
1	50.7	50.8[a]	35.6[b]
2	134.2	134.7	134.7
3	130.7	129.5	123.8
4	42.2	41.2	37.5
5	40.0	40.4	33.6
6	42.9 (42.9)[c]	35.9	30.6
7	43.5 (42.4)	25.4	35.5
8	39.4 (39.5)	32.5	35.5
Ph	144.8, 128.2, 127.1, 125.8		

[a] Data in this column was taken from Whitesell, J. K.; Matthews, R. S. *J. Org. Chem.* **1977**, *42*, 3878. [b] Data in this column was taken from ref 13. [c] The parenthesized values were calculated by adding +7 and +17 δ to the values for C-6, 8 and C-7, respectively, for the [3.3.0] parent system. These empirical substituent parameters were taken from Wehrli, F. W.; Wirthlin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden and Son Inc.: Philadelphia, PA, 1978; p 37.

nance of **9**–TFE (δ_c 81.8) and that for C-2 in bicyclo-[3.3.0]octan-2-ol[25] (δ_c 79.9 in the syn epimer, δ_c 75.3 for the anti) compared to C-3 in bicyclo[3.2.1]octan-3-ol (δ_c 66.2 in the exo epimer, δ_c 66.7 in the endo). On these bases the formulation of the solvolysis of 2-OTs was decided: *2-OTs solvolyzes with σ-participation and is therefore an inappropriate model for the necessity of ERO in these processes.* It appears that 2-OTs in fact behaves exactly as does its non-phenyl parent.[21] Presumably, the conformational bias against the "boat" conformer of 2-OTs, coupled with the ease of the competitive σ-participation pathway available to the "chair" conformer, obviate the LRAM route.

Our search for an appropriate model to test the necessity of ERO therefore continues. Incidentally, the occurrence of LRAMERO is not restricted to solvolysis reactions. The next paper in this series will describe its operation in various addition reactions.

Experimental Section

Melting points were taken on a calibrated Fisher–Johns block. Boiling points are uncorrected. Spectra were recorded on the following instruments: IR, Perkin-Elmer Model 700; ^1H NMR, Varian EM-360 and EM-360A; ^{13}C NMR, Varian FT-80. For IR spectra only structurally significant absorptions (in reciprocal centimeters) are given. Liquids were run as neat samples and solids as 1% mixtures in KBr disks. For NMR spectra the usual abbreviations for split resonances are employed. At times only partial spectra are given. Defined multiplets are listed at the centers, otherwise the range is given in δ units (Me_4Si = δ 0.00). The solvent was deuteriochloroform. Microanalyses were performed by Micro-Tech Laboratories, Skokie, IL. The petroleum ether used was 30–60 °C boiling material.

***syn*- and *anti*-3-Phenyl-*exo*-tricyclo[3.2.1.$0^{2,4}$]oct-*anti*-8-yl *tert*-Butyl Ether (*syn*-1-O-*t*-Bu and *anti*-1-O-*t*-Bu).** A run typical of many performed is described.[9] *anti*-7-*tert*-Butoxynorbornene[26] ("TBN", 9.03 g, 54.4 mmol) and benzyl chloride (2.97 g, 23.4 mmol) were dissolved in anhydrous ether (6 mL) and chilled to −20 °C under nitrogen. In an addition funnel was placed

(19) Schleyer, P. V. R.; Sliwinski, W. F.; Van Dine, G. W.; Schöllkopf, U.; Paust, J.; Fellenberger, K. *J. Am. Chem. Soc.* **1972**, 94, 125.
(20) Wilt, J. W.; Niinemae, R., unpublished work.
(21) Foote, C. S.; Woodward, R. B. *Tetrahedron* **1964**, 687.
(22) Noyce, D. S.; Casterson, R. L.; Meyers, D. A. *J. Org. Chem.* **1972**, *37*, 4222.
(23) We thank Professor David S. Crumrine of this Department for his generous and insightful assistance in this regard.
(24) Note that ^{13}C NMR spectra of 2-OH and its non-phenyl analogue also correlate well. See the Experimental Section. Clearly the presence of the phenyl group does not perturb seriously the δ_c values of more distant carbons in either of the bicyclooctane series, thereby allowing an easy differentiation between them.
(25) Whitesell, J. K.; Matthews, R. S., cited in Table II.
(26) Franzus, B.; Snyder, E. I. *J. Am. Chem. Soc.* **1965**, *87*, 3423. As we have commented before,[1] the synthesis of TBN is capricious, to put it mildly. At one time for over a month, *no* reduction of 7-*tert*-butoxynorbornadiene by lithium aluminum hydride was observed, in spite of all sorts of changes in sources and conditions. Then, just as mysteriously, the reduction succeeded once again and did so for the completion of this work. Our advice to those interested is to prepare as large a batch as needs anticipate while the "getting is good".

2,2,6,6-tetramethylpiperidine ("TMP", Aldrich, 4.31 g, 30.5 mmol) in dry ether (4 mL). A solution of methyllithium in ether (Aldrich, 1.4 M, 20 mL, 28 mmol) was then slowly injected through a septum into the TMP solution to form the lithium salt (gas evolution). The solution of this salt was slowly added (1.5 h) to the stirred TBN–benzyl chloride mixture at −30 to −10 °C. The yellow solution was allowed to warm to room temperature and stirred for a further 3.5 h. Water (30 mL) was then added carefully to dissolve the precipitate present and the resultant layers were separated. The aqueous material was extracted with ether (2 × 20 mL) and the combined ethereal material was washed with hydrochloric acid (5%, 2 × 25 mL), sodium bicarbonate (5%, 1 × 25 mL), water (1 × 25 mL), and then brine (1 × 25 mL) and finally dried over $MgSO_4$. After removal of the ether, the residual oil was distilled first at 3 mm (bp 47–52 °C), then at 1 mm (bp 33–35 °C) until no further distillate was obtained. The distillates from nine such runs were combined and dissolved in minimal hexane (some insoluble material was removed) and chromatographed on silica gel with mixtures of ether and petroleum ether as eluant. The epimeric ethers were obtained in 51% yield with a ratio of syn:anti ≃ 2. The syn epimer was recrystallized from ethanol–water: mp 50–50.5 °C; ^{1}H NMR (partial) δ 7.27 (s, Ph), 2.93 (br s, H-8), 0.7 (s, *t*-Bu).

Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.56; H, 9.50.

The anti epimer was not obtained pure by this route and was better prepared elsewise (see later). A contaminant in this reaction (removable by precipitation with hexane) was an incompletely identified material which appeared from its spectra to be α-benzyl ethyl ether, an insertion product not involving TBN.[27]

***syn*-3-Phenyl-*exo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl Tosylate (*syn*-1-OTs).** The conversions of *syn*-1-O-*t*-Bu to acetate *syn*-1-OAc [^{1}H NMR (partial) δ 3.97 (s, H-8), 1.80 (s, OAc), 75%], alcohol *syn*-1-OH [^{1}H NMR (partial) δ 3.15 (s, H-8), 97%], and finally to tosylate *syn*-1-OTs (80%) followed the procedures described earlier for the diphenyl analogue[10] and for brevity will be omitted here. The tosylate was recrystallized from hexane–ether: mp 135–135.5 °C; ^{1}H NMR δ 7.13 (sharp m, Ar H), 3.77 (br s, H-8), 2.37 (s, Ar CH_3), 2.3 (sharp m, H-1,5), 2.07–1.17 (m, all other H's); IR (KBr) 1350, 1170 (SO_2).

Anal. Calcd for $C_{21}H_{22}O_3S$: C, 71.16; H, 6.26. Found: C, 71.19; H, 6.33.

***syn*-3-*p*-Tolyl-*exo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl Tosylate.** The preparation of this tosylate mirrored that of the phenyl analogue both in the procedures used and the yields obtained. Use of *p*-methylbenzyl chloride, LiTMP, and TBN, as described above, again led to a mixture of syn and anti ethers, from which the former was isolated by chromatography. By procedures previously reported,[10] the ether was converted to the acetate [^{1}H NMR δ 7.13 (s, Ar H), 4.0 (br s, H-8), 2.43 (sharp m, M-1,5), 2.27 (s, Ar CH_3), 1.80 (s, OAc), 2.0–1.13 (br m, all other H's) and thence to the alcohol. The alcohol was recrystallized from petroleum ether–hexane: mp 127–127.5 °C; ^{1}H NMR δ 7.03 (s, Ar H), 3.27 (br s, H-8), 2.30 (s, Ar CH_3), 2.20 (sharp m partially obscured, H-1,5), 2.0–1.0 (br m, all others H's); IR (KBr) 3350 (OH) 1080 (CO).

Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.33; H, 8.62.

Conversion of the alcohol in the described manner[10] led to the tosylate, which was recrystallized from hexane–ether: mp 130–131.5 °C; IR (KBr) 1360, 1170, 1190 (SO_2).

Anal. Calcd for $C_{22}H_{24}O_3S$: C, 71.71; H, 6.56. Found: C, 71.93; H, 6.59.

Reaction of TBN and Phenyldiazomethane. *anti*-10-*tert*-Butoxy-5-phenyl-3,4-diazatricyclo[5.2.1.0^{2,6}]dec-3-ene (TBN-P).[28] Again, a typical run is described. TBN (2.43 g, 14.6 mmol) and freshly distilled phenyldiazomethane[11] (1.29 g, 10.9 mmol) were mixed in pentane (2 mL) and allowed to stand. When the originally red solution became bright yellow (overnight or longer depending upon the quantities used), petroleum ether was added to precipitate the adduct. Recrystallization from ether–petroleum ether afforded white, shiny crystals: mp 128–129 °C (yield averaged 65% over some five preparations); ^{1}H NMR (partial) δ 5.03 (m, H-2); IR (KBr) 1550 (N=N).

Anal. Calcd for $C_{18}H_{24}ON_2$: C, 76.06; H, 8.45. Found: C, 76.38; H, 8.55.

***anti*-3-Phenyl-*exo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl *tert*-Butyl Ether (*anti*-1-O-*t*-Bu).** Pyrazoline TBN-P (1.52 g, 5.4 mmol) was equally distributed among five quartz tubes. Each portion was dissolved in acetone (6 mL) in four of the tubes and acetone-d_6 (6 mL) in the fifth. The tubes were irradiated at 300 nm in a Rayonet Carousel Minireactor using the acetone-d_6 tube to monitor the reaction by ^{1}H NMR. After 40 h no further TBN-P remained so the acetone was removed by rotary evaporation. The oily residue (~100% yield) possessed an ^{1}H NMR spectrum essentially identical with *anti*-1-O-*t*-Bu prepared by carbenoid addition (see above), although some acetone-derived contaminants were present.

Use of benzophenone[8] as photosensitizer at 366 nm in cyclohexane solvent was advantageous in rate but led to difficulties in its separation from the photoproduct.

***anti*-3-Phenyl-*exo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl Tosylate (*anti*-1-OTs).** By methods previously reported,[10] the crude ether was converted to the acetate *anti*-1-OAc [80%; ^{1}H NMR (partial) δ 4.63 (broad s, H-8)] and thence to the alcohol *anti*-1-OH [80%; ^{1}H NMR δ 7.3–6.8 (m, Ph), 3.8 (br s, H-8), 2.33 (br s, H-1,5), 2.1 (t, J = 3 Hz, H-3), 1.83–1.2 (m, H-6, 7, OH), 1.03 (d, J = 3 Hz, H-2, 4); IR (KBr) 3350 (OH), 1070 (CO)]. The alcohol was recrystallized from hexane–ether, mp 126–127 °C.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.80; H, 8.05.

Conversion of the alcohol to the tosylate *anti*-1-OTs, 75%, was performed as described.[10] The tosylate was recrystallized from ether–petroleum ether, mp 129–130 °C: ^{1}H NMR (partial) δ 4.42 (br s, H-8).

Anal. Calcd for $C_{21}H_{22}O_3S$: C, 71.16; H, 6.26. Found: C, 71.18; H, 6.30.

***anti*-7-*tert*-Butoxy-*exo*-2-benzyl-*endo*-2-norbornanol (5).** Conversion of TBN to anti-7-*tert*-butoxy-*exo*-2-norbornanol (3, bp 108–111 °C (8 mm)) was achieved via hydroboration–oxidation or oxymercuration–demercuration as described.[29] The yields either way were comparable (80–85%), but the latter method was more convenient. Oxidation of 3 to *anti*-7-*tert*-butoxy-2-norbornanone [4, 80%, bp 116–118 °C (15 mm); mp 35–36 °C; ν_{co} 1720 cm^{-1}] was accomplished as described[29] or by means of pyridinium chlorochromate in the usual way. Benzylmagnesium chloride, prepared from magnesium (1.2 g) and benzyl chloride (5.8 mL) in dry ether (25 mL), was then stirred as ketone 4 (8.2 g, 45 mmol) was added dropwise. After the addition the solution was refluxed for 12 h, cooled, and decomposed with water (50 mL). Conventional workup afforded alcohol 5: 4.3 g; 35%; bp 157–158 °C (0.1 mm); ^{1}H NMR δ 7.25 (s, PhH), 3.9 (broad s, H-7), 2.8 broad s, H-1, 4), 2.0–0.7 (m, H-3,5,6, CH_2Ph, OH), 1.2 (s, *t*-Bu); IR 3500 (OH).

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.89; H, 9.18.

***anti*-8-*tert*-Butoxy-*exo*-3-phenylbicyclo[3.2.1]octan-2-one (7).** Alcohol 5 (13.7 g, 50 mmol) was added to a solution of benzoyl peroxide (0.5 g) and *N*-bromosuccinimide (8.9 g, 50 mmol) in dry carbon tetrachloride (100 mL). The solution was heated gently under reflux until the amount of floating succinimide seemed maximized. The cooled solution was filtered and the solvent was removed. The yellow residual 6 (δ 6.3, CHBr) was used without further purification. To a stirred, cold (0 °C) solution of 6 in dry benzene (100 mL) was added dropwise a solution of isopropylmagnesium bromide, prepared from isopropyl bromide (4.69 mL) and magnesium (1.2 g) in dry ether (25 mL). After the addition the solution was stirred at room temperature for 12 h and then refluxed for 1 h. The cooled solution was then decomposed with water and processed in the described manner.[12] Chromatography of the yellow oily product on alumina with petroleum ether–benzene (1:1 v/v) as the eluant afforded ketone 7 as a yellow oil:

(27) Professor Creary has observed this byproduct also and suggested the proposed structure (private communication).

(28) The structure for TBN-P shown in Scheme I is based upon the generally observed exo addition of dipoles to norbornenes in 1,3-dipolar cycloadditions. The epimeric position of the phenyl group was not determined.

(29) Flanyak, J. R. Dissertation, Loyola University of Chicago, 1973.

4.5 g; 33%; ^{1}H NMR δ 7.3–6.8 (m, PhH), 3.7 (broad s, H-8), 3.6–3.1 (m, H-3), 2.65 (broad s, H-1), 2.25 (m, H-4,5), 2.1–1.0 (m, H-6,7), 1.15 (s, *t*-Bu); IR 1735 (CO). A small sample was distilled in a Hickman still (bath 150 °C (0.2 mm)) to obtain an analytical sample.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.12; H, 8.87.

The **2,4-dinitrophenylhydrazone** derivative, mp 200–202 °C, was also prepared and analyzed.

Anal. Calcd for $C_{24}H_{28}O_5N_4$: N, 12.38. Found: N, 12.16.

***exo*-3-Phenylbicyclo[3.2.1]oct-8-*anti*-yl *tert*-Butyl Ether (2-O-*t*-Bu).** A mixture of ketone **7** (13.4 g, 50 mmol), potassium hydroxide (85%, 6.7 g), hydrazine hydrate (95%, 45 mL), and triethylene glycol (TEG, 50 mL) was refluxed for 2 h. The excess hydrazine and water were distilled off as the temperature rose to 200 °C. After 4 h at this temperature, the solution was cooled and extracted with ether (4 × 50 mL). The washed and dried ethereal material was concentrated in vacuo and distilled to afford ether 2-O-*t*-Bu as a colorless oil: bp 128–131 °C (0.1 mm); ^{13}C NMR[30] δ 146.1, 128.5–125.0 (Ph), 81.8 (C-8), 72.9 ($OCMe_3$), 42.1 (C-1,5), 39.9 (C-2,4), 35.7 (C-3), 28.7 (C-6,7) 27.1 (CH_3).

***exo*-3-Phenylbicyclo[3.2.1]octan-*anti*-8-ol (2-OH) and Tosylate (2-OTs).** Ether 2-O-*t*-Bu was converted as described[10] to the corresponding acetate 2-OAc (75%, ν_{co} 1745 cm^{-1}) and thence to alcohol 2-OH (75%, methylmagnesium bromide was used to cleave the acetate instead of lithium aluminum hydride in this instance). Alcohol 2-OH formed white crystals from hexane: mp 124–125 °C; ^{1}H NMR δ 7.2 (s, PhH), 3.8 (s, H-8), 2.2 (m, H-1,5), 2.0–1.4 (m, H-2,3,4,6,7), 1.3 (s, OH); ^{13}C NMR[30] δ 145.8, 130.4–124.0 (Ph), 81.9 (C-8), 42.4 (C-1,5), 39.2 (C-2,4), 35.4 (C-3), 26.4 (C-6,7); IR (KBr) 3290 (OH), 1000 (CO).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.21; H, 8.97. Found: C, 82.95; H, 8.90.

In the customary fashion, alcohol 2-OH was converted to its tosylate 2-OTs (5 day reaction time at 25 °C): 83%; mp 128–129 °C (petroleum ether); ^{1}H NMR (partial) δ 4.65 (br s, H-8); IR (KBr) 1340, 1170 (SO_2).

Anal. Calcd for $C_{12}H_{24}O_3S$: C, 70.76; H, 6.79. Found: C, 70.72; H, 6.77.

Solvolysis of Tosylates. The procedure followed has been described in detail.[1] The kinetic and activation parameter data were obtained by computer. The data are collected in Table I.

(30) Reference 13 lists the ^{13}C NMR spectrum of bicyclo[3.2.1]octan-*anti*-8-ol (the non-phenyl analogue of the 2 system): δ_c 42.2 (C-1,5), 31.3 (C-2,4), 17.1 (C-3), 26.2 (C-6,7), 82.2 (C-8).

Tosylate *anti*-1-OTs showed no change after 24 h at 84.2 °C or after 1 week at 119–120 °C.

Solvolysis Products. The ampoule contents comprising the titrated aliquots of tosylate *syn*-1-OTs were combined and extracted thoroughly with ether. Chromatography on silica gel led to recoverable starting material and to enriched product samples that were characterized by ^{1}H NMR spectra only. The products observed were: ***syn*-8-phenylbicyclo[3.2.1]oct-3-en-*endo*-2-ol** (8-OH) [86%; ^{1}H NMR (partial) δ 6.3 (m, H-3,4), 4.47 (m, H-2)] and ***syn*-8-phenylbicyclo[3.2.1]oct-2-en-*endo*-4-yl trifluoroethyl ether** (8-TFE) [14%; ^{1}H NMR (partial) δ 6.3 (m, H-2,3), 4.23 (m, H-4), 3.33 (q, J = 9 Hz, CH_2CF_3)]. Tosylate 2-OTs (73 mg 0.2 mmol) was heated in the solvolysis solvent (10 mL) for 48 h. The solvent was evaporated and the residue was diluted with water and extracted with ether (2 × 25 mL). The washed and dried ethereal extracts were freed of solvent and the residual oil was then chromatographed on Florisil with hexane and ether mixtures as eluants. Although separations were not as desired, resonably pure ***syn*-7-phenyl-*cis*-bicyclo[3.3.0]oct-2-ene (9)** was isolated: 28 mg; 75%; ^{1}H NMR δ 7.2 (s, PhH), 5.65 (m, H-2,3), 3.5–1.7 (series of multiplets, all other H's); ^{13}C NMR see Table II; IR 3090, 2890, 1610, 1510, 1460, 1360, 1280, 1170, 1100, 1080, 1040, 970, 910, 810, 760, 700.

Anal. Calcd for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 89.68; H, 9.87.

Lack of material prevented further purification, but even so the above analysis served to establish the hydrocarbon nature of **9** (%C + %H observed = 99.55%). Also isolated was an even smaller amount of a poorly resolved mixture of ***syn*-7-phenyl-*cis*-bicyclo[3.3.3]octan-2-ol**, OH configuration unknown (9-OH), and ***syn*-7-phenyl-*cis*-bicyclo[3.3.0]oct-2-yl trifluoroethyl ether**, ether configuration unknown (9-TFE), ca. 25% of product. Several milligrams of the latter were isolated in reasonable purity to observe its spectra: ^{1}H NMR (partial) δ 3.8 (q, J = 9 Hz, CH_2CF_3); ^{13}C NMR (partial) 81.8 (C-3); IR 1340 (CF_3). Insufficient material was available for combustion analysis.

Reaction of 2-OTs (169 mg, 0.474 mmol) in dioxane–water (80:20 v/v, 2.0 mL) containing distilled 2,6-lutidine (52 mg, 0.485 mmol) in a sealed tube at 110 °C for 70 h led to the isolation of essentially only **9** (75 mg, 86%). Its spectral properties were identical with those of **9** isolated from the kinetic studies.

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Convenient Synthesis of 3-Methyl-2,3,4,4aα,5,6,7,7aα-octahydro-1*H*-benzofuro[3,2-*e*]isoquinoline

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A new synthesis of 3-methyl-2,3,4,4aα,5,6,7,7aα-octahydro-1*H*-benzofuro[3,2-*e*]isoquinoline (**3**) has been developed. The synthesis utilizes the acylation of anion **5** with γ-butyrolactone preferentially at the 4-position. Reduction of the resulting keto alcohol **9** afforded two diastereomeric azabicyclooctanes **11a** and **11b**. Synthetic transformation of both of these compounds gave the desired product **3** in respectable yields. The structure of one of the intermediates (**14a**) was confirmed by single-crystal X-ray diffraction analysis.

The search for potent, nonaddictive analgesics based on the morphine ring system **1** (Scheme I) has been an area of considerable interest for many years.[1] The morphine fragment 2,3,4,4aα,5,6,7,7aα-octahyro-1*H*-benzofuro[3,2-*e*]isoquinoline (**3**), which contains the complete morphine skeleton with the exception of C-10, was synthesized by one of us[2] using the intramolecular Diels–Alder reaction

† Contribution No. 3382.

(1) Johnson, M. R.; Michne, G. M. In "Medicinal Chemistry", 4th ed.; Wolff, M. E., Ed.; Wiley Interscience: New York, 1981; Part III, p 699.

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