(35) H. C. Brown and Nung Min Yoon, *J. Am. Chem. Soc.*, **88**, 1464 (1966).
(36) E. C. Ashby, J. R. Sanders, P. Claudy, and R. Schwartz, *J. Am. Chem. Soc.*, **95**, 6485 (1973).
(37) E. C. Ashby, P. Claudy, and R. D. Schwartz, *Inorg. Chem.*, **13**, 192 (1974).
(38) J. Klein and H. Stollar, *Tetrahedron Lett.*, 2541 (1974).
(39) J. Klein, *Tetrahedron Lett.*, 3349 (1974).
(40) R. C. Bingham and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **93**, 3187 (1971).
(41) N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, *J. Am. Chem. Soc.*, **88**, 2999 (1966).
(42) E. C. Ashby, R. D. Schwartz, and B. D. James, *Inorg. Chem.*, **9**, 325 (1970).
(43) E. C. Ashby and R. D. Schwartz, *Inorg. Chem.*, **10**, 355 (1971).
(44) E. C. Ashby and B. D. James, *Inorg. Chem.*, **8**, 2468 (1969).
(45) E. C. Ashby and J. Watkins, *Inorg. Chem.*, **12**, 2493 (1973).
(46) E. C. Ashby and J. J. Watkins, *Inorg. Chem.*, submitted.
(47) E. C. Ashby and S. Srivastava, *Inorg. Chem.*, in press.
(48) E. C. Ashby, G. Brendel, and H. E. Redman, *Inorg. Chem.*, **2**, 499 (1963)

Stereochemical Control of Reductions. 5.[1] Effects of Electron Density and Solvent on Group Haptophilicity[2]

Hugh W. Thompson,* Eugene McPherson, and Barbara L. Lences[3]

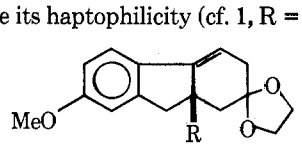
Carl A. Olson Memorial Laboratories, Department of Chemistry, Rutgers University, Newark, New Jersey 07102

Received February 17, 1976

7-Methoxy-10a-hydroxymethyl-1,2,3,9,10,10a-hexahydrophenanthrene (**2**) was synthesized and the stereochemistry of its cis (**8**) and trans (**5**) reduction products established. The directive effect of the CH_2OH group was examined by heterogeneous catalytic hydrogenation of **2** over a Pd/C catalyst, leading to cis–trans mixtures whose proportion of **8** increased (6–61%) as the solvent dielectric constant was lowered (DMF, EtOH, THF, DME, diglyme, Bu_2O, dioxane, hexane). This is interpreted primarily in terms of competition between substrate CH_2OH and solvent for active catalyst sites. Use of a Pt/C catalyst gave a nearly identical solvent order, but with higher proportions of **8** throughout (9–80%). Compound **2** was converted to its Li, Na, and K alkoxides and these, when hydrogenated over Pd/C in diglyme, gave increasing proportions of **8** (60–69%) in the product mixture compared to the protonated group (23%). This is interpreted as reflecting increasing electron density available to bind oxygen to the catalyst surface during reduction. These principles may be useful in improving stereochemical control in catalytic hydrogenation.

Numerous reports[4] of heterogeneous catalytic hydrogenations deal with instances in which the presence of certain functional groups in the substrate molecule has led to product stereochemistry opposite that expected on the basis of steric hindrance.[4b] This evidently can arise from a propensity of the functional group, most frequently hydroxyl, to bind to the catalyst surface during reduction in such a way as to enforce addition of hydrogen from its own side of the molecule, an effect we have termed haptophilicity.[5]

Our previous work[5] on the directing effects of various substrate functional groups during hydrogenation led us to the general conclusion that a group's haptophilicity is probably directly related to, among other things, its ability to donate electrons toward the catalytic surface. This conclusion suggested to us several specific ways in which the haptophilicities of groups might be altered so as to affect predictably the stereochemistry of reductions. For example, conversion of an acidic group to its anion should increase its electron-donating ability and hence its haptophilicity (cf. **1**, R = COOH, COOLi,



1

COONa).[5] Additionally, the effective haptophilicity of many R groups would probably be increased if competition from polar and especially hydroxylic solvents were eliminated, since OH has a high haptophilicity.

Synthesis and Stereochemistry of Materials. We wished to test these ideas experimentally; however, it was clear that for several R groups the system **1** would be insensitive to increases in haptophilicity, leading to higher percentages of cis product, simply because the percentage of cis product was already very high (e.g., R = CH_2OH → 95% cis).[5,6] For this reason we have turned our attention to the closely related system **2**, which was prepared by reduction of the known ester **3**.[7] Compound **2** not only was soluble in a variety of solvents of low polarity but, on catalytic hydrogenation under reaction conditions similar to those used with **1**, gave a product mixture rich in the trans isomer (94% trans, 6% cis), allowing us ample leeway in enhancing the haptophilicity of the CH_2OH group. This relatively high percentage of trans product obtained from **2** supports our previous speculation[5] that the ketal group in **1** may be haptophilically involved in the contrastingly high cis specificity (95%) observed in hydrogenation of **1**, R = CH_2OH.[5,6] Scheme I shows the sequences by which the

Scheme I

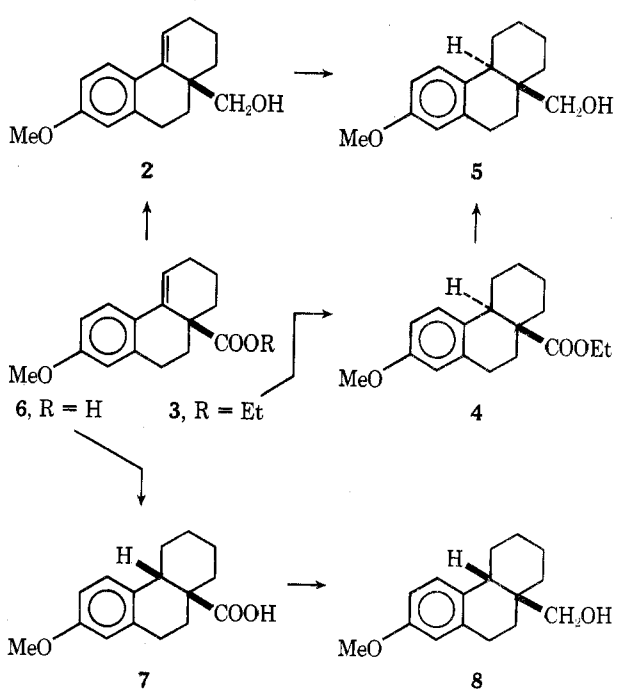


Table I. Products from Hydrogenation of 2 at 1 atm and 25 °C

Solvent	Dielectric constant[a]	Pd/C catalyst		Pt/C catalyst	
		% yield	Ratio of 8:5[b]	% yield	Ratio of 8:5[b]
Hexane	1.9	89	61:39	90	80.5:19.5
Dioxane	2.2	96	26:74	95	46.5:53.5
Bu_2O	3.1	94	26.5:73.5	90	50.5:49.5
Diglyme	7.2	81	18.5:81.5	98	43:57
DME	7.2	94	20:80	96	36:64
THF	7.6	93	18:82	90	30:70
EtOH	24.6	96	6:94		
DMF	36.7	99	6:94	90	9:91

[a] Values taken from ref 11. [b] Values considered accurate to ±2%, e.g., 61 ± 2:39 ± 2.

stereochemistries of the reduction products of **2** were established.

Our stereochemical assignments for **4** and **7**, and hence for **5** and **8**, are based as follows. The unsaturated ethyl ester **3** has a single infrared carbonyl absorption at 1720 cm^{-1}. Catalytic reduction with Pd/C yielded a major product whose ir spectrum has a carbonyl doublet (1735, 1720 cm^{-1}), indicating rotation which is more severely restricted than in **3**. This is consistent only with trans stereochemistry in the reduction product, and conforms to the spectral patterns found for the corresponding compounds of series **1** (where the cis product lacks such a doublet).[6] This stereochemical result also fulfilled our expectations based on the established low haptophilicity of the ester function.[5,6]

Lithium–ammonia reduction of the unsaturated carboxylic acid **6** was expected to yield products representing protonation of an equilibrium mixture of the conformers of the benzylic anion reduction intermediate. The cis and trans forms of this should provide equally good ring overlap with the benzylic anion, so that conformational preferences should be controlled here by steric and electrostatic repulsions. While the latter are very difficult to assess, the cis juncture is known to be favored in decalin and octalin systems by introduction of angular substituents more bulky than H.[8] Hence, on the assumption that rates of protonation are comparable, this equilibrium mixture was expected to give largely or entirely cis product. This reduction yielded at least 80% of a single carboxylic acid, whose $LiAlH_4$ reduction product (**8**) was not identical with that from $LiAlH_4$ reduction of **4**, but melted some 50° lower, consistent with the less planar and less rigid cis structure.

Solvent Effects on Haptophilicity. Little of the existing data[9,10] concerning solvent effects on hydrogenation stereochemistry is derived from compounds specifically chosen to elucidate mechanisms. Much of it was gleaned incidentally during synthetic studies and is far from exhaustive, and much, stemming from the period before VPC and NMR, suffers "from both inadequate product analysis and isomerization of initially formed products".[9] The best that can be safely summarized from the morass of available, often conflicting, data is that the interrelationship of the solvent's functional group, bulk, viscosity, dielectric constant, pH, etc., with catalyst, substrate, pressure, and temperature is so intricate that prediction of results is frequently hazardous even when only one variable is changed.

Against this background we wished to examine with compound **2** the proposition that substrate haptophilicity may be diminished by competition with the solvent. We envisioned this as a preempting of active sites on the catalyst surface by solvents containing polar functional groups, particularly ones of known high haptophilicity. However, such a process might operate by several mechanisms, not only making sites unavailable for haptophilic substrate interactions, but probably also increasing steric interactions by adding bulk at the catalyst surface near whatever sites are available. A similar result could also be produced by the fact that such solvents could solvate and thus mask the substrate haptophilic group, making it bulkier.

Although they do not allow us to distinguish among these mechanisms, our results, shown in Table I, are strikingly consistent with the basic idea of solvent competition and indicate that dielectric constants seem to provide a rough guide to this sort of solvent effect. It seems clear that some of the previously observed solvent effects on stereochemistry may have been of this origin, which we may call competitive solvent haptophilicity. It is not our intention to present here a complete or rigid solvent haptophilicity series, since so specific a ranking might well fail when other variables are changed. In fact, since **2** has been chosen specifically to illustrate haptophilic effects by eliminating complicating structural features, most other systems will probably present situations which are less clear-cut. Rather, we wish to suggest that, in the absence of perturbing factors, to the extent that haptophilic effects operate in a given system the extremes of stereospecificity are likely to be achieved with extremes of solvent dielectric constant.

It should be pointed out that the data for palladium and for platinum closely parallel each other, but with the platinum series giving consistently higher percentages of cis product. Although in general Pd catalysts seem to favor the thermodynamic product epimer more frequently than does Pt,[10] our results appear consistent with the general observation that Pt catalysts are the more sensitive to poisoning.[10a]

Haptophilic Enhancement by Anion Formation. We had already demonstrated in the case of **1** that increasing the electron density on a carboxyl group by anion formation leads to increased haptophilicity, which varies with the cation used.[5] We wished also to apply this idea to the hydromethyl group of **2**. For these experiments it seemed clear that alcohols, for reasons of proton exchange, and hydrocarbons, because of substrate insolubility, would be inappropriate solvents. Diglyme was finally chosen because of its combination of low dielectric constant with ability to dissolve salts by cation solvation. It was found that at 25 °C and 1 atm conversions in the hydrogenation of salts of **2** with our Pd/C catalyst were essentially nil. This did not surprise us unduly, as we had already speculated upon the relationship between haptophilicity and catalyst poisoning,[5] and we found that by increasing the pressure to 3 atm the reductions could be carried to completion, although isolated yields were only in the 70–80% range (Table II). The small difference in cis–trans isomer ratio obtained for R = CH_2OH here and in Table I is the result of this change in hydrogen pressure.

The results in Table II coincide remarkably with those found for carboxylate in system **1**: an increase in the amount of cis product on going from the protonated group to the alkali metal salts, and an increase in cis product as the size of the cation is increased. These results, together with the mild

Table II. Products from Hydrogenation of Salts of 2 with Pd/C Catalyst at 3 atm and 25 °C

Group	Solvent	% yield	Ratio of 8:5[a]
CH_2OH	Diglyme	95	23:77
CH_2OLi	Diglyme	71	60:40
CH_2OLi	Bu_2O	95	63:37
CH_2ONa	Diglyme	74	66.5:33.5
CH_2OK	Diglyme	81	69:31

[a] Values considered accurate to ±2%, e.g., 23 ± 2:77 ± 2.

catalyst-poisoning effect of the salts, speak eloquently for the idea that the adhesion of acidic functional groups to the catalyst surface can be enhanced by anion formation[12] and further controlled by choice of cation.

The two effects demonstrated here extend considerably our fundamental understanding of the concept and nature of haptophilicity and the practical usefulness of the ranking of group haptophilicities we previously presented.[5] Even for nonideal cases our results suggest a systematic basis for attempting to exploit more fully the steric and electronic features of a given system to achieve stereochemical control.

Experimental Section[13]

Catalytic Hydrogenation of 7-Methoxy-10a-carbethoxy-1,2,3,9,10,10a-hexahydrophenanthrene (3). A solution of 577 mg (2.02 mmol) of 3[7] in 30 ml of absolute EtOH was hydrogenated at 25 °C and 1 atm over 60 mg of 5% Pd/C catalyst. Concentration of the filtered reaction solution provided material recrystallized from pentane to give 351 mg (60.5%) of 4 as rhombic platelets: mp 41–42 °C; ir 1735, 1720 cm^{-1}; NMR δ 1.05 (3 H t, J = 7 Hz), 1.2–2.9 (13 H complex), 3.7 (3 H s), 3.95 (2 H q, J = 7 Hz), 6.35–6.7 (2 H complex), 7.1 (1 H d, J = 9 Hz); MS m/e 288 (33%, M^+), 215 (29%), 214 (100%), 171 (32%).

Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.77; H, 8.39.

$LiAlH_4$ Reduction of 4. Compound 4 (234 mg, 0.81 mmol), when treated with 66 mg (1.65 mmol) of $LiAlH_4$ in Et_2O, gave incompletely reduced material after 1 h of reflux and was recovered and resubjected to $LiAlH_4$ (133 mg, 3.3 mmol) by refluxing in 50 ml of dry THF for 6 h under N_2. The mixture was worked up by titration with saturated aqueous Na_2SO_4, filtration, and concentration to give material melting at 110–116 °C. Two recrystallizations from pentane produced 46 mg (23%) of 5 as fine felted needles, mp 117–120.5 °C, identical with material produced by hydrogenation of 2. An analytical sample melted at 121–123 °C: ir ($CHCl_3$) 3620, 3460 cm^{-1}, no C=O absorption; uv 212, 224, 281, 289 nm; NMR δ 0.8–3.1 (14 H complex), 3.3 (1 H d, J = 11.5 Hz), 3.7 (1 H d, J = 11.5 Hz), 3.8 (3 H s), 6.55–6.8 (2 H m), 7.1 (1 H d, J = 9 Hz); MS m/e 246 (100%, M^+), 228 (51%), 215 (99%), 171 (68%), 147 (99%).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.12; H, 8.91.

$LiAlH_4$ Reduction of 3. A slurry of 200 mg (5.0 mmol) of $LiAlH_4$ in 40 ml of dry Et_2O was stirred under N_2 during dropwise addition of 572 mg (2.0 mmol) of 3 in 10 ml of dry Et_2O. After addition the mixture was refluxed for 2 h, stirred overnight at 25 °C, and worked up by titration with saturated aqueous Na_2SO_4. The decantate was combined with the hexane washings of the precipitate and passed through a short Al_2O_3 column. Concentration gave a solid recrystallized from MeOH to provide 465 mg (95%) of 2 as fine felted needles: mp 116–116.5 °C; ir 3660 cm^{-1}, no carbonyl absorption; uv 218, 262.5, 297 nm; NMR δ ca. 1.4 (1 H s, disappears on shaking with D_2O), 1.1–3.0 (10 H complex), 3.55 (2 H s), 3.8 (3 H s), 6.2 (1 H t, J = 4 Hz), 6.6–6.9 (2 H complex), 7.45 (1 H d, J = 8 Hz); MS m/e 244 (62%, M^+), 226 (25%), 214 (43%), 213 (100%), 198 (38%).

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.58; H, 8.35.

Catalytic Hydrogenation of 2. A preparative hydrogenation was carried out involving 490 mg (2.0 mmol) of 2, 62.5 mg of 5% Pd/C catalyst, and 30 ml of absolute EtOH. After 45 min of stirring at 25 °C and 1 atm, uptake of H_2 had ceased and the usual filtration and concentration procedure yielded 478 mg (97%) of 5, mp 115–118 °C. Recrystallization from Et_2O gave material melting at 121–123 °C, which was identical (ir, mixture melting point) with that obtained by $LiAlH_4$ reduction of 4.

Saponification of 3. Compound 3 (858 mg, 3.0 mmol), when treated with 2.0 g of 85% KOH in 80 ml of EtOH–H_2O, gave primarily starting material after 24 h of reflux and was recovered and resubjected to 85% KOH (2.30 g, 35 mmol) by refluxing in 90 ml of methoxyethanol (bp 124 °C) for 24 h under N_2. Acidification with aqueous HCl, extraction with Et_2O, and concentration gave 751 mg (97%) of crude solid which was recrystallized from absolute EtOH to provide 569 mg (73.5%) of 6 as white needles: mp 174–176 °C dec; ir 3300–2100, 1690 cm^{-1}; uv 218, 262, 297 nm; NMR δ 0.8–2.95 (10 H complex), 3.75 (3 H s), 6.2 (1 H t, J = 5 Hz), 6.65 (2 H complex), 7.5 (1 H d, J = 9 Hz); MS m/e 258 absent, 214 (80%, $M^+ - CO_2$), 213 (100%), 212 (80%), 186 (55%), 171 (67%).

Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.59; H, 7.16.

Li–NH_3 Reduction of 6. A solution of 100 mg (0.39 mmol) of 6 in 10 ml of dry 1:1 THF–Et_2O was added over 1 min to a stirred solution of 39 mg (5.6 mg-atoms) of Li in 16 ml of liquid NH_3. After 15–20 min the blue reaction mixture was quenched with solid NH_4Cl, and NH_3 was allowed to evaporate. Addition of aqueous HCl and extraction with Et_2O provided 100 mg (99%) of crude solid, which was sublimed at 160 °C (0.08 mm) and recrystallized from Et_2O–pentane to give 81 mg (80%) of 7 as flat matted crystals: mp 150–151 °C; ir 3600–2300, 1700 cm^{-1}; uv 212, 224, 282.5, 290 nm; NMR δ 1.0–3.35 (13 H complex), 3.75 (3 H s), 6.7 (2 H complex), 7.05 (1 H d, J = 8 Hz); MS m/e 260 (100%, M^+), 215 (72%), 214 (98%), 213 (74%), 186 (40%), 171 (65%).

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.67; H, 7.83.

$LiAlH_4$ Reduction of 7. A slurry of 40 mg (1.0 mmol) of $LiAlH_4$ in 10 ml of dry Et_2O was stirred under N_2 during dropwise addition of 100 mg (0.385 mmol) of 7 in 15 ml of dry Et_2O. After addition the mixture was refluxed for 3 h, stirred overnight at 25 °C, and worked up by titration with saturated aqueous Na_2SO_4. The organic filtrate was concentrated to a viscous oil which was purified by chromatography on Al_2O_3 and distilled at 150 °C (1.0 mm) to give ca. 80 mg (85%) of solid. Repeated recrystallization from hexane yielded pure 8: mp 71 °C; ir 3660, 3510 cm^{-1}, no carbonyl absorption; uv 211, 223, 281, 288.5 nm; NMR δ 1.0–3.0 (13 H complex), 3.3 (1 H d, J = 11 Hz), 3.45 (1 H d, J = 11 Hz), 3.8 (3 H s), 6.65 (2 H complex), 6.95 (1 H d/d, J = 2, 7 Hz); MS m/e 246 (100%, M^+), 228 (61%), 215 (51%), 171 (58%), 147 (51%).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.92; H, 9.02.

Procedure for Hydrogenations. Table I. Hydrogenations were carried out with a low-pressure apparatus at 1 atm (76 ± 2 cm) and room temperature (25 ± 2 °C) using 5% Pd/C and 5% Pt/C catalysts supplied by Engelhard Industries, Newark, N.J. Diglyme, DME, THF, and Bu_2O (distilled from $LiAlH_4$) and benzene, hexane, and dioxane (distilled from Na) were stored over 4A molecular sieves. Toluene and DMF were distilled from CaH_2 and stored over molecular sieves or CaH_2. Absolute EtOH (Commercial Solvents Corp. Gold Shield) was used without further purification.

To a flask containing a Teflon-covered magnetic stirring bar and 3.4 mg of catalyst was added a solution of 24.4 mg (0.10 mmol) of 2 in 1.6 ml of solvent. The flask was then alternately evacuated and filled with H_2 several times to remove air. The final charge of H_2 was adjusted to 1 atm with a mercury leveling bulb and stirring was begun. When at least the theoretical quantity of H_2 had been absorbed and uptake had ceased (typically ca. 1 h, occasionally longer), the product was isolated by filtration (catalyst washed with additional solvent) and removal of all solvent under vacuum. The residue was sublimed at ca. 110 °C (ca. 0.05 mm) and the cold finger weighed immediately before and after removal of the sublimate.

Table II. Compound 2 (24.4 mg, 0.10 mmol) was dissolved in 1.0 ml of dry solvent and 1.0 equiv of base was introduced under N_2. The mixture was stirred for 5 min at 35 °C for formation of the Li salt (ethereal MeLi, diglyme), refluxed for 24 h to produce the Na salt (NaH, diglyme), and refluxed for 2–3 h in the case of the K salt (KH, THF). In each instance the mixture was evaporated to dryness under vacuum and the residue was weighed. Infrared analysis verified complete alkoxide formation by lack of OH absorption.

Salts were used immediately after isolation, employing the amounts of catalyst and solvent described above, but with a Parr apparatus at 25 °C and 3.0 atm for 3 h. Workup was by filtration, dilution with water, adjustment of pH to 3 with aqueous HCl, and extraction with Et_2O. After being dried and concentrated, the extract was sublimed and weighed as described above.

Analysis of Product Mixtures. The entire sublimate was washed from the cold finger with dry MeOH and this solution was used directly for VPC analysis. NMR did not provide adequate resolution

of the appropriate peaks at 60 MHz to be useful for mixture analysis. Typical VPC retention times for **2**, **8**, and **5**, respectively, were 6, 10, and 13 min with the Apiezon column at 270 °C and 6, 13, and 16 min for the SE-30 column at 235 °C. Traces were integrated by planimeter and calibrated with traces from prepared mixtures of **8** and **5**.

Control Hydrogenations. Except in one instance control hydrogenations to establish absence of equilibration were run on the trans product (**5**), since evidence suggests that it is the less stable epimer.[8] These reactions employed substrate, catalyst, and solvent (diglyme) in the ratio indicated above, with material recoveries of 98–100%, and in no instance gave detectable evidence for epimerization: **5**, Pd/C, 1 atm; **8**, Pd/C, 1 atm; **5**, Pt/C, 1 atm; **5**, Pd/C, 3 atm; Na salt of **5**, Pd/C, 3 atm. Isomerizations through catalyst-associated states (e.g., double-bond migration) were tested for and found absent or negligible in the closely related system **1**;[5] for this reason such processes are believed also to be unimportant in the reactions of **2**.

Acknowledgments. Financial support from the Rutgers Research Council is gratefully acknowledged. In addition, thanks is due to Lever Brothers Research Center, Givaudan Corp., and Hoffmann-La Roche Inc. for making facilities available to E. M. Gratitude is expressed to Gree L. Spoog for helpful consultations.

Registry No.—**2**, 53547-99-2; **3**, 59434-75-2; **4**, 59434-76-3; **5**, 59434-77-4; **6**, 59434-78-5; **7**, 59434-79-6; **8**, 59434-80-9.

References and Notes

(1) Part 4: H. W. Thompson and E. McPherson, *J. Am. Chem. Soc.*, **96**, 6232 (1974).
(2) Taken in part from the Ph.D. Thesis of E. M., Rutgers University, 1975.
(3) Undergraduate Research Participant, spring 1968.
(4) (a) For references, see previous papers in this series and R. J. Sehgal, R. U. Koenigsberger, and T. J. Howard, *J. Org. Chem.*, **40**, 3073 (1975). (b) However, see S. Siegel and J. R. Cozort, *ibid.*, **40**, 3594 (1975).
(5) H. W. Thompson and R. E. Naipawer, *J. Am. Chem. Soc.*, **95**, 6379 (1973).
(6) H. W. Thompson, *J. Org. Chem.*, **36**, 2577 (1971).
(7) R. A. Barnes, H. P. Hirschler, and B. R. Bluestein, *J. Am. Chem. Soc.*, **74**, 32 (1952); see also S. J. Daum, P. E. Shaw, and R. L. Clarke, *J. Org. Chem.*, **32**, 1427 (1967), and P. N. Chakrabortty, R. Dasgupta, S. K. Dasgupta, S. R. Ghosh, and U. R. Ghatak, *Tetrahedron*, **28**, 4653 (1972).
(8) (a) F. Sondheimer and D. Rosenthal, *J. Am. Chem. Soc.*, **80**, 3995 (1958); R. J. Balf, B. Rao, and L. Weiler, *Can. J. Chem.*, **49**, 3135 (1971); (b) A. J. Birch, H. Smith, and R. E. Thornton, *J. Chem. Soc.*, 1339 (1957); W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi, and Y. Hayase, *J. Am. Chem. Soc.*, **89**, 1483 (1967); W. S. Johnson, *Acc. Chem. Res.*, **1**, 1 (1968); (c) H. W. Thompson, G. E. Linkowski, and J. M. Gottlieb, unpublished results.
(9) H. O. House, "Modern Synthetic Reactions", 2d ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 26–28.
(10) (a) R. L. Augustine, "Catalytic Hydrogenation", Marcel Dekker, New York, N.Y., 1965, pp 34–49; (b) P. N. Rylander, "Catalytic Hydrogenation over Platinum Metals", Academic Press, New York, N.Y., 1967, pp 104–107.
(11) J. A. Riddick and W. B. Bunger, "Technique of Organic Chemistry—Organic Solvents", Vol II, 3d ed, Wiley-Interscience, New York, N.Y., 1970; I. P. Gol'dshtein, E. N. Gur'yanova, N. M. Alpatova, and Yu. M. Kessler, *Elektrokhimiya*, **3**, 1011 (1967); *Chem. Abstr.*, **68**, 99624v (1968).
(12) Such an effect may be at least partly responsible for the increased β-hydrogenation reported when reduction of 4-cholesten-3β-ol is carried out using a base-treated catalyst: M. C. Dart and H. B. Henbest, *J. Chem. Soc.*, 3563 (1960).
(13) Melting points were determined with a Mel-Temp apparatus and are uncorrected, as are boiling points. Infrared spectra were taken using a Beckman IR-10 spectrometer and, unless otherwise specified, CCl_4 solutions. Ultraviolet spectra were taken with a Beckman DB-5 grating spectrometer, with 95% EtOH as the solvent. NMR spectra were taken on a Varian A-60 instrument, using CCl_4 or $CDCl_3$ solutions with Me_4Si and/or CH_2Cl_2 internal standards. Mass spectra were determined with an Atlas CH-5 magnetic sector instrument at 70 eV ionization potential. VPC analyses were carried out using 4 ft × 0.25 in. columns packed with 10% Aplezon L on 80–100 mesh firebrick (Hewlett-Packard 5750) and with SE-30 on 80–100 mesh firebrick (Varian Aerograph 1520). Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Steric Effects. 6. Hydrolysis of Amides and Related Compounds

Marvin Charton

Department of Chemistry, School of Science, Pratt Institute, Brooklyn, New York 11205

Received November 10, 1975

Data for eight sets of acidic and basic hydrolysis of amides, 18 sets of acidic and basic hydrolysis of *N*-acylimidazoles, and one set of acidic hydrolysis of hydroxamic acids were correlated with the modified Taft equation $\log k_X = \psi\upsilon_X + h$. Data for one set of basic hydrolysis of amides were correlated with the equation $\log k_X = \alpha\sigma_{IX} + \beta\sigma_{RX} + \psi\upsilon_X + h$. Best results were obtained upon the exclusion of the *tert*-butyl group from the correlations. The magnitude of the steric effect upon acid-catalyzed amide or *N*-acylimidazole hydrolysis is the same as the magnitude of the steric effect upon the base-catalyzed hydrolysis of amides or *N*-acylimidazoles. This is in contrast to the behavior of esters, for which a significant difference in the magnitude of the steric effect upon esterification of acid-catalyzed hydrolysis and upon base-catalyzed hydrolysis exists. The magnitude of the steric effect upon the acidic or basic hydrolysis of amides and related compounds is roughly comparable to the magnitude of the steric effect upon esterification, acidic or basic ester hydrolysis, and ester alcoholysis.

In previous papers of this series we have examined steric effects upon rates of esterification and acid-catalyzed hydrolysis of esters[1] and upon rates of base-catalyzed hydrolysis of esters.[2] It seemed of interest to extend these investigations to the question of steric effects upon the rates of hydrolysis of amides and related compounds. The objectives of this work are twofold: first, to determine whether the magnitude of the steric effect upon rates of acid-catalyzed hydrolysis of amides and related compounds is significantly different from the magnitude of the steric effect upon the rates of base-catalyzed hydrolysis; second, to compare the magnitude of the steric effect upon amide hydrolysis rates with the magnitude of the steric effect upon ester hydrolysis rates and upon esterification rates.

Twenty-seven sets of data taken from the literature for the rates of acid-catalyzed or base-catalyzed hydrolysis of amides, *N*-acylimidazoles, and hydroxamic acids were correlated with the modified Taft equation[1]

$$\log k_X = \psi\upsilon_X + h \quad (1)$$

by means of linear regression analysis. The data used in the correlations are set forth in Table I. The υ values required were generally taken from the first paper in this series;[1] some υ values are from our unpublished results. The results of the correlations are presented in Table II. The data for set 2 were correlated with the equation

$$\log k_X = \alpha\sigma_{IX} + \beta\sigma_{RX} + \psi\upsilon_X + h \quad (2)$$

as this set includes a number of nonalkyl substituents and involves base-catalyzed hydrolysis. Presumably the mechanism of amide hydrolysis is similar to that of ester hydrolysis. In that event, acid-catalyzed amide hydrolysis should be a