on silica gel with petroleum ether as eluent to afford 510 mg (41%) of **14** which was identical (IR, ^{1}H NMR, and GLC) with the sample obtained by the pyrolysis of **2a**.

Pyrolysis of 14. Pyrolysis of **14** under usual conditions at 380 °C gave a mixture of **14** and **15** in a ratio of 1:4.

Preparation of 19. A solution of 239 mg (2.34 mmol) of acetic anhydride in 1 mL of dichloromethane was added dropwise to a solution of 178 mg (1.17 mmol) of **16** and 319 mg (2.34 mmol) of 4-(dimethylamino)pyridine[18] in 3 mL of the same solvent, and the mixture was stirred at room temperature for 12 h. The solution was diluted with ether and washed with 5% HCl, 5% $NaHCO_3$, and water. After being dried ($MgSO_4$), the solvent was evaporated to give 224 mg (99%) of the acetate **19**: IR (neat) 3070, 1735, 1645, 1245, 1020, 950, 915, 885 cm^{-1}; MS, *m/e* (relative intensity) 194 (M^+, not detected), 153 (16), 134 (39), 111 (78), 93 (100); ^{1}H NMR (CCl_4) δ 1.19–1.65 (m, 2 H), 1.92 (s, 3 H), 2.00–2.44 (m, 6 H), 2.59 (d, J = 8 Hz, 2 H), 4.55 (br s, 2 H), 4.84–5.18 (m, 2 H), 5.44–5.92 (m, 1 H). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.04; H, 9.52.

Pyrolysis of 19. Pyrolysis of **19** under usual conditions at 380 °C gave a mixture of **13–15** quantitatively in a ratio of about 6:1:3.

Pyrolysis of 20. Pyrolysis of **20**[3c] was carried out at 380 °C to afford a mixture of unreacted **20** (conversion 16%) and the alcohol **16** which was identical (IR, ^{1}H NMR, and GLC) with the sample prepared from **7**.

Registry No. 2a, 73626-91-2; **2b**, 73626-92-3; **2c**, 73648-76-7; **3**, 82353-64-8; **4a**, 82353-65-9; **4b**, 82353-66-0; **5**, 82353-67-1; **7**, 29648-66-6; **8**, 84215-13-4; **9**, 84215-14-5; **10**, 84215-15-6; **11**, 84215-16-7; **11** disemicarbazone, 84215-17-8; **13**, 84215-18-9; **14**, 84215-19-0; **15**, 84237-45-6; **16**, 84215-20-3; **19**, 84215-21-4; **20**, 77871-16-0; 5-bromo-1-pentene, 1119-51-3; allyl bromide, 106-95-6; triphenyl(2-propenylidene)phosphorane, 15935-94-1.

(18) Holfe, G.; Steglich, W. *Synthesis* **1973**, 619.

Stereoselectivity in Organoborane Rearrangement: Relationship to the Mechanism of Hydroboration

Stanley E. Wood and Bruce Rickborn*

Department of Chemistry, University of California, Santa Barbara, California 93106

Received September 9, 1982

Hydroboration of 1,2-dimethylcyclohexene and subsequent rearrangement of the tertiary to the primary alkylborane occur with substantial (≥99:1) suprafacial selectivity. Similar though less pronounced behavior is found for the rearrangement of the tertiary to the secondary alkylborane. These results rule out, as the lowest energy pathway, dissociation (dehydroboration) to the free olefins followed by readdition with reversed regiochemistry, since hydroborations of these olefins exhibit little selectivity. The observed stereoselectivity provides strong support for an intramolecular process, most likely involving an intermediate π complex, which must give rearranged alkylborane faster than dissociated entities. Similar stereochemical results are obtained for the rearrangement in the presence or absence of THF, showing that solvent plays no critical role in the intramolecular migration. As a further mechanistic probe, B_2D_6 was employed, and the deuterium content was examined in various products. Evidence for an exchange process at the tertiary center β to boron was found. In general, the results are compatible with the proposed π-complex mechanism. An unusual feature is the incorporation of deuterium at the borane migration terminus, for which a free-radical mechanism is suggested. The rearrangement results are considered in the context of the mechanism of hydroboration. Although a π-complex intermediate has been suggested for hydroboration, it is concluded that such an intermediate (if it exists) must be fundamentally different from that involved in the rearrangement. This conclusion is surprising considering the close similarities of the two processes.

The mechanisms of hydroboration and of organoborane rearrangement are thought to be closely related, in that the latter can be viewed as a sequence of elimination (dehydroboration) followed by readdition reactions with the opposite regiochemistry.[1] The rearrangement process has recently been shown by Brown and co-workers[2] to be greatly speeded by bulky substituents on boron, with concurrent improvement in product selectivity for a series of reactions starting with 3-hexene. In earlier work Brown demonstrated that the thermal isomerization of boranes leads to migration to the least substituted carbon; in simple acyclic examples 90–99% primary alcohols result from subsequent alkaline peroxide oxidation.[3] Methylcyclohexenes show a similar but less pronounced preference for rearrangement to cyclohexylmethylborane, with 50–60% primary product being formed. The latter rearrangements were found to be relatively slow, presumably due to the required formation of the unfavorable tertiary alkylborane as an intermediate.[4] All these observations were readily explained by a dehydroboration–readdition mechanism in which free olefin intermediate is formed.[3] Further support of this gross mechanistic feature is found in the olefin exchange process whereby heating a mixture of high-boiling alkene and organoborane derived from a more volatile alkene allows the isolation of lower boiling olefin by distillation.[5] Similar conclusions have been drawn by Midland[6] in a recent study using *B*-alkyl 9-BBN derivatives.

The detailed mechanism of the very important hydroboration reaction continues to be a matter of interest and considerable speculation. The net stereochemistry of the reaction appears to be generalizable as involving either

(1) Brown, H. C. "Hydroboration"; W. A. Benjamin: New York, 1962.
(2) Brown, H. C.; Racherla, U. S.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 4313.
(3) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1966**, *88*, 1433.
(4) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1967**, *89*, 561.
(5) Brown, H. C.; Bhatt, M. V. *J. Am. Chem. Soc.* **1966**, *88*, 1440.
(6) Midland, M. M.; Petre, J. E.; Zderic, S. A. *J. Organomet. Chem.* **1979**, *182*(4), C53.

0022-3263/83/1948-0555$01.50/0

strong or exclusive preference for syn addition to both cyclic[7] and acyclic olefins.[8,9] This statement holds for reactions involving both BH_3·THF and dialkylboranes.[10] The limits of this syn selectivity are of interest from a mechanistic viewpoint, since anti addition product could represent leakage from a common intermediate in the dominant syn route; alternatively, anti product might result from an unrelated mechanistic path, or in the usual case where alkylboranes are oxidized prior to analysis, lack of total specificity in the basic peroxide step. Analyses in simple acyclic examples have been limited by the sensitivity of the NMR method, whereas cyclic olefin hydroboration processes are amenable to the more sensitive VPC technique. There appears to be no thoroughly documented example of anti hydroboration/oxidation, although 0.8% of *cis*-2-methylcyclohexanol (by VPC retention time) has been reported arising from the reaction of 1-methylcyclohexene and "traces" of the analogous product in the reaction of 1-methylcyclopentene.[11] The hydroboration/oxidation of 1,2-dimethylcyclohexene has been reported[11] to yield "pure" syn addition product, but the experimental evidence (boiling point, melting point) would likely not be sensitive to small amounts of isomer.

Several theoretical treatments of the prototype ethylene–borane reaction mechanism have led to the suggestion of a π complex or otherwise designated three-centered intermediate, with varying energy relationships to the ground state and transition state.[12-16] The most recent of these[16] favors an energy minimum π complex followed by a rate-determining four-centered transition state. A similar proposal was put forward some time ago on the basis of orbital symmetry arguments by Jones.[17] Pasto and co-workers[18] have also discussed orbital symmetry features for the proposed four-centered transition state in the context of isotope effects for the reaction. The significant kinetic hydrogen isotope effects found by Pasto support the view that transfer of this atom from boron to carbon is involved in the rate-determining step (conversely, π-complex formation, if any, would not be rate limiting). A π complex has been suggested by Seyferth[19] and invoked by Streitwieser[20] to rationalize the asymmetric induction observed in the reaction of 1-deuterio-1-butene.

For the alkylborane rearrangement reaction, only two studies address the question of a possible π-complex intermediate. Rossi et al.[21] suggested a dissociative process for the interconversion of $(t\text{-Bu})B(i\text{-Bu})_2$ to $(i\text{-Bu})_3B$, and an intramolecular (π-complex intermediate) mechanism for the rearrangement of $(i\text{-Pr})B(n\text{-Pr})_2$ to $(n\text{-Pr})_3B$, based on differences in $\Delta S^{\ddagger}$ for the two processes. While this argument is plausible, the use of activation parameters for these potentially complex reactions is subject to considerable uncertainty.[22] In 1971, we reported[23] the apparent high suprafacial selectivity observed in the rearrangement of the alkylborane generated from 1,2-dimethylcyclohexene. This reaction was examined in the context of another study (the diborane cleavage of cyclopropanes) and involved the use of a mixture of 1,2-dimethylcyclohexene (77%) and 1,6-dimethylcyclohexene (23%). Certain (reasonable) assumptions were needed to discuss the outcome in terms of alkylborane rearrangement stereochemistry.[24]

Table I. Hydroboration/Oxidation of 1

run	1[a]	B_2H_6[a]	T, °C	time	% 2	% 3
1	4	2.1 (3.4)	25	0.5 h	1.6	98.4
2	4	2.0 (0.5)	0	0.55 h	1	99
3	2	2.2[b]	25	20 days	1.5	98.5
4	2	2.1[c]	25	18 h	4	96
5	2	0.9 (0.9)[d]	25	0.9 h	1.5	98.5

[a] Millimoles of 1 and B_2H_6 are tabulated. In runs 1, 2, and 5 THF was present, and the concentration of BH_3·THF is shown (M). [b] The initial pressure was ca. 1 atm. [c] The initial pressure was ca. 10 atm. This reaction was carried out in a 3-mL heavy-walled glass tube. On opening, the contents were pyrophoric, suggesting the formation of higher boranes. [d] $NaBH_4$, 0.4 g, was present; the volume of THF was 2.0 mL.

The purpose of the present study was to examine the stereochemistry of rearrangement using highly purified material to resolve this ambiguity. Recognizing the overall common features of alkylborane rearrangement and the hydroboration of an olefin, it is of particular interest to determine whether mechanistic features of the former could be applied to the latter process, i.e., could evidence for a π complex in the rearrangement be used to demonstrate the existence of the intermediate in hydroboration. Put another way, the issue is whether one can apply microscopic reversibility arguments to link the detailed mechanisms of the two reactions.[18] One might expect this to be appropriate, since free olefin is clearly implicated in rearrangement reactions that have attained overall equilibrium. However, the question remains whether a distinct lower energy pathway might be available for rearrangement, i.e., an energy surface that does not appreciably intercept the associative–dissociative path followed by hydroboration–dehydroboration of the like olefin.

In addition to examining stereochemical features with protonated materials, we have also used B_2D_6 to provide further insight into the details of the alkylborane rearrangement reaction.

Results and Discussion

Highly purified 1,2-dimethylcyclohexene (1) was obtained by dehydration of 1,2-dimethylcyclohexanol,[25] distillation, and VPC preparative collection. The material used exhibited no vinyl proton absorption in NMR and was judged to be ≥99.5% pure by VPC.

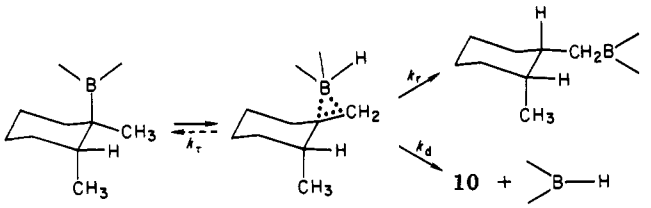
(7) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1959**, *81*, 247.
(8) Kabalka, G. W.; Bowman, N. S. *J. Org. Chem.* **1973**, *38*, 1607.
(9) Bergbreiter, D. E.; Rainville, D. P. *J. Org. Chem.* **1976**, *41*, 3031.
(10) Kabalka, G. W.; Newton, R. J., Jr.; Jacobus, J. *J. Org. Chem.* **1978**, *43*, 1567.
(11) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 2544.
(12) Dasgupta, S.; Datta, M. K.; Datta, R. *Tetrahedron Lett.* **1978**, 1309.
(13) Dewar, M. J. S.; McKee, M. L. *Inorg. Chem.* **1978**, *17*, 1075.
(14) Clark, T.; Schleyer, P. v. R. *J. Organomet. Chem.* **1978**, *156*, 191.
(15) (a) Sundberg, K. R.; Graham, G. D.; Lipscomb, W. N. *J. Am. Chem. Soc.* **1979**, *101*, 2863. (b) Graham, G. D.; Freilich, S. C.; Lipscomb, W. N. *Ibid.* **1981**, *103*, 2546.
(16) Nagase, S.; Ray, N. K.; Morokuma, K. *J. Am. Chem. Soc.* **1980**, *102*, 4536.
(17) Jones, P. R. *J. Org. Chem.* **1972**, *37*, 1886.
(18) Pasto, D. J.; Lepeska, B.; Cheng, T. C. *J. Am. Chem. Soc.* **1972**, *94*, 6083.
(19) Seyferth, D. *Prog. Org. Chem.* **1962**, *3*, 210.
(20) Streitwieser, A., Jr.; Verbit, L.; Bittman, K. *J. Org. Chem.* **1967**, *32*, 1530.
(21) Rossi, F. M.; McCusker, P. A.; Hennion, G. F. *J. Org. Chem.* **1967**, *32*, 450. We thank a referee for calling this paper to our attention.
(22) Perhaps the most striking feature of this study[21] is the close similarity of rate constants for the two processes mentioned. These were determined over the range of 120–150 °C, using an open flask under N_2. Experimental uncertainties involve the possible differential loss of olefin (propylene or isobutylene) under these conditions and the catalytic effect of traces of R_2BH at the temperature used. Rather small changes in rate constants can of course significantly alter derived activation entropies.
(23) Rickborn, B.; Wood, S. E. *J. Am. Chem. Soc.* **1971**, *93*, 3940.
(24) The mixture used may also have contained up to 4% of 2-methyl-1-methylenecyclohexane, which can account for the somewhat lower selectivity reported earlier[23] when compared to the results of the present study.
(25) Hammond, G. S.; Nevitt, T. D. *J. Am. Chem. Soc.* **1954**, *76*, 4121.

Table II. Hydroboration/Rearrangement/Oxidation of 1

run	B_2H_6[a]	T, °C	time[b]	% 2[c]	% 3	% 4	% 5[d]	% 6[d]	% 7[d]	% 8	% 9	8/9
1	2.2	20	20 days	1	99							
2	1.0	100	0.6 h	0.5	74		0.3	6	1	0.3	18	1.5/98.5
3	1.0	100	2 h	0.5	34		1.4	16	2	0.8	45.3	1.5/98.5
4	1.1	100	13 days	0.5	10	15	6	23	7	32	5	86.5/13.5
5	1.6	100	2 h	0.5	34		4.5	17	3	0.4	41	1/99
6	0.1[e]	100	0.5 h	0.5	45	17	13	5	2	0.5	17	3/97
7	1.0[f]	100	0.6 h	0.4	36		2.9	14.5	1.7	0.5	44	1/99

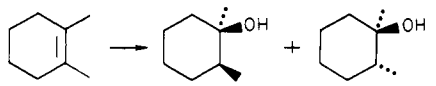
[a] All reactions involved 2.0 mmol of 1; millimoles of B_2H_6 are shown. [b] The mixtures were kept at ambient temperature for a minimum of 12 h before heating, except for run 7; this is sufficient for extensive or complete hydroboration. [c] Alcohol percentages were determined by peak area measurement from VPC traces. A 22-ft, 0.25-in. 20% Carbowax 20M column was used. [d] While the tertiary (2, 3) and primary (8, 9) alcohols are widely separated from the secondary isomers of 3,4-dimethylcyclohexanol, and the values shown are presumed to include, especially in the runs involving more extensive rearrangement, some amounts of the latter. With the 3,4-methyl groups trans related, one isomer falls under peak 5 and the other under peak 6. The isomers having the 3,4-methyl groups cis related are especially difficult to separate, with both falling under peak 7 on this column. [e] In addition to the diborane, 0.8 mmol of B_4H_{10} was added. [f] THF, 2.0 mL, was used in this run.

Scheme I



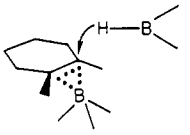
11

(a) Stereochemistry of the Hydroboration/Oxidation of 1. The hydroboration/oxidation of 1 was examined in detail, since the outcome of the first step is critical to discussion of the subsequent rearrangement. The results are shown in Table I.



1 2 3

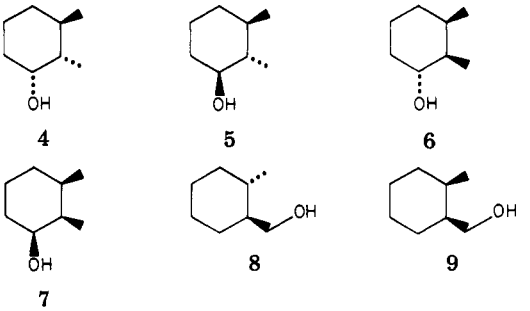
In all cases, with and without THF being present, some anti addition product 2 is formed, identified by VPC retention time. Since the same oxidative workup was used in all instances, we believe the differences in outcome are a result of the hydroboration step, although the changes are too small to be definitive. One possible route to 2 is intermolecular anti reduction of a π complex, viz.,



Run 4 tests this idea by increasing the initial diborane concentration (pressure), and indeed this does lead to an increase in the relative amount of 2. This result, however, is complicated by the probable formation of higher boranes under these high-pressure conditions. Reasoning that a more active hydride donor might enhance anti attack of an intermediate, a hydroboration was carried out in the presence of $NaBH_4$ (run 5). The result failed to lend support to this notion, perhaps in part due to the limited solubility of $NaBH_4$ in THF (ca. 0.1 g/100 g).

While the origin of anti addition product remains uncertain, we assume in further discussion that ca. 1% of the borane analogue of 2 is formed in the initial hydroboration of 1.

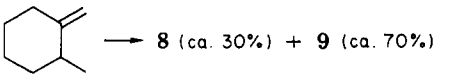
(b) Stereochemistry of the Rearrangement. The hydroboration/rearrangement/oxidation sequence of 1 was carried out in sealed tubes, using both BH_3·THF and neat B_2H_6, with subsequent alkaline peroxide oxidation. The alcohol mixtures were analyzed by VPC, giving the results shown in Table II, in which the products are displayed in order of retention time for structures 2–9.



4 5 6

7 8 9

The distinction between the intramolecular suprafacial rearrangement pathway and a mechanism involving dissociation to free olefin of course depends on the selectivity of product formation in the hydroboration of the olefin. We earlier established[23] that the reaction of 2-methyl-1-methylenecyclohexane (10), using either B_2H_6 or BH_3·THF, gives both 8 and 9, with the latter constituting a



10

maximum of 73% of the mixture. More recently Senda and co-workers[26] reported that BH_3·THF at 0 °C gives 8/9 in a ratio of 17/83. We have repeated the reaction of 10 using B_2D_6 in THF (BD_3·THF) at ambient temperature and again find a ratio of 29/71. The differences between Senda's result and ours may be associated with somewhat higher selectivity at lower temperature, although we have not explored this question. We also found[23] that the bulky reagent dicyclohexylborane exhibits somewhat lower selectivity in reaction with 10 (8/9 = 37/63). In addition, the use of thexylborane[27] gave comparable results (8/9 = 28/72, THF, 2 h, 25 °C) to those obtained with the other reagents.

Thus we conclude that the hydroboration of free olefin 10 by any borane species reasonably anticipated under our rearrangement conditions will exhibit no greater than this same limited selectivity.

The results in Table II show clearly that the rearrangement of the initially formed tertiary borane to the

(26) Senda, Y.; Kamiyama, S.; Imaizumi, S. *Tetrahedron* **1977**, *33*, 2933.
(27) Zweifel, G.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2066.

Table III. Hydroboration/Rearrangement/Oxidation of 12[a]

run	B_2H_6[b]	T, °C	t, h	% 2	% 3	% 4	% 5[d]	% 6[d]	% 7	% 8	% 9
1	2.2	20	16	1	3	1.5	61	33	0.5		
2	1.05[c]	20	0.3	1	2	1.5	47	49	0.5		
3	1.0	100	2	0.5	1.5	1	69	24	1	1	2
4	1.6	100	0.5	0.5	2.5	0.5	75	20		0.5	1
5	1.0[c]	100	2	<0.5	0.5	0.5	76	17	3	0.5	2

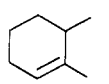
[a] The material used (2.0 mmol in each run) contained <1% of 1 by VPC. [b] Millimoles of diborane. [c] Runs 2 and 5 were done in 2.0 mL of THF. [d] See footnote d of Table II.

primary derivative occurs with substantial syn selectivity; a minimum factor of 99:1 favoring suprafacial migration is established directly. Taking into account the ca. 1% of **2** (again, assuming this arises in the hydroboration step), an even higher selectivity seems likely. Note that this conclusion holds for both the diborane and BH_3·THF reactions. The role of ethereal solvent in the rearrangement process is not obvious; although the BH_3·THF reaction appears to be somewhat more rapid (compare runs 2, 3, and 7) than those involving B_2H_6 with neat olefin, the large kinetic enhancement caused by ethereal solvent in the hydroboration reaction[1] is not experienced. Run 4 establishes the expected result that prolonged heating leads to equilibration, presumably involving free olefin, in which **8** is favored over **9** by at least 86/14. Finally, we note that the use of a mixture of B_2H_6 and B_4H_{10} (run 6) causes more rapid overall rearrangement, but the suprafacial selectivity in migration to the primary center is still evident.

This stereoselectivity is most readily accommodated by an intramolecular migration involving a π complex (**11**; Scheme I).

In this mechanism (Scheme I) the tertiary alkylborane is converted through a four-centered transition state to **11**; on the basis of analogy to the outcome of hydroboration of **10**, which leads essentially only to primary product under nonrearranging conditions, the slowest process would presumably be return to the tertiary alkylborane (k_t). Most important to establishing the viability of **11** as an intermediate is the ratio of rearrangement (k_r) to dissociation (k_d). On the basis of the data in Table II and the 70/30 ratio of primary alcohol isomers found in the hydroboration of **10**, we conclude that the minimum k_r/k_d ratio is ca. 30, and it may be significantly larger, depending on how one accounts for the anti addition product formed on hydroboration of olefin **1**. The upper limit on this ratio is difficult to establish, but cannot be too large because of the experimental evidence that dissociation does occur on prolonged treatment under these conditions to attain eventually overall equilibrium.

The stereochemistry of tertiary to secondary alkylborane rearrangement is more difficult to ascertain in this system, because of the possible formation of 3,4-dimethylcyclohexanols (secondary–secondary rearrangement; see footnote *d* of Table II). To examine this question, a sample of 1,6-dimethylcyclohexene (**12**) was collected by preparative VPC, and reactions with this substance are shown in Table III. The ambient temperature reactions (runs 1 and 2) show some differences in olefin face selectivity between B_2H_6 and BH_3·THF, while the formation of small amounts of **4** and **7** again imply the existence of a minor anti addition pathway. Under rearrangement conditions (runs 3–5) the most noticeable features are the loss of the peak corresponding to **6**, the increase in **5**, and the negligible buildup of **7**. These observations are clouded by the possible formation of 3,4-dimethylcyclohexanols, but to the extent that they represent the true increase in compound **5** at the expense of **6**, they suggest that the dissociative pathway of the borane precursor of **6** to olefin **12** is of lower energy than intramolecular rearrangement processes. The small amounts of peak **7** support this view and also imply that dissociation to **12** is more facile than rearrangement paths to *cis*-3,4-dimethylcyclohexanols.

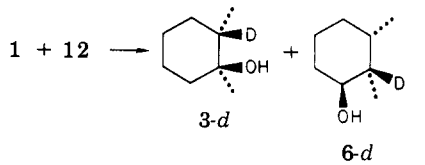


12

Returning to Table II, one would predict that intramolecular rearrangement of the dominant tertiary alkylborane corresponding to **3** would lead to **6**, while a dissociative process forming **12** would result in nearly equal (BH_3·THF) amounts of **5** and **6**, or a predominance of **5** with B_2H_6. Since **6** predominates in all rearrangements with these reagents, the data again support a suprafacial intramolecular process. The lower observed selectivity for tertiary–secondary than for tertiary–primary rearrangement may be caused by the relatively facile conversion of **6**–borane to **5**–borane (via **12**), as shown by the data in Table III.

(c) Reactions with B_2D_6. In the hope of gaining further insight into the details of the rearrangement mechanism, some reactions were carried out with B_2D_6. This material was prepared by treatment of $NaBD_4$ with BF_3·Et_2O. Determination of the isotopic composition of the B_2D_6 by MS was complicated by the absence of a parent molecular ion, requiring high-resolution analysis of the M – H and M – D ions (see Experimental Section). This treatment assumes no equilibrium isotope effect on bridging vs. terminal H/D, and no isotope effect on the fragmentation to produce the species examined. The value obtained (93.5% D, 6.5% H) would represent an upper limit on deuterium content if loss of hydrogen is preferred in the fragmentation.

This material was used in THF at room temperature with a mixture of olefins **1** and **12**, and after oxidation the products **3**-*d* and **6**-*d* were collected by VPC. The deuterium contents were assessed by 100-MHz proton NMR, focusing on the $CDCH_3$ absorption; in each case the downfield leg of the $CHCH_3$ doublet appeared as a distinct peak, while the upfield leg partially overlapped the $CDCH_3$ triplet. The percentage of $CHCH_3$ was estimated by doubling the area of the downfield leg and comparing this value to the total integral. Since the tertiary proton causing the coupling lies downfield of the doublet in question, this procedure will overestimate the amount of H at the tertiary center. The upper limits for H obtained in this way were 12% for both **3-d** and **6-d**.



3-*d* 6-*d*

Taking the 6.5% hydrogen content of the B_2D_6 as a minimum, and the 12% hydrogen content for the products as a maximum, allows one to calculate an H/D isotope

Table IV. B_2D_6 Rearrangement Reactions[a]

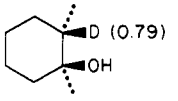
run	olefin[b]	B_2D_6[b]	% 2	% 3	% 4	% 5	% 6	% 7	% 8	% 9	8/9
A	1 (2.4)	1.2	0.5	27	0.5	4	15	2.7	3	47	6/94
B	mix (2.0)[c]	2.45	0.5	28	0.5	21	21	2.5	0.5	26	2/98
C	1 (2.9)	2.0	0.5	40		0.5	16	<0.5	<0.5	42	1/99
D	mix (2.0)[c]	*d*	0.5	21	1	23	16	2.5	0.5	35	1.5/98.5

[a] All reactions were run at 100 °C for 2 h. [b] Millimoles of total olefin and of B_2D_6 are shown. [c] The mixture consisted of 75% 1, 21% 12, and 4% 10. [d] Initially 1.9 mmol of B_2D_6 was added. After the mixture stood for 24 h at room temperature, the removable B_2D_6 was pumped off (0.55 mmol), and 1.1 mmol of B_2H_6 was added. The mixture was then subjected to the rearrangement conditions.

effect for the hydroboration of 1 and 12 of ≤1.8. A modest isotope effect is in keeping with those reported by Pasto and co-workers.[18]

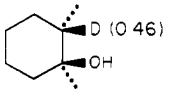
Addition/rearrangement reactions using the same B_2D_6 were carried out in the absence of solvent, using both purified 1 and an olefin mixture of known composition. The product distributions obtained by VPC analysis are given in Table IV. Several interesting features emerge from these data. Importantly, but not unexpectedly, the gross aspects of the reaction (percent loss of starting material and distribution of various products) are not significantly different in comparing B_2H_6 and B_2D_6 reactions run under similar conditions. Thus in the first entry of Table IV, we note that ca. 75% of the starting tertiary alkylborane has been converted to products, with rearrangement to primary alkylborane favored over rearrangement to secondary alkylborane by approximately a factor of 2. In the time (2 h) used in the Table IV runs, the system is far from attaining overall equilibrium, and this is again reflected in the stereoselectivity exhibited by the ratios of 8/9. To reiterate, the amount of isomer 8 formed establishes an upper limit (i.e., 70/30 × 8) for the amount of 9 that could have been generated through formation of olefin 10 as an intermediate.

Proton NMR analysis of 3-A (alcohol 3, run A, Table IV) was accomplished as described above and indicated that this material contained 79% deuterium at the tertiary center, as shown. Significantly, proton-decoupled ^2H

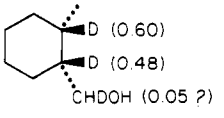


3-A

NMR of 3-A exhibited only one peak (1.63 ppm), and specifically, there is no measurable (estimated ≤1%) deuterium incorporation in the methyl groups of this product. The loss of some tertiary deuterium as compared to the 88% found in the room temperature deuterioboration of 1 suggested the existence of an exchange mechanism. In run D of Table IV this question was explored by carrying out the deuterioboration of mixed olefin at room temperature, pumping off the excess volatile B_2D_6, adding B_2H_6 such that the ratio of total BH/BD was approximately 1.0, and then heating to effect rearrangement. The tertiary alcohol 3-D obtained in this case had lost

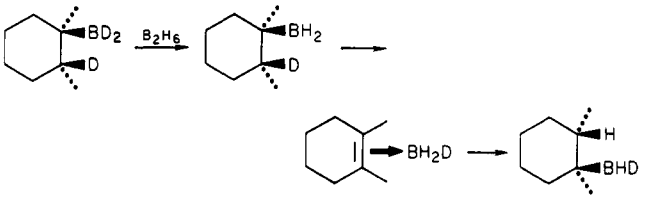


3-D



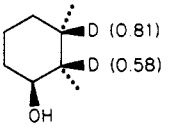
9-D

significantly more deuterium, and the primary alcohol 9-D similarly contained appreciably less deuterium at both tertiary centers than in runs using B_2D_6 alone, as discussed below. The two most likely mechanisms for this exchange involve either (a) elimination to olefin, scrambling of the isotopically labeled diboranes, and readdition, or (b) H–D exchange between B_2H_6 and "RBD_2", reversible conversion of the tertiary alkylborane to the symmetrical π complex of olefin 1, followed by collapse to the two equivalent tertiary alkylboranes. The latter process is illustrated:



Note that the exchange process must operate with reasonable facility to account for the observed diminution of deuterium at an overall rate that is competitive with rearrangement to primary alkylborane. Assuming complete scrambling of hydrogen and deuterium on all borane species and statistical distribution in the products would lead to ca. 1/1 H/D ratio at the positions in question; within experimental error this is observed in 3-D (46%) and at the tertiary position closest to the migration terminus of 9-D (48%). The 60% deuterium at the other tertiary position in 9-D suggests that rearrangement to primary alkylborane is somewhat faster than the tertiary center exchange process.

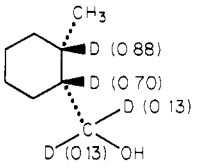
Returning to run A of Table IV, the secondary alcohol 6-A was also collected for analysis. By proton NMR the 3-position was estimated to be 81% deuterated, with 58% deuterium at the 2-position, as shown. The ^2H NMR of



6-A

this material gave a good cross check on these relative values (81% assumed, 60% by integration at C-2). The ^2H NMR also indicated no measurable incorporation of deuterium at either methyl group. Another feature of interest was a third peak at 3.72 ppm, constituting ≤2.5% deuterium, which could be interpreted as incorporation at the carbinol (C-1) center. If this is correct, it should be noted that there is no known mechanistic explanation for substitution at this site with this geometry; no syn addition, syn elimination sequence could accomplish this without incorporating deuterium at other ring carbons, and the system is far from the overall equilibrium that such a multistep process would imply.

Primary alcohol 9-B (run B, Table IV) proved especially informative. The proton NMR of this material indicated 88% deuterium at C-3, 66% at C-2, and 25% at the carbinol carbon. The ^2H NMR, assuming 88% at C-3, gave by integration 73% at C-2, and very interestingly, two equal height incompletely resolved peaks at 3.54 and 3.58



9-B

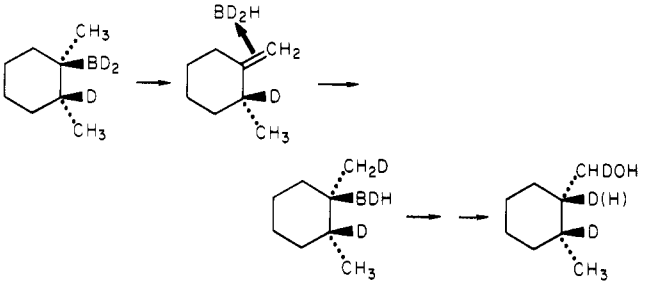
ppm, comprising a total of 26% deuterium. We assign these as the two diastereotopic carbinol deuterons, as shown. No other absorptions were discernable, and specifically the remaining methyl group is clearly devoid of deuterium.[28]

(d) Mechanism. The high degree of suprafacial selectivity in alkylborane rearrangement, notably demonstrated in the tertiary to primary process but also evident in the tertiary to secondary conversion, is most simply explained by an intermediate involving significant bonding interaction between the incipient borane and olefin. A π complex provides a rational model for this intermediate.

Most features of the B_2D_6 results are compatible with this view of the rearrangement mechanism. In particular, the observed increase in the H/D ratio (over that available in the total BH/BD pool) at the carbon origin of the rearrangement is evidenced in most of the cases examined. These results are explicable in terms of a π complex involving "BD_2H" that more or less randomly deposits deuterium or hydrogen at the migration origin somewhat faster than it exchanges with the external pool. Such an exchange process is operating, but the evidence (see **9-D**) supports the view that exchange coupled with tertiary–tertiary rearrangement occurs somewhat less rapidly than rearrangement to the primary alkylborane.

The reactions described here are potentially very complex and involve many unknowns. These include the nature of the species undergoing rearrangement (monoalkylborane, monomer or dimer, alkyldiborane, and dialkylborane are the most likely candidates), and even the composition of the reactants (diborane itself decomposes at 100 °C to form hydrogen and various higher boranes). These complicating factors cannot be addressed in any obvious manner. It should be recognized that the terms we use to discuss mechanism may involve significant oversimplification.

The most surprising result from the B_2D_6 work is the incorporation of deuterium at the migration terminus, the carbinol center. This is clearly demonstrated in the primary alcohol **9-B** and may be occuring to a small extent in the secondary alcohol **6-A**. At first glance, it might seem that incorporation of deuterium at the carbinol position of **9** could be accommodated by formation of a tertiary–primary π complex that partially reverts to tertiary alkylborane, as illustrated:



This mechanism is, however, faulty on several grounds:

(1) To the extent that deuterium is incorporated at the carbinol center of secondary alcohol **6**, no such syn rearrangement or syn elimination–readdition process can accommodate the stereochemical features.

(2) Significant reversion of the π complex to tertiary alkylborane is not in line with the specificity for primary borane formation in the hydroboration of **10** and similar olefins. While a very small amount of tertiary alkylborane intermediate is presumably formed from any of several precursors in overall equilibration, we observe substantial rearrangement and deuterium incorporation at the carbinol site of **9**, when the system is far from overall equilibrium. This comment would apply to either a π-complex process or elimination–readdition.

(3) Evidence has been presented that shows that the tertiary alkylborane can undergo exchange of D/H at the adjacent tertiary center. Whether this occurs via a π complex or elimination–readdition, we infer interconversion of the two equivalent tertiary alkylboranes. The mechanism shown above would then require deuterium incorporation not only at the carbinol center but also in the remaining methyl group. No indication of such incorporation was found in any of the products examined, even with the especially sensitive ^2H NMR technique.

The mechanism of incorporation of deuterium at the carbinol site remains unclear, but a likely possibility is that it occurs after formation of the primary borane. A free-radical process could account for the results, and some support for this view is found in Brown's observation that bromine reacts rapidly with alkylboranes by an α-hydrogen abstraction mechanism[29]. The fact that tri-*sec*-butylborane reacts with bromine more rapidly than tri-*n*-butylborane is in keeping with an α-radical process. We find greater incorporation of deuterium at the primary site (in **9-B**) than in the secondary borane leading to **6-A**, in reactions run under similar conditions. While this is contrary to the order of radical stability, steric requirements of the unknown radical initiator and the secondary alkylborane precursor of **6** could explain the differences between our observations and those involving bromine.

With regard to the overall mechanism of the rearrangement process, the stereochemical and deuterium incorporation results generally are in accord with a pathway involving a π-complex intermediate. It is tempting to extend the principle of microscopic reversibility to draw conclusions about the mechanism of hydroboration, but there are problems in doing so. The two reactions differ in usual conditions (temperature, possibly the structure of reactants), and in the outcome of systematic changes that have been examined. For example, the very large rate enhancement of hydroboration caused by ethereal solvents is well-documented, while we find that the presence or absence of THF in the rearrangement has only a small effect on rate, and no detectable effect on stereochemistry.

(28) The chemical shifts of the tertiary deuterons in **6** and **9** deserve comment, since in both compounds the C-2 D is found at higher field than the C-3 D (in **6**, 1.76 and 2.17 and in **9**, 1.78 and 2.08 ppm, respectively.) This is contrary to the order expected on the basis of proximity to the hydroxyl group. However, in addition to the generally good agreement between ^1H NMR and ^2H NMR integrations, the assignment has been verified for **9** by carrying out a room temperature reaction of olefin **10** with BD_3-THF; the **9** isolated by VPC exhibited a single peak in ^2H NMR, at 1.78 ppm (D at C-2). A reasonable explanation for the observed shifts may be the conformational preference of these materials. If the OH of **6** and the CH_2OH of **9** prefer the equatorial position, perhaps due to intermolecular hydrogen bonding in CCl_4, the C-2 D would be axial and the C-3 D equatorial in both compounds. The well-established greater shielding experienced by axial protons (or D) would accommodate both the direction and magnitude of the shifts observed.

(29) Lane, C. F.; Brown, H. C. *J. Am. Chem. Soc.* **1970**, *92*, 7212.

Further, the rearrangement process is known to be speeded by excess diborane (or other BH species), while no such "catalytic" effect has been reported for hydroboration, which seems to be well-behaved kinetically. Also, the kinetic H/D isotope effect in hydroboration (admittedly with different reagents and conditions) provides strong evidence for rate-determining hydrogen transfer in this reaction.[18,30]

Our stereochemical results require that rearrangement of the π complex occurs more rapidly than dissociation to olefin and some form of borane. Note again that this holds regardless of whether or not THF is present. If it is assumed that the same π complex is involved as an intermediate in rearrangement and in hydroboration, our results would dictate that π-complex formation be rate-determining in the latter, contrary to the kinetic isotope effects reported by Pasto. The different species involved in our work and studies where kinetic isotope effects have been determined limit generalization, i.e., it is conceivable (though considered unlikely) that π-complex formation is rate limiting in the hydroboration of olefin **10**. Assuming this is not the case, one must conclude that the same π complex cannot be involved in the hydroboration of **10** and the stereospecific rearrangement of the related tertiary to primary alkylboranes (otherwise the complex would preferentially dissociate and subsequently lead to the nonselective mixture of **8** and **9** characteristic of the hydroboration of **10**). This is a surprising conclusion given the overall similarities of the two processes. Nonetheless, we conclude that either a different intermediate, or none at all, is involved in hydroboration, while a distinct lower energy intramolecular pathway is available for the rearrangement. Eventual complete equilibration of an alkylborane must involve leakage over a higher barrier dissociative pathway, the reverse of hydroboration.

Experimental Section

The olefin preparations and VPC analyses on these and alcohol products were done as described previously.[23] Proton NMR spectra were obtained on Varian T-60 and XL-100 instruments. Noise proton decoupled ^2H NMR spectra were run on a Nicolet NT-300 instrument; deuterium chemical shifts were estimated by setting the resonance from a sample of $CDCl_3$ to 7.24 ppm and with no adjustments of any instrumental parameters, changing to the sample of interest. High-resolution MS was done on a VG Micromass ZAB-2F instrument.

Structural Assignments of 4–7. The general procedure of Ulery and Richards[31] was employed for the identification of the *cis*-dimethyl and *trans*-dimethyl alcohols as follows. A commercial sample of the four diastereomeric alcohols was oxidized with Jones reagent to give the isomeric ketones. Equilibration of these with $NaOCH_3$ in methanol gave a mixture consisting of the major (trans) isomer and the minor (cis) 2,3-dimethylcyclohexanones. Sodium borohydride reduction of the major ketone gave **4** and **5**, while the minor isomer gave **6** and **7**. Hydroboration/oxidation of pure olefin **12** gave **5** and **6** (see Table III), thus completing the stereochemical assignments of all four isomeric alcohols. The relative retention times on our VPC column coincided with those reported earlier.[31]

Olefin Purification. The distilled olefin mixture from the phosphoric acid dehydration of 1,2-dimethylcyclohexanol was separated by manual preparative VPC, using repeated injections on a 25-ft, 0.25-in. 15% DBTCP column. The 1,2-dimethylcyclohexene (**1**) obtained in this manner was ≥99.5% pure by VPC analysis; its proton NMR spectrum had no absorption in the vinyl proton region and exhibited a methyl singlet at 1.58 ppm. The 1,6-dimethylcyclohexene (**12**) obtained in the first pass was resubjected to preparative VPC, giving material judged to be ≥99% pure by analytical VPC. Its proton NMR spectrum had a vinyl proton multiplet at 5.3 ppm. Further evidence of purity is found in the data of Table III. The preparation of **10** by Wittig reaction of 2-methylcyclohexanone was done as described earlier.[23]

B_2D_6. Boron trifluoride etherate was distilled [bp 67 °C (40 torr)], using a 30-cm column packed with Raschig rings. The first distillate (ca. 10%) was discarded and a center cut collected directly in the dropping funnel attached to the reaction vessel. Lithium tetradeuteridoborate (Ventron, 99% isotopic purity) was handled and weighed in a dry N_2 atmosphere. The preparation and purification of B_2D_6 was accomplished as described earlier for diborane.[21] The product was stored in a 1-L bulb equipped with a condensing tube and a Teflon plug glass valve. The yield of purified material was approximately 50%.

Isotopic analysis of the B_2D_6 by MS is complicated by the absence of a parent molecular ion, making necessary the assumption of no isotope effect in formation of the M − D and M − H ions measured. The high-resolution peaks at $m/e \simeq 30$ consist of $^{10}B_2D_5$, $^{11}B^{10}BD_4H$, and $^{11}B_2D_4$, while those at $m/e \simeq 31$ are $^{11}B^{10}BD_5$ and $^{11}B_2D_4H$. With use of the natural abundances of ^{10}B (18.98%) and ^{11}B (81.02%), the probabilities of $^{10}B_2$, $^{10}B^{11}B$, and $^{11}B_2$ species are calculated to be, respectively, 0.0360, 0.3075, and 0.6564. Multiplying the measured intensities by the appropriate probability factor gives the ratio of ions B_2D_5/B_2D_4H = 0.738/0.262. Since the B_2D_5 ion can arise from either B_2D_6 or B_2D_5H, while B_2D_4H is derived principally from B_2D_5H ($B_2D_4H_2$ is a low probability species at low H/D ratios), the relative amounts of B_2D_6 and B_2D_5H are, respectively, **6**/**7**(0.738) = 0.633, and 0.262 + 1/7(0.738) = 0.367. The H/D ratio is then calculated as 0.367[**6**(0.633) + **5**(0.367)] = 0.065/0.935.

Rearrangement Reactions. The olefins, THF, and boranes were kept in appropriate bulbs attached to a high vacuum gas handling system. Measured amounts were vacuum transferred into tubes of ca. 20-mL volume, which were sealed and allowed to stand at room temperature to effect hydroboration, for an appropriate period as established by control experiments. The tubes were transferred to an oil bath kept in a hood and heated as indicated in the tables. For quenching, the tubes were removed from the oil bath and allowed to cool to room temperature before opening. Ethanol was carefully added, and the contents transferred to an Erlenmeyer flask with rinsing. A few milliliters of 3 N NaOH was added, followed by dropwise addition of 30% H_2O_2. The mixtures were extracted repeatedly with CH_2Cl_2 after the addition of 25 mL of water. The combined organic phase was dried and evaporated on a steam bath through a Vigreux column. The resulting residues were subjected to VPC analysis and in some cases preparative collection of individual products. Yields were good in all cases checked.

For run D, Table IV, the procedure was altered as follows. The reaction tube was attached with a Teflon plug glass valve between it and the vacuum manifold. Two millimoles of olefin was transferred to the tube, followed by 1.9 mmol of B_2D_6. The valve was closed and the mixture kept at room temperature for 24 h. After the mixture was cooled in an ice bath, excess B_2D_6 (0.55 mmol) was recovered by vacuum transferring out of the tube and subjected to MS analysis. It contained 6.3% H, within probable experimental error identical to the starting B_2D_6. Again by standard gas handling techniques, 1.1 mmol of B_2H_6 was added to the reaction tube, which was then sealed and treated as described in Table IV.

Hydroboration/Rearrangement of 10. As a control experiment on the reversibility of the tertiary to primary alkylborane rearrangement, a sealed tube containing 4.0 mmol of olefin **10** and 0.7 mmol of B_2H_6 was prepared and allowed to stand at room temperature for 14 h. It was then subjected to rearrangement conditions, 100 °C, for 11 h, and worked up in the usual way. No detectable levels (≤0.5%) of tertiary alcohols **2** or **3** were observed; secondary alcohol **4** was also absent. The mixture consisted of the following: **5**, 2%; **6**, trace; **7**, 1%; **8**, 56%; and **9**, 40%. The borane mixture before rearrangement consisted of ca. 30% **8**, 70% **9** precursors, as shown in several room temperature hydroboration controls. The interconversion of **9** to **8**, presumably by elimination to **10** and readdition from the opposite face of the olefin, thus occurs much more rapidly than conversion to tertiary alkylborane.

Acknowledgment. We are grateful to the U.S. Naval

(30) Pasto, D. J.; Kang, S. Z. *J. Am. Chem. Soc.* **1968**, *90*, 3797.
(31) Ulery, H.; Richards, J. H. *J. Am. Chem. Soc.* **1964**, *86*, 3113.

Weapons Center, China Lake, CA, for providing a special leave to S.E.W. We thank Professor J. T. Gerig and Allan Kershaw for indispensible help in obtaining the ^2H NMR spectra, Dr. Robert Miller (IBM Corp., San Jose, CA), and Professors D. H. Aue and W. Palke for helpful discussions. The instrument used to record the ^2H NMR spectra was funded in part by the NSF.

Registry No. 1, 1674-10-8; 3, 19879-12-0; 6-d_2, 84195-31-3; 9-d_2, 84195-32-4; 10, 2808-75-5; 12, 1759-64-4.

Electrochemical Study of the Oxidation of α-Methyldopamine, α-Methylnoradrenaline, and Dopamine

Thomas E. Young* and Brion W. Babbitt

Department of Chemistry, Lehigh University, Bethlehem, Pennsylvania 18015

Received June 2, 1982

The anodic melanization reactions of α-methyldopamine (**1b**), α-methylnoradrenaline (**1c**), and dopamine (**1d**) were studied at the carbon-paste electrode in 1 M $HClO_4$ and in McIlvaine buffers of varying pH at 15, 20, 25, and 30 °C. Cyclic voltammetry showed that each catecholamine underwent an ECC mechanistic sequence involving an initial two-electron oxidation to a quinone (**2**), which after deprotonation to the free amines (**3**) cyclized rapidly to the 5,6-dihydroxyindolines (**4**). A further two-electron redox transfer gave the aminochromes (**5**), which in two series (**1b** and **1d**) rearranged to electrochemically detectable 5,6-dihydroxyindoles (**6b**, **6d**). In all cases melanin-like pigments were ultimately formed. Chronoamperometry of **1b**, **1c**, and **1d** afforded first-order rate constants for the cyclizations of the *o*-quinones (**2** ⇌ **3**) of each catecholamine to the corresponding indolines (**4**). The detailed conformity of these systems to the electrochemical-kinetic treatment associated with the ECC process indicates that variegation of the polymeric melanin structure, as reported by Swan, probably involves condensations of precursor molecules with electrophilic quinones formed subsequent to the dihydroxyindoles (**6**).

Metabolism of the clinically important[1] antihypertensive drug L-α-methyldopa, L-(3,4-dihydroxyphenyl)-2-methylalanine (**1a**), occurs primarily in the catecholaminergic neurons of the central nervous system[2,3] to produce the metabolites L-α-methyldopamine (**1b**) and α-methylnoradrenaline (**1c**). Investigations involving both acute and chronic administration of α-methyldopa (**1a**) to hypertensive rats have demonstrated the accumulation of these two metabolites (**1b** and **1c**) and the depletion of natural neurotransmitters, including dopamine (**1d**) and noradrenaline, in rat brain tissues.[4] The α-methylated catecholamines (**1b** and **1c**) are currently considered as false neurotransmitters, and recent experiments have suggested that, of the two, α-methyldopamine (**1b**), an effective dopamine agonist, is the responsible hypotensive agent.[5,6]

All of these catecholamines (**1a–d**) may form melanin-like pigments under oxidative conditions,[7] and we have previously reported a detailed study of the melanization reactions of α-methyldopa (**1a**),[8] as well as of dopa itself,[9] using fast sweep electrochemical techniques. Only abbreviated studies of the oxidation of the metabolite catecholamines **1b**,[10] **1c**,[11] and **1d**[10,11] have appeared in the literature. Hence, it was of interest to conduct a more extensive kinetic–mechanistic investigation of the anodic oxidation of these physiologically important catecholamines.

Cyclic voltammetry of 1.0 mM α-methyldopamine (**1b**) in 1 M perchloric acid (pH 0.60) at 25 °C indicated that the system **1b** → **2b** is irreversible at the carbon paste electrode. A typical voltammogram at a scan rate of 0.050 V/s is shown in Figure 1. The anodic peak (A) for the process **1b** → **2b** occurred at E_{pa} = 0.679 V (SCE) and the cathodic peak (A′) for the reverse process **2b** → **1b** at E_{pc} = 0.518 V, yielding a peak separation of 161 mV. Calculation of the theoretical anodic peak current (i_{pa}),[12,13] assuming an irreversible charge transfer involving two electrons and that the transfer coefficient (α) = 0.5 and using a diffusion coefficient derived from chronoamperometry ($D = 0.53 \times 10^{-5}$ cm^2/s), gave a value of i_{pa} = 118.2 μA. This value correlated well with the experimentally determined quantity of 117.5 μA.

Similar cyclic voltammograms for α-methylnoradrenaline (**1c**) and dopamine (**1d**) in 1 M perchloric acid at a scan rate of 0.050 V/s showed that these redox systems are also irreversible. α-Methylnoradrenaline (**1c**) exhibited a peak for the oxidative process **1c** → **2c** at E_{pa} = 0.703 V and a cathodic peak at E_{pc} = 0.473 for the reduction **2c** → **1c**, with a wide peak separation of 230 mV. A 178-mV peak separation was found for dopamine (**1d**): oxidation (**1d** → **2d**, E_{pa} = 0.648 V) and reduction (**2d** → **1d**, E_{pc} = 0.470 V). Chronoamperometry experiments carried out at 25 °C for α-methylnoradrenaline (**1c**) and dopamine (**1d**) provided diffusion coefficients of $D = 0.51 \times 10^{-5}$ and 0.54×10^{-5} cm^2/s, respectively. By making the same assumptions as previously for α-methyldopamine, theoretical anodic peak currents of i_{pa} = 112.6 and 114.8 μA were calculated for α-methylnoradrenaline (**1c**) and dopamine

(1) Oates, J. A.; Gillespie, L.; Udenfriend, S.; Sjoersdma, A. *Science* **1960**, *131*, 1890.
(2) Carlsson, A.; Lindquist, M. *Acta Physiol. Scand.* **1962**, *54*, 87.
(3) Henning, M.; Rubenson, A. *J. Pharm. Pharmacol.* **1971**, *23*, 407.
(4) Conway, E. L.; Louis, W. J.; Jarrott, B. *Neuropharmacology* **1979**, *18*, 279; **1979**, *18*, 287.
(5) Freed, C. R.; Quintero, E.; Murphy, R. L. *Life Sci.* **1978**, *23*, 313.
(6) Karashima, D.; Cockerline, R. L.; Melmon, K. L.; Castagnoli, N., Jr., *Recent Dev. Mass. Spectrom. Biochem. Med.* **1979**, *2*, 317.
(7) Nicolaus, R. A. "Melanins"; Hermann: Paris, 1968.
(8) Young, T. E.; Babbitt, B. W.; Wolfe, L. A. *J. Org. Chem.* **1980**, *45*, 2899.
(9) Young, T. E.; Griswold, J. R.; Hulbert, M. H. *J. Org. Chem.* **1974**, *39*, 1980.
(10) Chavdarian, C. G.; Karashima, D.; Castagnoli, N., Jr. *J. Med. Chem.* **1978**, *21*, 548.
(11) Hawley, M. D.; Tatawawadi, S. V.; Piekarski, S.; Adams, R. N. *J. Am. Chem. Soc.* **1967**, *89*, 447.
(12) Nicholson, R. S.; Shain, I. *Anal. Chem.* **1964**, *36*, 706.
(13) Adams, R. N. "Electrochemistry at Solid Electrodes"; Marcel Dekker: New York, 1969.

0022-3263/83/1948-0562$01.50/0