Structural Effects in Solvolytic Reactions. 32. Effect of Increasing Electron Demand on the Rates of Solvolysis of 2-Aryl-3-methylene-2-norbornyl *p*-Nitrobenzoates. High Exo/Endo Rate and Product Ratios for Tertiary Derivatives of the Accepted Classical 3-Methylene-2-norbornyl System

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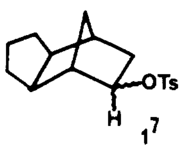
The secondary 3-methylene-2-norbornyl system, with its low exo/endo solvolytic rate ratio of 3.9, has been proposed as a model norbornyl system which undergoes solvolysis through the intermediacy of classical carbocations, the allylic double bond of the 3-methylene group swamping out any possible σ participation by the 1,6-bonding electron pair. It follows that the more stabilized tertiary 2-aryl derivatives must also undergo solvolysis through classical cationic intermediates. Accordingly, 2-aryl-3-methylene-2-norbornyl *p*-nitrobenzoates, containing representative substituents in the 2-aryl ring, were synthesized and their rates of solvolysis in 80% aqueous acetone determined. These derivatives reveal high exo/endo rate ratios of 407 for *p*-OCH_2CH_2-*m* (5-coumaranyl), 357 for *p*-H, 214 for *p*-CF_3, and 454 for 3,5-$(CF_3)_2$. The reaction products are ≥99% exo. It follows that the high exo/endo rate and product ratios in this system cannot be the result of σ participation leading to the formation of a σ-bridged species but must be the result of the unique steric characteristics of the U-shaped norbornyl system. Both the 2-aryl-3-methylene-*exo*- and -*endo*-norbornyl derivatives yield almost identical values of ρ^+: −3.79 for the exo isomers and −3.76 for the endo isomers, quite similar to the previously established values of −3.82 and −3.76 for the 2-aryl-*exo*- and -*endo*-norbornyl derivatives, respectively.

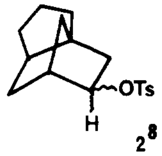
The high exo/endo rate and product ratios in the solvolyses of 2-norbornyl derivatives have long been considered to be the strongest argument favoring σ bridging in such systems.[2] The observation that 2-methyl- and 2-phenyl-2-norbornyl derivatives also undergo solvolysis with high exo/endo rate and product ratios[3,4] led to a questioning of this interpretation.[3-5] However, it was argued that even the solvolysis of the stabilized tertiary derivatives, such as 2-methyl- and 2-phenyl-*exo*-norbornyl, could proceed through the formation of nonclassical intermediates.[6]

A number of 2-norbornyl systems have been observed to undergo solvolysis with relatively low exo/endo rate ratios. It has been proposed that these systems should be considered to be models of the behavior to be anticipated for classical 2-norbornyl systems. The unique structural features of these systems are believed to resist σ bridging either because of steric constraints (**1**, **2**) or because of special electronic effects (**3**, **4**).

For example, in **1** and **2** σ bridging would require the *exo*-5,6- and the *exo*-4,5-trimethylene groups to move toward the more crowded endo environment, increasing the strain.[11] The system resists this change, resulting in a decreased rate for the exo isomer and a decreased exo/endo rate ratio.[11]


1[7]

exo/endo 9.5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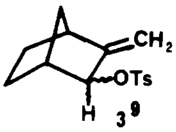
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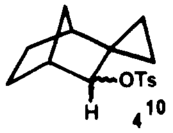
exo/endo 3.9

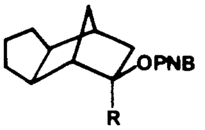

4[10]

1.2

In the case of **3** and **4**, it is proposed that delocalization of charge from the 2-position into the double bond of the 3-methylene group of **3** (allylic stabilization) or into the cyclopropane ring of **4** (cyclopropylcarbinyl stabilization) reduces the positive charge on C2 and reduces its ability to form a nonclassical bridge with the 1,6-bonding pair.[9-10] Again a low exo/endo rate ratio results.

It occurred to us that these systems provide a critical test for the position that high exo/endo rate ratios are diagnostic of σ bridging. If the secondary derivatives undergo solvolysis via classical intermediates, because of the steric or electronic constraints incorporated into the structures, surely the more stable tertiary derivatives should solvolyze through classical intermediates. Would the exo/endo rate ratio be high, as observed for the 2-aryl-2-norbornyl derivatives, or would they be low, corresponding to the low exo/endo rate ratios observed for the secondary derivatives (**1**–**4**)?

We selected two of these systems for detailed study: **1** as an example of steric constraint and **3** as an example of electronic constraint. The results for the 2-methyl-, 2-phenyl-, and 2-(5′-coumaranyl)-*exo*-5,6-trimethylene-2-norbornyl *p*-nitrobenzoates (**5**, **6**) have been previously reported.[12,13] In the present paper we report our results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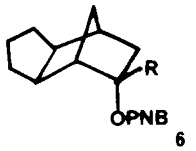
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[1] Postdoctoral research associate on a grant provided by the Exxon Research and Engineering Co.

[2] Winstein, S.; Trifan, D. *J. Am. Chem. Soc.* **1952**, *74*, 1147, 1154.

[3] Brown, H. C.; Chloupek, F. J.; Rei, M. H. *J. Am. Chem. Soc.* **1964**, *86*, 1247.

[4] Brown, H. C.; Chloupek, F. J.; Rei, M. H. *J. Am. Chem. Soc.* **1964**, *86*, 1248.

[5] Brown, H. C. "The Nonclassical Ion Problem"; Plenum: New York, 1977; Chapter 7 (comments by Schleyer, P. von R.).

[6] Winstein, S. *J. Am. Chem. Soc.* **1965**, *87*, 381.

[7] Takeuchi, K.; Oshika, T.; Koga, Y. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 1318.

[8] Corey, E. J.; Glass, R. S. *J. Am. Chem. Soc.* **1967**, *89*, 2600.

[9] Wilcox, C. F., Jr.; Jesaitis, R. G. *Chem. Commun.* **1967**, 1046.

[10] Wilcox, C. F., Jr.; Jesaitis, R. G. *Tetrahedron Lett.* **1967**, 2567.

[11] Sargent, G. D. *Carbonium Ions*, **1972**, *3*, 1154.

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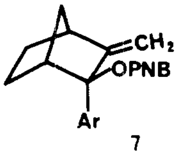
Table I. Rate Data for the Solvolysis of the 2-Aryl-3-methylene-2-norbornyl *p*-Nitrobenzoates in 80% Aqueous Acetone

		$10^6 k_1$, s^{-1}					
substituent on aryl	isomer	T_1, °C	T_2, °C	25 °C	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu	exo/endo at 25 °C
p-OCH$_2$CH$_2$-*m*	X			67600^a			407
	N	6.86 (0)		166	20.0	−8.6	
p-H	X	300 (50)		16.5	21.6	−7.9	357
	N	270 (100)	22.7 (75)	$4.62 \times 10^{-2\ b}$	24.9	−8.3	
p-CF$_3$	X	403 (100)	32 (75)	$5.64 \times 10^{-2\ b}$	25.6	−6.0	214
	N	42 (125)	3.84 (100)	$2.64 \times 10^{-4\ b}$	27.7	−9.6	
3,5-(CF$_3$)$_2$	X	400 (125)	33 (100)	$1.5 \times 10^{-3\ b}$	28.9	−2.1	454
	N	25.7 (150)	2.39 (125)	$3.3 \times 10^{-6\ b}$	31.2	−6.4	

^{a} Calculated by multiplying the rate of the benzoate by the factor 20.8. ^{b} Extrapolated from data at higher temperatures.

with the 2-aryl-3-methylene-2-norbornyl *p*-nitrobenzoates (**7**, **8**). In the present study we selected a range of substituents to permit the application of the tool of increasing electron demand[14] to this system and comparison of the results with those previously realized for the parent 2-aryl-2-norbornyl system.[15,16]



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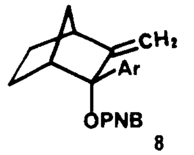

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Results

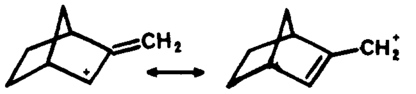
Synthesis. Addition of 5-coumaranyllithium, phenyllithium, *p*-(trifluoromethyl)phenyllithium, and 3,5-bis(trifluoromethyl)phenylmagnesium bromide to 3-methylene-2-norbornanone gave the tertiary endo alcohols following hydrolysis of the intermediate. The purified alcohols were converted into the lithium alkoxides, and these were treated with *p*-nitrobenzoyl chloride to form the *p*-nitrobenzoates. Solvolysis of the *p*-nitrobenzoates in 80% aqueous acetone containing a 10% molar excess of sodium acetate yielded the corresponding exo alcohols. These exo alcohols were purified and converted into the *p*-nitrobenzoates as described for the endo isomers. 2-(5′-Coumaranyl)-3-methylene-*exo*-norbornyl *p*-nitrobenzoate was too unstable to be isolated. Hence the more stable benzoate was synthesized and utilized for the solvolytic studies.

Rate Studies. The *p*-nitrobenzoates were solvolyzed in 80% aqueous acetone at appropriate temperatures, and the rates were calculated to 25 °C for ready comparison. The rate constant for the solvolysis of 2-(5′-coumaranyl)-3-methylene-*exo*-norbornyl *p*-nitrobenzoate was determined by multiplying the rate constant for the benzoate by the usual factor 20.8.[16] The rate data and the thermodynamic parameters are listed in Table I.

Solvolytic Products. The *p*-nitrobenzoates were solvolyzed in 80% aqueous acetone in the presence of a 10% molar excess of sodium acetate for 10 half-lives. After the usual workup, the product was analyzed by ^{1}H NMR.

Discussion

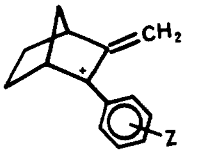
The low exo/endo rate ratio, 3.9, observed for the acetolyses of 3-methylene-2-norbornyl tosylates[9] (**3**) is in sharp contrast to the much higher ratio, 280, observed for the parent 2-norbornyl tosylates.[17] The higher value has been attributed to σ bridging in the transition state for *exo*-norbornyl tosylate, leading to the σ-bridged carbocation.[2] The lower value has been attributed to the absence of such σ bridging in the transition state for the 3-methylene-*exo*-norbornyl tosylate resulting from delocalization of charge from the 2-position to the allylic position (**9** ↔ **10**).



9 **10**

It is proposed that such stabilization of the cation by delocalization of charge from C2 to the allylic position makes σ bridging insignificant.[9] Consequently, the 3-methylene-2-norbornyl system provides a 2-norbornyl cationic intermediate which is clearly classical.

Exo/Endo Rate Ratios in the 2-Aryl-3-methylene-2-norbornyl Derivatives. The introduction of an aryl group into the 2-position of the 3-methylene-2-norbornyl cation should further delocalize charge from C2 into the aryl group. Clearly, if there is no driving force for σ bridging in the secondary ion (**9** ↔ **10**), there should be no driving force for σ bridging in the tertiary ion (**11**).



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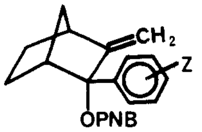
Yet the 2-aryl-3-methylene-2-norbornyl *p*-nitrobenzoates reveal a high, essentially constant exo/endo rate ratio for solvolysis in 80% aqueous acetone at 25 °C (Table I), a ratio which does not change significantly with increasing electron demand (**12**, **13**). These exo/endo rate ratios are



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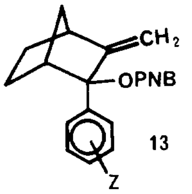

13

Z		
p-OCH$_2$CH$_2$-*m*	1.00	407
p-H	1.00	357
p-CF$_3$	1.00	214
3,5-(CF$_3$)$_2$	1.00	454
2-H	1.00	3.9

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(12) Brown, H. C.; Gundu Rao, C.; Vander Jagt, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 1780.

(13) The tool of increasing electron demand[14] has been applied to the 2-aryl-*exo*-5,6-trimethylene-2-norbornyl system by K. Takeuchi and his co-workers and will be reported shortly.

(14) Gassman, P. G.; Fentiman, A. F., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 2549.

(15) Brown, H. C.; Gundu Rao, C. *J. Org. Chem.* **1979**, *44*, 133.

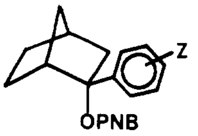
(16) Brown, H. C.; Takeuchi, K. *J. Am. Chem. Soc.* **1977**, *99*, 2679. Brown, H. C.; Takeuchi, K.; Ravindranathan, M. *Ibid.* **1977**, *99*, 2684.

(17) See Chapter 8, ref 5.

very similar to those realized for the tertiary *exo*-5,6-trimethylene-2-norbornyl derivatives.[12] (**5**, **6**). Finally, the

Z	6	5
p-OCH$_2$CH$_2$-m	1.00	286
p-H	1.00	118
2-Me	1.00	420
2-H	1.00	9.5

values are also very similar to the ratios realized for the corresponding 2-norbornyl derivatives (**14**, **15**). These



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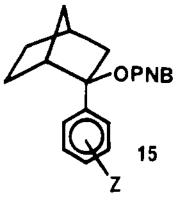

15

Z		
p-OCH$_2$CH$_2$-m	1.00	240
p-H	1.00	127
p-CF$_3$	1.00	187
3,5-(CF$_3$)$_2$	1.00	176
2-Me	1.00	885
2-H	1.00	280

similar rate ratios in the three systems argue for a similar physical basis.

As was pointed out earlier, Winstein had proposed that the mere existence of a high exo/endo rate ratio argued for σ bridging, and he proposed that even 2-phenyl- and 2-methyl-2-norbornyl should be considered to undergo solvolysis via nonclassical (σ-bridged) cationic intermediates.[6] However, the present studies reveal that even systems **1** and **3**, systems which have been proposed as involving classical intermediates even for the secondary derivatives,[7,9] exhibit high exo/endo rate ratios in the solvolyses of the more stable tertiary derivatives. Clearly these high exo/endo rate ratios exhibited by the tertiary derivatives cannot be the result of σ bridging. Steric hindrance to ionization in these U-shaped systems, resulting in sharply reduced rates for the endo isomers, has been proposed as an explanation for the resulting high exo/endo rate ratios of the tertiary derivatives.[17]

Secondary Derivatives. This steric explanation for the high exo/endo rate ratios in tertiary 2-norbornyl derivatives has been accepted by P. von R. Schleyer.[17] However, he argues that this explanation should not be extrapolated to explain the high exo/endo rate ratio in 2-norbornyl itself.[18] The low exo/endo rate ratios for the secondary derivatives **1** and **3** provide a challenge to the steric interpretation. We are examining the solvolyses of these derivatives under a wide variety of conditions in the hope of attaining an understanding of the behavior of these secondary systems.

Effect of the 3-Methylene Substituent. A puzzling feature of the present results is the observation that the 3-methylene group has very little effect on the rates of reactions either of the exo derivatives or of the endo derivatives.

Z	13/15	12/14
p-OCH$_2$CH$_2$-m	1.0	0.6
p-H	2.2	0.8
p-CF$_3$	1.3	1.2
3,5-(CF$_3$)$_2$	1.3	0.5

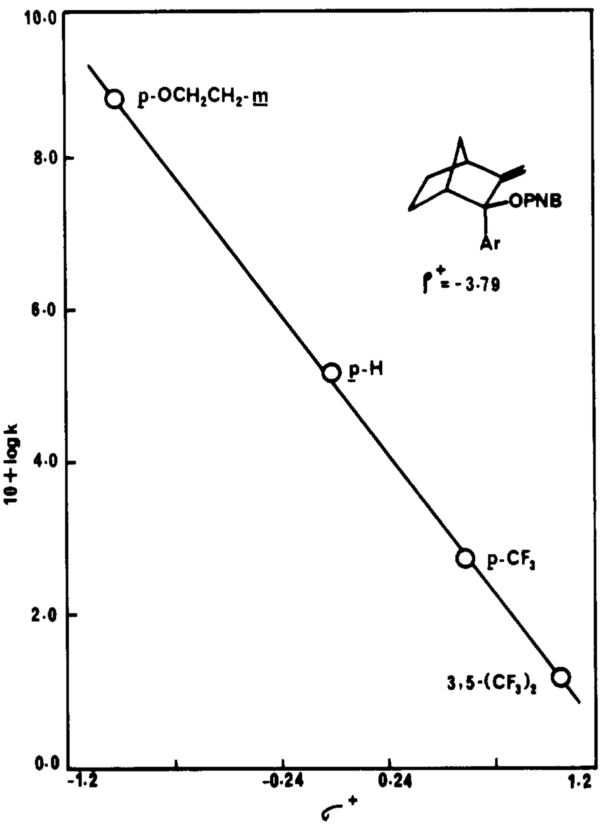

Figure 1. Linear free energy relationship for the solvolysis of the 2-aryl-3-methylene-*exo*-norbornyl p-nitrobenzoates in 80% aqueous acetone at 25 °C.

On the other hand, the introduction of an allylic double bond in representative aliphatic and alicyclic systems results in major enhancements of the solvolytic rates.[19] Clearly we must understand this greatly reduced effect of the allylic double bond in the norbornyl system if we are to arrive at a satisfactory understanding of the behavior of the 3-methylene derivatives, both secondary and tertiary.

σ^+ Correlation of the Rate Constants. The rate data for both the *exo*- and *endo*-2-aryl-3-methylene-2-norbornyl derivatives provide excellent linear correlations with σ^+ (Figures 1 and 2). The exo derivatives (**13**) yield a value of ρ^+ of −3.79 (correlation coefficient 0.999), and the endo derivatives (**12**) yield a ρ^+ value of −3.76 (correlation coefficient 0.999). The striking similarity in the values of ρ^+ of these derivatives with those of the parent norbornyl derivatives (**15** and **14**), ρ^+_{exo} −3.82 and ρ^+_{endo} −3.72, is noteworthy. Therefore, both systems, 2-norbornyl and 3-methylene-2-norbornyl, exhibit similar sensitivities to the tool of increasing electron demand. It follows that similar factors must be responsible for the high exo/endo rate ratios. Since σ bridging cannot be a factor in the 2-aryl-3-methylene-2-norbornyl system,[9] it follows that σ bridging should not be a factor in the 2-aryl-2-norbornyl derivatives.

Exo/Endo Product Ratios. The solvolyses of the *exo*- and *endo*-norbornyl brosylates yield essentially pure *exo*-norbornyl product.[2,20] Such high stereoselectivity favoring the exo product was also considered to provide major support for σ bridging.[2] Consequently, it was of interest to examine carefully the products of the solvolyses of the 2-aryl-3-methylene-2-norbornyl derivatives (**12** and

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[18] Brown, H. C.; Ravindranathan, M.; Gundu Rao, C.; Chloupek, F. J.; Rei, M. H. *J. Org. Chem.* **1978**, *43*, 3667 discusses the several proposals which have been advanced to account for the very similar exo/endo rate ratios of 2-norbornyl and 2-methyl-2-norbornyl in terms of very different physical origins.

[19] Brown, H. C.; Gundu Rao, C.; Ravindranathan, M. *J. Org. Chem.* **1978**, *43*, 4939.

[20] Goering, H. L.; Schewene, C. B. *J. Am. Chem. Soc.* **1965**, *87*, 3516.

Table II. Properties of the 2-Aryl-3-methylene-2-norbornyl *p*-Nitrobenzoates

substituent on aryl	isomer	mp, °C	formula	calcd, % C	calcd, % H	calcd, % N	calcd, % F	found, % C	found, % H	found, % N	found, % F
p-OCH_2CH_2-*m*	N	130-131	$C_{23}H_{21}NO_5$	70.59	5.37	3.58		70.26	5.31	3.32	
p-H	X	126-127	$C_{21}H_{19}NO_4$	72.2	5.44	4.01		72.04	5.36	3.95	
	N	114-115	$C_{21}H_{19}NO_4$	72.2	5.44	4.01		72.04	5.52	3.80	
p-CF_3	X	137-138	$C_{22}H_{18}F_3NO_4$	63.3	4.32	3.36	13.67	63.19	4.58	3.09	13.85
	N	149-150	$C_{22}H_{18}F_3NO_4$	63.3	4.32	3.36	13.67	63.46	4.46	3.14	13.90
3,5-$(CF_3)_2$	X	104-105	$C_{23}H_{17}F_6NO_4$	56.9	3.5	2.89	23.5	56.96	3.73	3.10	23.73
	N	116-117	$C_{23}H_{17}F_6NO_4$	56.9	3.5	2.89	23.5	56.72	3.54	3.03	23.40

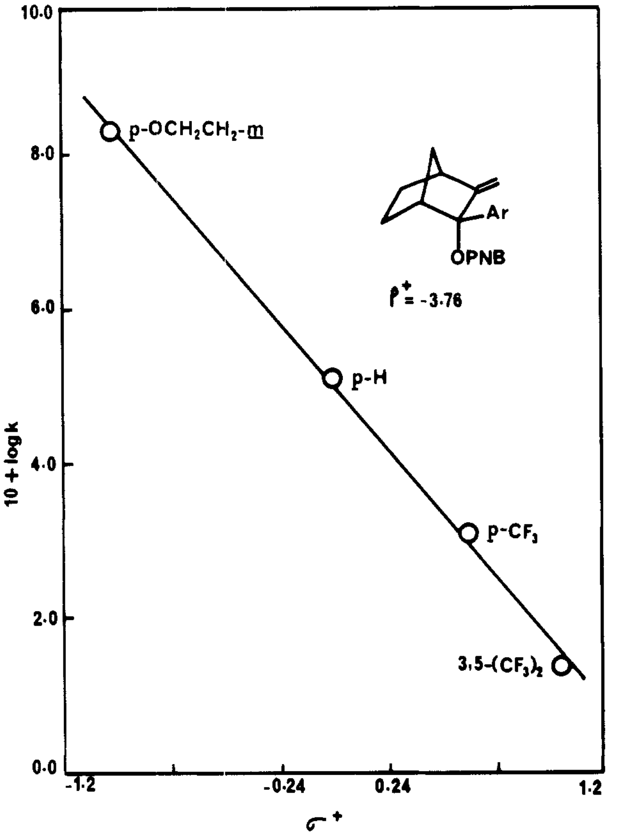

Figure 2. Linear free energy relationship for the solvolysis of the 2-aryl-3-methylene-*endo*-norbornyl *p*-nitrobenzoates in 80% aqueous acetone at 25 °C.

13). Would these compounds, solvolyzing to give highly stable classical cations, provide pure exo products or a mixture of exo and endo compounds?

The solvolyses of the 2-aryl-3-methylene-2-norbornyl *p*-nitrobenzoates in 80% aqueous acetone in the presence of a 10% molar excess of sodium acetate yield the corresponding exo alcohols exclusively, as indicated by ^1H NMR examination of the products. Therefore, even these highly stabilized derivatives, which must undergo solvolysis through classical non-σ-bridged cations, exhibit predominant substitution from the exo face. Predominant substitution to give the exo product can no longer be used to argue for the intermediacy of a σ bridged intermediate.

Goering–Schewene Diagram. It was of interest to construct the Goering–Schewene diagram for the solvolyses of the 2-(5′-coumaranyl)-3-methylene-2-norbornyl *p*-nitrobenzoates. The rate data for the two epimeric derivatives reveal a difference in the free energy of activation of 3.5 kcal mol^{-1}. The difference in the ground-state energies was assumed to be 0.4 kcal mol^{-1}, similar to that determined for the 2-phenyl-2-norbornyl system.[21] This results in a difference of 3.9 kcal mol^{-1} in the energies of the two transition states (Figure 3). Since it has been argued that σ bridging must be absent in the parent secondary system (**3**, **9** ↔ **10**), it must also be absent in the more stable tertiary system (**11**). Consequently, it is not possible to account for the difference in energy of the two transition states in terms of a stabilization of the exo transition state by σ bridging. It is more reasonable to account for the observed difference in energy of the two transition states in terms of an increase in the energy of the endo transition state arising from the steric difficulties in the ionization of the *endo*-*p*-nitrobenzoate group.

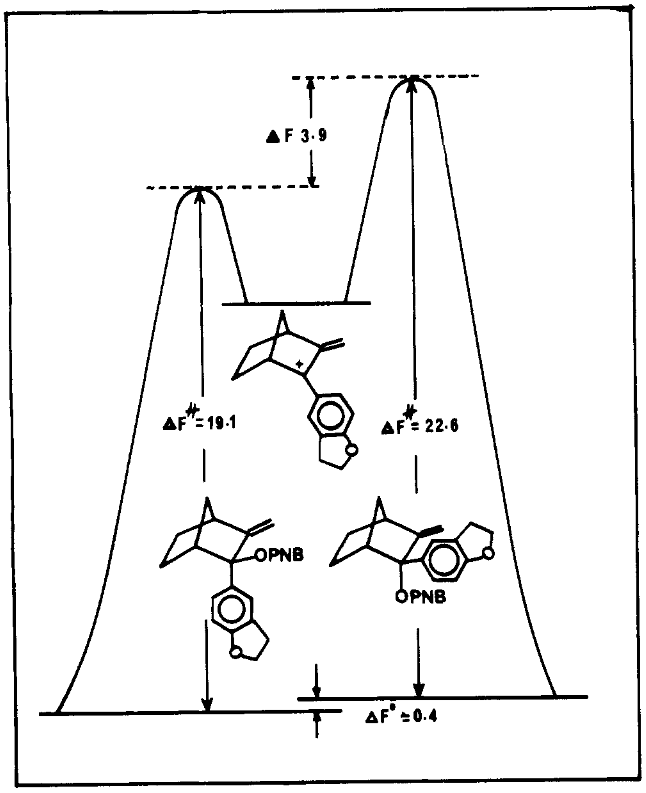

Figure 3. Free energy diagram for the solvolysis of the 2-(5′-coumaranyl)-3-methylene-2-norbornyl *p*-nitrobenzoates in 80% aqueous acetone at 25 °C.

The difference of 3.9 kcal mol^{-1} in the energies of the two transition states nicely accounts for the distribution of the common cationic intermediate essentially completely into the exo product. The predicted distribution would be approximately 1000:1 for exo/endo.

Conclusion

We started with acceptance of the argument that the low exo/endo rate ratios for the systems **1**–**4** reveal the absence of σ bridging, either because of steric restraint to bridging (**1** and **2**) or because the electronic stabilization of the cationic center negates bridging (**3** and **4**). If these secondary derivatives do not involve bridging, the more stable tertiary derivatives cannot involve bridging. Yet the tertiary derivatives of **1** and of **3** reveal high exo/endo

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[21] Rei, M. H.; Brown, H. C. *J. Am. Chem. Soc.* **1966**, *88*, 5335.

rate and product ratios. It is clear from these results that high exo/endo rate and product ratios can be present in 2-norbornyl derivatives without the involvement of σ bridging. Steric hindrance to ionization provides an alternative explanation for such high exo/endo ratios in the tertiary derivatives. We are left with the question as to whether the high exo/endo rate and product ratios in the parent 2-norbornyl system can be explained in terms of similar factors and as to the precise nature of the factor or factors responsible for the low exo/endo rate ratios in systems 1–4. We are currently examining this question.

Experimental Section

2-Aryl-3-methylene-*endo*-norbornanols. Addition of 5-coumaranyllithium, phenyllithium, *p*-(trifluoromethyl)phenyllithium, and 3,5-bis(trifluoromethyl)magnesium bromide to 3-methylene-2-norbornanone (Aldrich) provided the corresponding endo alcohols. These alcohols were purified by distillation.

2-Aryl-3-methylene-*endo*-norbornyl *p*-Nitrobenzoates. These *p*-nitrobenzoates were made by the addition of *p*-nitrobenzoyl chloride to the lithium alkoxide of the endo alcohols in THF.[22] The physical properties and analytical data are summarized in Table II.

2-Aryl-3-methylene-*exo*-norbornanols. 2-Aryl-3-methylene-*endo*-norbornyl *p*-nitrobenzoates were solvolyzed in 80% aqueous acetone in the presence of a 10% molar excess of sodium acetate for 10 half-lives. After the usual workup, the exo alcohols obtained were used for the next reaction without any further purification.

2-Aryl-3-methylene-*exo*-norbornyl *p*-Nitrobenzoates. These *p*-nitrobenzoates were made by the addition of *p*-nitrobenzoyl chloride to the lithium alkoxide of the exo alcohol in THF.[22] The 2-(5′-coumaranyl)-3-methylene-*exo*-norbornyl *p*-nitrobenzoate could not be isolated because of its extreme reactivity; instead, the corresponding benzoate ester was made and used as such for the kinetic work. The physical and analytical data are summarized in Table II.

Kinetic Measurements. The method used for determining the rate constants of the *p*-nitrobenzoates and benzoates is essentially the same as that described earlier.[22] The rates and thermodynamic parameters are listed in Table I.

Solvolysis Products. The *p*-nitrobenzoates were solvolyzed in 80% aqueous acetone containing a 10% molar excess of sodium acetate for 10 half-lives. Then the reaction mixtures were worked up and analyzed by ^1H NMR. In all of the cases, the solvolysis products were almost exclusively the tertiary exo alcohols.

Registry No. 12 (Z = *p*-OCH_2CH_2-*m*), 71185-52-9; **12** (Z = *p*-H), 71185-53-0; **12** (Z = *p*-CF_3), 71243-01-1; **12** (Z = 3,5-$(CF_3)_2$), 71185-54-1; **13** (Z = *p*-OCH_2CH_2-*m*), 71185-55-2; **13** (Z = *p*-H), 71185-56-3; **13** (Z = *p*-CF_3), 71185-57-4; **13** (Z = 3,5-$(CF_3)_2$), 71185-58-5; **14** (Z = *p*-OCH_2CH_2-*m*), 68150-99-2; **14** (Z = *p*-H), 21845-81-8; **14** (Z = *p*-CF_3), 20530-03-4; **14** (Z = 3,5-$(CF_3)_2$), 56068-59-8; **14** (Z = 2-Me), 71185-59-6; **15** (Z = *p*-OCH_2CH_2-*m*), 68150-98-1; **15** (Z = *p*-H), 20550-35-0; **15** (Z = *p*-CF_3), 20530-02-3; **15** (Z = 3,5-$(CF_3)_2$), 56068-58-7; **15** (Z = 2-Me), 71185-60-9; 2-(5′-coumaranyl)-3-methylene-*endo*-norbornanol, 71185-61-0; 2-(5′-coumaranyl)-3-methylene-*exo*-norbornanol, 71185-62-1; 2-phenyl-3-methylene-*endo*-norbornanol, 30781-91-0; 2-phenyl-3-methylene-*exo*-norbornanol, 30781-92-1; 2-[4-(trifluoromethyl)phenyl]-3-methylene-*endo*-norbornanol, 71185-63-2; 2-[4-(trifluoromethyl)phenyl]-3-methylene-*exo*-norbornanol, 71185-64-3; 2-[3,5-bis(trifluoromethyl)phenyl]-3-methylene-*endo*-norbornanol, 71185-65-4; 2-[3,5-bis(trifluoromethyl)phenyl]-3-methylene-*exo*-norbornanol, 71185-66-5; *p*-nitrobenzoyl chloride, 122-04-3.

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(22) Brown, H. C.; Peters, E. N. *J. Am. Chem. Soc.* **1975**, *97*, 1927.

Internal Acid Catalysis in the Reactions of Monoprotonated Diamines with Cyclopentanone and 3-Pentanone to Give Imines[1a]

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Equilibrium constants for oxime formation in water at 35 °C have been determined for 3-pentanone (7.9×10^4 M^{-1}) and cyclopentanone (40×10^4 M^{-1}), as have the pK_a values for the protonated oximes. The kinetics of oximation and secondary deuterium kinetic isotope effects were determined in the pH range 6–11, where dehydration of the intermediate carbinolamine is rate controlling. With hydroxylamine to capture the relatively unstable imines, the kinetics of imine formation from seven primary amines were studied in this pH range. For amines of the type $XCH_2CH_2NH_2$, where X is neutral in charge and in acid–base behavior, plots of log *k* for imine formation vs. pK_a for the corresponding primary ammonium ions give straight lines. The monoprotonated forms of 2-(dimethylamino)ethylamine, 3-(dimethylamino)propylamine, and *N*,*N*,2,2-tetramethyl-1,3-propanediamine are too reactive to fit these lines, the tertiary-protonated form of 2-(dimethylamino)ethylamine being more than 2000 times too reactive. This is attributed to internal acid catalysis of dehydration of the intermediate carbinolamine $R_2C(OH)NH\sim NHMe_2^+$ by the dimethylammonio group. The effect of structure on reactivity is discussed.

The formation of iminium ions in the reactions of primary and secondary amines with aldehydes and ketones involves intermediate formation of a carbinolamine, which then loses a hydroxide ion.[2,3] This last step is ordinarily rate controlling in neutral or basic aqueous solutions. The loss of hydroxide ions is uncatalyzed in sufficiently basic solutions, but in less basic solutions it is catalyzed by hydrogen ions. The loss of hydroxide ion is brought about by an internal acidic hydrogen atom (eq 1) in the reactions of certain monoprotonated diamines with acetone[4,5] and isobutyraldehyde.[6] This increases the efficiency with which some monoprotonated diamines bifunctionally catalyze α-hydrogen exchange reactions that proceed via

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(2) Jencks, W. P. *Prog. Phys. Org. Chem.* **1964**, *2*, 63–128.

(3) Jencks, W. P. "Catalysis in Chemistry and Enzymology"; McGraw-Hill: New York, 1969; Chapter 10.B.

(4) Hine, J.; Cholod, M. S.; Chess, W. K., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 4270–6.

(5) Hine, J.; Li, W.-S. *J. Org. Chem.* **1975**, *40*, 2622–6.

(6) Hine, J.; Via, F. A. *J. Org. Chem.* **1977**, *42*, 1972–8.

0022-3263/79/1944-3540$01.00/0