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Stereospecific Palladium-Promoted Oxyamination of Alkenes

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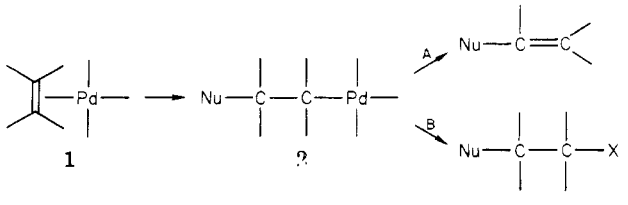
A method for direct oxyamination of olefins to vicinal amino alcohol derivatives is described. The reaction proceeds via an aminopalladation–oxidation sequence. Terminal olefins give good yields (60–80%) whereas internal olefins give lower yields (20–60%). The oxyamination reaction is stereospecific as shown by reaction of (*Z*)- and (*E*)-2-butene and (*E*)-1-deuterio-1-decene and proceeds by overall cis stereochemistry. The stereochemical outcome is a result of a trans aminopalladation followed by an oxidative cleavage of the palladium carbon bond with inversion of configuration at carbon. Oxidation of the organopalladium σ complex to give an oxidized palladium intermediate, which could be a Pd(IV) intermediate, followed by S_N2-type nucleophilic displacement of palladium is the most likely mechanism for the oxidative cleavage reaction.

Organometallic reagents, in particular those of transition metals, have become important tools in organic synthesis, and today a great number of organic transformations utilizing transition metals are known.[1,2] Because of their ability to coordinate and activate alkenes, transition-metal reagents are particularly useful for the functionalization of double bonds. We have recently been concerned with palladium-promoted functionalization of double bonds involving carbon–nitrogen bond formation to give amines, diamines, and amino alcohol derivatives.[3-5]

The general route for palladium-promoted or -catalyzed functionalization of olefins involves π-complex formation (1) followed by nucleophilic attack on the coordinated olefin (Scheme I). In this process the olefin may be attacked either by a coordinated nucleophile (e.g., alkyl) or by a free nucleophile (e.g., amine, acetate, or alcohol). Cleavage of the palladium–carbon bond in the intermediate σ complex **2** may take place in two principal ways: β elimination (A) or substitution of the palladium atom (B). Examples of the first type of reaction (A) include palladium-catalyzed arylation (Nu = Ar)[6] and the vinyl acetate process (Nu = OAc).[7] The Wacker process may also be considered as such a reaction (Nu = OH).[8]

Scheme I



Cleavage of the metal carbon bond according to the second path (B) may, for example, be a reduction (X = H),[5] an insertion (X = COOR),[9] or an oxidative cleavage process (X = OR, R_2N, Cl, Br).[3,4,10]

In a preliminary paper[3] we reported a method for vicinal cis oxyamination of olefins, which in principle takes place as depicted in Scheme I (path B; Nu = NR_2, X = OAc), using palladium in stoichiometric amounts. This procedure also required one equivalent of lead tetraacetate. We have now found that lead tetraacetate can be replaced by other oxidants (e.g., NBS, Br_2, I_2), which in the presence of an oxygen nucleophile (CH_3COO^-, OH^-, ArO^-) readily cleave the palladium–carbon bond in the aminopalladation adduct to give the desired product. In this paper we report these new results and also give full details of the previous report.

Results and Discussion

Olefins were transformed in a "one-pot" reaction to a vicinal amino alcohol derivative (e.g., amino acetate). A β-aminopalladium complex is readily obtained from the corresponding olefin by aminopalladation[5] at −40 °C. The oxidative cleavage of the palladium–carbon bond in such adducts was studied by using different oxidants in the presence of an oxygen nucleophile. Most such cleavage

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Table I. Oxyamination of Olefins

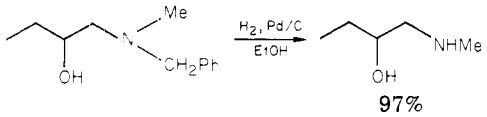
olefin	amine	oxidant[a]	amino acetate or amino alcohol[b]	yield[c] of amino acetate or amino alcohol, %
ethene	Et_2NH	NBS	$Et_2NCH_2CH_2OAc$	50
1-butene	Me_2NH	$Pb(OAc)_4$	$C_2H_5CH(NMe_2)CH_2OH$ (88), $C_2H_5CH(OH)CH_2NMe_2$ (12)	84[d]
1-butene	$PhCH_2NHMe$	NBS	$C_2H_5CH(MeNCH_2Ph)CH_2OAc$ (53), $C_2H_5CH(OAc)CH_2N(CH_2Ph)Me$ (47)	62
(*Z*)-2-butene	Me_2NH	$Pb(OAc)_4$	*erythro*-$MeCH(OH)CH(NMe_2)Me$ (>99% *erythro*)	29[d]
(*E*)-2-butene	Me_2NH	$Pb(OAc)_4$	*threo*-$MeCH(OH)CH(NMe_2)Me$ (>99% *threo*)	58[d]
(*E*)-2-butene	Me_2NH	Br_2	*threo*-$MeCH(OH)CH(NMe_2)Me$ (92:8 *threo/erythro*)	50[d]
(*E*)-2-butene	Et_2NH	NBS	*threo*-$MeCH(OAc)CH(NEt_2)Me$	44[e]
(*E*)-2-butene	Et_2NH	Br_2	*threo*-$MeCH(OAc)CH(NEt_2)Me$	37
1-hexene	Me_2NH	$Pb(OAc)_4$	n-$C_4H_9CH(NMe_2)CH_2OAc$ (83), n-$C_4H_9CH(OAc)CH_2NMe_2$ (17)	77
1-hexene	Et_2NH	Br_2	n-$C_4H_9CH(NEt_2)CH_2OAc$ (47), n-$C_4H_9CH(OAc)CH_2NEt_2$ (53)	32
1-hexene	Et_2NH	NBS	n-$C_4H_9CH(NEt_2)CH_2OAc$ (42), n-$C_4H_9CH(OAc)CH_2NEt_2$ (58)	71
1-hexene	Et_2NH	$Pb(OAc)_4$	n-$C_4H_9CH(NEt_2)CH_2OAc$ (43), n-$C_4H_9CH(OAc)CH_2NEt_2$ (57)	44
1-decene	Me_2NH	$Pb(OAc)_4$	n-$C_8H_{17}CH(NMe_2)CH_2OAc$ (84), n-$C_8H_{17}CH(OAc)CH_2NMe_2$ (16)	80
1-decene	Me_2NH	NBS	n-$C_8H_{17}CH(NMe_2)CH_2OAc$ (80), n-$C_8H_{17}CH(OAc)CH_2NMe_2$ (20)	62
1-decene	Et_2NH	$Pb(OAc)_4$	n-$C_8H_{17}CH(NEt_2)CH_2OAc$ (55), n-$C_8H_{17}CH(OAc)CH_2NEt_2$ (45)	56
styrene	Et_2NH	NBS	$PhCH(OAc)CH_2NEt_2$	61[e]
styrene	Et_2NH	Br_2	$PhCH(OAc)CH_2NEt_2$	40
(*E*)-1-phenylpropene	Me_2NH	$Pb(OAc)_4$	$PhCH(OAc)CH(NMe_2)Me$ (6:1 *threo/erythro*)	21[e]
allyl phenyl ether	Me_2NH	$Pb(OAc)_4$	$PhOCH_2CH(OAc)CH_2NMe_2$	60
allyl phenyl ether	Et_2NH	$Pb(OAc)_4$	$PhOCH_2CH(OAc)CH_2NEt_2$	49[e]

[a] All oxidations of the aminopalladation adducts were performed in the presence of acetic acid. [b] Relative yields indicated in parentheses were generally determined by GLC and checked in some cases by NMR. [c] Yields are based on the amount of palladium used. Unless otherwise noted, yields were determined by GLC using appropriate internal standards. [d] Reductive workup with $LiAlH_4$. [e] Isolated yield.

reactions were found to result in stereospecific replacement of palladium by an oxygen function.

Results from the oxyamination of some olefins are given in Table I. Terminal olefins give higher yields than internal olefins, and among internal olefins the trans isomers give higher yields than the cis isomers. This difference is most likely due to the different reactivities of the olefins in the aminopalladation step.[5b] Among the amines used, primary amines did not give the desired amino alcohol derivative on oxidation in the presence of an oxygen nucleophile but rather gave aziridines.[4c] Secondary amines gave good to moderate yields of vicinal *N,N*-dialkylamino alcohols, depending on the size of the amine used.

Because *N*-alkylamino alcohols could not be prepared directly by the normal procedure by amination with primary amines, a modified route must be applied to obtain these compounds. Oxyamination using *N*-alkylbenzylamine followed by debenzylation of the product formed gave the desired product. This was demonstrated by debenzylation of *N*-benzyl-*N*-methyl-1-amino-2-butanol (one of the regioisomers from the oxyamination of 1-butene using *N*-methylbenzylamine) to *N*-methyl-1-amino-2-butanol.



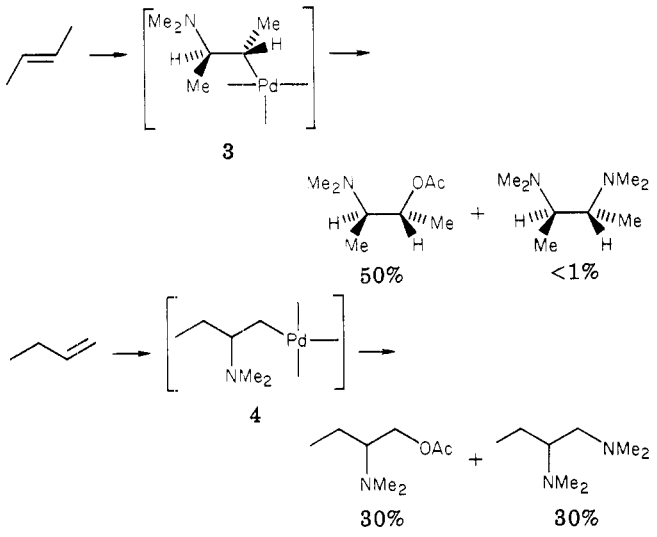
97%

The oxidative cleavage of the palladium–carbon bond appears to be dependent on the size of the amino group in the β position. Thus, diethylamino adducts generally reacted slower than the dimethylamino adducts, the difference being most pronounced for adducts having primary carbon–palladium bonds. Of the oxidants used, lead tetraacetate was the most efficient oxidant for dimethylamino adducts, whereas NBS (*N*-bromosuccinimide) seemed to be best for diethylamino adducts. Furthermore, there is a marked difference in the cleavage of primary and secondary carbon–palladium bonds. The oxidative cleavage of secondary carbon–palladium bonds in the presence of acetate ions is effective, replacing the metal selectively by acetate. On the other hand, the acetate cleavage of primary carbon–palladium bonds was slower, and in this case competing replacement of palladium by amine took place if amine was used in excess. The difference is illustrated by the experiments shown in Scheme II. The complexes **3** and **4**, generated from (*E*)-2-butene and 1-butene,[11] respectively, were oxidized under similar conditions. The secondary alkyl complex **3** gave exclusively an amino acetate, whereas the primary alkyl complex **4** gave amino acetate and diamine in equal amounts.

The low reactivity of primary carbon–palladium bonds in the oxidative acetate cleavage is probably responsible for the low yield of 2-(diethylamino)-1-acetoxy adducts. The expected ratio 2-amino-1-ol/1-amino-2-ol from the known[5a] ratio of regioisomers of the (diethylamino)palladation adduct is 1.3, whereas the observed ratio is 0.7–1.2.

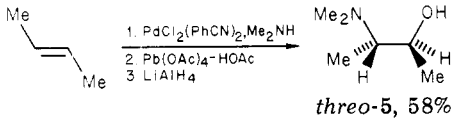
(11) In this case a small fraction (~1/7) of anti-Markovnikov adduct is also formed, which on oxidation gives $CH_3CH_2CH(OAc)CH_2NMe_2$.

Scheme II[a]



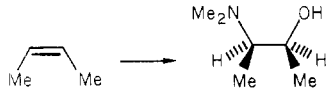
[a] $[AcO]_{tot} = [NHMe_2] = 10$ equiv; oxidizing agent, Br_2 (1 equiv).

The stereochemistry of the reaction was studied using (*Z*)- and (*E*)-2-butene and (*E*)-1-deuterio-1-decene as the substrates. These olefins were chosen because they yield stereochemical information on the cleavage of secondary and primary carbon–palladium bonds, respectively. Oxyamination of (*Z*)- and (*E*)-2-butene using dimethylamine and lead tetraacetate as the oxidizing agent gave in each case a different diastereoisomer as shown by NMR and GLC analyses (eq 1 and 2). By comparison with authentic



(1)

threo-**5**, 58%

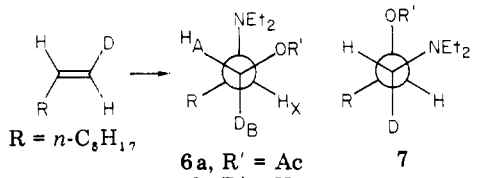


(2)

erythro-**5**, 29%

samples of *threo*- and *erythro*-**5**, prepared from (*Z*)- and (*E*)-2-butene oxide, respectively (see Experimental Section), the product from (*E*)-2-butene was shown to be *threo*-**5** and the product from (*Z*)-2-butene to be *erythro*-**5**. Thus the overall result is a cis oxyamination. The stereoselectivity was >99%. When bromine was used as the oxidant in the analogous reaction [(*E*)-2-butene, Me_2NH], a slightly lower stereoselectivity was observed, and *threo*-**5** and *erythro*-**5** were formed in a ratio of 92:8.

Oxyamination of (*E*)-1-deuterio-1-decene using diethylamine gave two regioisomers (eq 3). The regioisomer



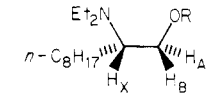
(3)

6a, R′ = Ac
b, R′ = H

7

6a, resulting from cleavage of the primary carbon–palladium bond, was isolated and analyzed by NMR spectroscopy. The acetate **6a** was transformed to the alcohol **6b** which also was analyzed by NMR spectroscopy. The proton H_A of **6a** appeared at 4.13 ppm (J = 6.6 Hz), and the corresponding H_A proton of **6b** appeared at 3.22 ppm (J = 10.3 Hz). From the NMR data of the undeuterated parent compounds of **6a** and **6b** (Table II) we were able

Table II. NMR Data[a] for



	R = OAc	R = OH		R = OAc	R = OH
δ_{HA}	4.16	3.22	J_{AB}	11.2	10.5
δ_{HB}	3.94	3.54	J_{AX}	6.6	10.3
δ_{HX}	2.55	2.55	J_{BX}	5.6	4.9

[a] Shifts are given in parts per million relative to Me_4Si, and coupling constants are in hertz. Spectra were run in $CDCl_3$.

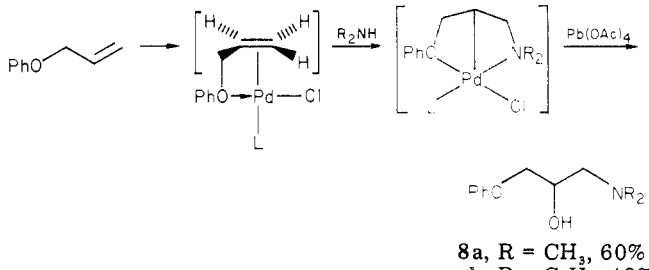
Table III. Results from Pd-Promoted Oxyamination of (*E*)-1-Deutereo-1-decene

oxidant	% yield[a,b] 6a	7a
NBS	23 (>95% threo)	32
$Pb(OAc)_4$	31 (>95% threo)	25
Br_2	15 (>95% threo)	13

[a] Determined by gas chromatography. [b] Figures in parentheses indicate isomeric purity as determined by NMR.

to assign **6a** and **6b** as the threo isomers. β-Amino alcohols are known to prefer a conformation in which the amino group and the alcohol group are gauche to each other.[12] The coupling constants J_{AX} = 10.3 Hz and J_{BX} = 4.9 Hz of the undeuterated amino alcohol (Table II) are consistent with the amino and alcohol groups mainly occupying the less hindered of the two possible gauche conformations.[13] The results from oxyamination of (*E*)-1-deuterio-1-decene are given in Table III. The stereochemical results thus show that in this case too the oxyamination is an overall cis addition, a result of trans aminopalladation[5] followed by oxidative cleavage of the primary carbon–palladium bond with inversion.

Oxyaminations of (*E*)-1-phenyl-1-propene (Me_2NH) and allyl phenyl ether were highly regiospecific, giving *N*-methyl-ψ-ephedrin and oxy amines 8, respectively. Com-



8a, R = CH_3, 60%
b, R = C_2H_5, 49%

pounds of the latter type, (aryloxy)propanolamines, are important β-adrenoceptor blocking drugs,[14] and the direct oxyamination procedure presented here seems to be a convenient method for the preparation of this class of compounds. The exclusive formation of **8a** from allyl phenyl ether is remarkable, since oxyamination of other terminal olefins using dimethylamine gives mainly the regioisomer in which the alcohol group is bonded to the

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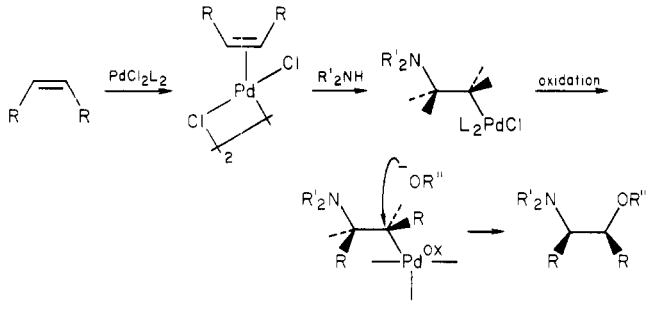
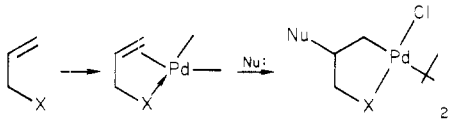
Scheme III[a]



[a] $R''O^- = AcO^-, PhO^-, OH^-$.

terminal carbon (cf. Table I). This directive effect of the phenoxy group may reflect a coordination of the ether oxygen to palladium in the amination step or may be a result of simple polarization by the oxygen substituent.[15] If such a coordination takes place, it must be weak, since related additions to allylamines and allyl sulfides, where strong coordination occurs, are known to result in adducts where palladium is bonded to the terminal carbon (eq 4).[15b,16]



(4)

X = NR_2, SR; Nu = CH_3O^-, $^-CH(COOR)_2$

In a preliminary report[3] we considered three different pathways for the formation of an amino acetate in the lead tetraacetate oxidation of (β-aminoalkyl)palladium complexes: (a) alkyl transfer to give a (β-aminoalkyl)lead(IV) intermediate followed by S_N2 attack by acetate on carbon, (b) coordination of lead tetraacetate to palladium, resulting in electron transfer from palladium to lead (inner-sphere electron transfer)[17] followed by acetate attack, (c) direct oxidation (outer-sphere electron transfer) to an alkylpalladium(IV) complex followed by acetate attack. It is likely that the oxidative cleavage of palladium–carbon bonds by the different oxidants used here proceeds by a common mechanism, as is also suggested by the stereochemical results. Thus a mechanism similar to b or c in which the palladium–carbon bond is retained during an initial electron-transfer process seems most likely (Scheme III). This electron-transfer process would activate the metal–carbon bond and transform the metal into a good leaving group. Recent results[18] on the cupric chloride cleavage of palladium–carbon bonds support such a mechanism. The slight loss of stereospecificity in the bromine-induced oxidative cleavage of secondary palladium–carbon bonds is not clearly understood but may reflect a reductive coupling to give a β-haloalkylamine, which on workup would yield the amino acetate by a neighboring-group-assisted nucleophilic substitution. β-Haloalkylamines have, in fact, been isolated from [β-(diethylamino)alkyl]platinum complexes on oxidation by bromine.[19a] It is still unclear why acetate does not cleave the palladium–carbon bond in the aminopalladation adducts formed from primary amines where the only products are aziridines. One could argue that the intramolecular displacement of palladium to give aziridines is much faster. Attempts to inhibit aziridine formation by protonating nitrogen in these adducts with an excess of acetic acid or trifluoroacetic acid were unsuccessful, and the main product was still aziridine. One explanation is that reductive coupling takes place to give a salt of a β-haloalkylamine, which on workup would yield the aziridine. Another possibility is that intramolecular coordination of nitrogen to palladium occurs which would inhibit protonation of the nitrogen. Similar intramolecular coordination of nitrogen to give four-membered rings has been observed in the analogous platinum complexes.[19] A four-membered-ring chelate might in our case decompose to aziridine under the conditions used.

Although a number of methods[20] are available for synthesis of β-amino alcohols, only a few procedures for direct oxyamination of olefins are known.[20,21] The method presented here for direct cis oxyamination has the advantage over other direct methods that ordinary amines can be used, and thus more variation of the nitrogen moiety is possible.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 421 spectrometer. NMR spectra were obtained with a Varian EM-360 or a Bruker WP 200 FT spectrometer. GLC analyses were performed on a 6 ft × $^1/_8$ in. steel column packed with 20% Apiezon L with 10% KOH on Chromosorb W (60/80 mesh). $(PhCN)_2PdCl_2$ was prepared according to Kharasch.[22] Tetrahydrofuran was distilled over potassium/benzophenone under nitrogen. Lead tetraacetate containing ~20% acetic acid was obtained from Merck Schuchhardt. Reference samples of *N,N*-diethyl- and *N,N*-dimethylethanolamine were purchased from Merck Schuchhardt. All olefins were purchased from Fluka AG. (*E*)-1-Deuterio-1-decene was prepared by hydroalumination[23] of 1-decyne followed by D_2O quenching. (*E*)- and (*Z*)-2-butene oxides were prepared by epoxidation of the corresponding 2-butene with *m*-chloroperbenzoic acid in dioxane.[24] 1-Hexene oxide,[25] styrene oxide,[26] 1-decene oxide,[25] and (*E*)-5-decene oxide[27] were prepared by reaction of the appropriate olefin with *m*-chloroperbenzoic acid in CH_2Cl_2.

Preparation of Authentic Amino Alcohols. 1-(Dimethylamino)-2-hexanol. A solution of 1-hexene oxide (0.85 g, 8.5 mmol) and dimethylamine (1.45 g, 32 mmol) in methanol (10 mL) was refluxed for 8 h. The reaction mixture was poured into 25 mL of ether and extracted with 2 M HCl (3 × 10 mL). The aqueous layer was washed with ether (2 × 5 mL), made alkaline with NaOH pellets, and extracted with ether. The organic phase was dried (K_2CO_3) and evaporated. The residue was purified by distillation to give 635 mg (52%) of product: bp 95–96 °C (42 mm) [lit.[28] 89–90 °C (25 mm)]; NMR ($CDCl_3$) δ 3.7 (s, 1, OH), 3.7–3.5 (m, 1, CH–O), 2.3–2.1 (m, 2, CH_2–N), 2.27 (s, 6, $(CH_3)_2N$), 1.4 (m, 6, $(CH_2)_3$), 0.9 (br t, 3, CH_3); IR (neat) 3600–3200 (OH), 2950, 2930, 2860, 2820, 2770, 1420, 1210, 1080, 1050, 880 cm^{-1}.

The same procedure was used for the preparation of the following β-amino alcohols:

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(16) (a) Cope, A. C.; Kliegman, J. M.; Friedrich, E. C. *J. Am. Chem. Soc.* **1967**, *89*, 287. (b) Takahashi, A.; Tokuda, A.; Sakai, S.; Ishii, Y. *J. Organomet. Chem.* **1972**, *35*, 415.

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(18) Bäckvall, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1980**, *102*, 393.

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(20) Patrick, D. W.; Truesdale, L. K.; Biller, S. A.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2628 and references cited therein.

(21) (a) Sharpless, K. B.; Chong, A. O.; Oshima, K. *J. Org. Chem.* **1976**, *41*, 177. (b) Herranz, E.; Biller, S. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1978**, *100*, 3596.

(22) Kharasch, M. S.; Seyler, R. C.; Mayo, F. R. *J. Am. Chem. Soc.* **1938**, *60*, 882.

(23) Wilke, G.; Müller, H. *Justus Liebigs Ann. Chem.* **1958**, *618*, 267.

(24) Pasto, D. J.; Cumbo, C. C. *J. Org. Chem.* **1965**, *30*, 1271.

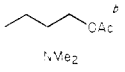
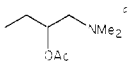
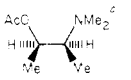
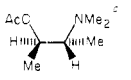
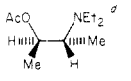
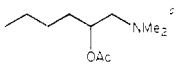
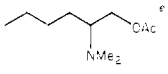
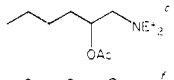
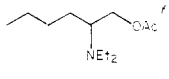
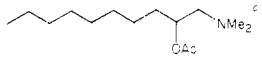
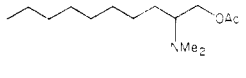
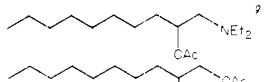
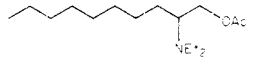
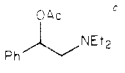
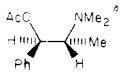
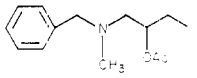
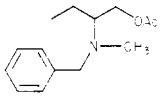
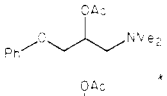
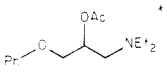
(25) Rothstein, B. *Bull. Soc. Chim. Fr.* **1935**, *2*, 1936.

(26) Hibbert, H.; Burt, C. P. *J. Am. Chem. Soc.* **1925**, *47*, 2243.

(27) Pankova, M.; Sicher, J. *Collect. Czech. Chem. Commun.* **1965**, *30*, 388.

(28) Major, R. T.; Bonnet, H. T. *J. Am. Chem. Soc.* **1936**, *58*, 23.

Table IV. Spectral Data for β-Amino Acetates

compd[a]	IR (CCl_4) ν, cm^{-1}	NMR ($CDCl_3$), δ
	2363, 1742, 1229	4.20, 4.12 (2, AB part of ABX), 2.6 (m, 1, CH-N), 2.32 (s, 6, $(CH_3)_2N$), 2.07 (s, 3, CH_3), 1.5 (m, 2), 0.95 (t, 3)
	2970, 2820, 2770, 1737, 1460, 1235	4.92 (m, 1, CH-O), 2.4-2.2 (m, 2, CH_2N), 2.25 (s, 6, $(CH_3)_2N$), 2.05 (s, 3, CH_3), 1.4 (m, 2), 0.9 (br t, 3, CH_3)
	2985, 1735, 1365, 1235, 1090, 1035	4.92 (m, 1, CH-O), 2.45 (m, 1, CH-N), 2.25 (s, 6, $(CH_3)_2N$), 2.03 (s, 3, CH_3), 1.23 (d, 3, CH_3), 0.97 (d, 3, CH_3)
	2975, 1740, 1370, 1240	4.98 (m, 1, CH-O), 2.50 (m, 1, CH-N), 2.27 (s, 6, $(CH_3)_2N$), 2.03 (s, 3, CH_3), 1.17 (d, 3, CH_3), 0.91 (d, 3, CH_3)
	2985, 1735, 1370, 1240	4.95 (m, 1, CH-O), 2.9-2.0 (m, 5), 2.03 (s, 3, CH_3), 1.17 (d, 3, CH_3), 0.92 (d, 3, CH_3)
	2955, 1738, 1468, 1370, 1239	4.9 (m, 1, CH-O), 2.4-2.2 (m, 2, CH_2-N), 2.22 (s, 6, $(CH_3)_2N$), 2.01 (s, 3, CH_3), 1.4 (m, 6), 0.9 (br t, 3, CH_3)
	2958, 1742, 1232	4.14, 4.05 (2, AB part of ABX), 2.6 (m, 1, CH-N), 2.32 (s, 6, $(CH_3)_2N$), 2.07 (s, 3, CH_3), 1.3 (m, 4), 0.9 (br t, 3)
	2960, 1736, 1235	4.9 (m, 1, CH-O), 2.7-2.3 (m, 6), 2.00 (s, 3, CH_3), 1.3 (m, 6), 1.0 (t over br t, 9)
	2960, 1742, 1231	4.19, 3.88 (2, AB part of ABX), 2.9-2.3 (m, 5), 2.01 (s, 3, CH_3), 1.3 (m, 6), 1.0 (t over br t, 9)
	2920, 1736, 1240	5.0 (m, 1, CH-O), 2.6-2.2 (m, 2, CH_2-N), 2.24 (s, 6, $(CH_3)_2N$), 2.05 (s, 3, CH_3), 1.3 (m, 14), 0.88 (br t, 3, CH_3)
	2930, 1742, 1230	4.13, 4.06 (2, AB part of ABX), 2.7 (m, 1, CH-N), 2.32 (s, 6, $(CH_3)_2N$), 2.07 (s, 3, CH_3), 1.2 (m, 14), 0.9 (br t, 3, CH_3)
		4.9 (m, 1, CH-O), 2.6-2.2 (m, 6), 1.99 (s, 3, CH_3), 1.2 (m, 14), 0.9 (t over br t, 9)
	2960, 2925, 1740, 1335, 1240	4.16, 3.94 (2, AB part of ABX, CH-O), 3.0-2.2 (m, 5), 2.00 (s, 3, CH_3), 1.2 (m, 14), 1.0 (t over br t, 9)
	2970, 1742, 1370, 1235, 1028	7.3 (br s, 5), 5.83 (dd, 1, CH-O), 3.0-2.4 (m, 6), 2.07 (s, 3, CH_3), 1.0 (t, 3, CH_3)
	2965, 1735, 1370, 1235, 1025	7.3 (br s, 5), 5.70 (d (J = 9 Hz), 1, CH-O), 2.98 (m, 1, CH-N), 2.32 (s, 3, $(CH_3)_2N$), 2.07 (s, 3, CH_3), 0.68 (t, 3, CH_3)
	2960, 1740, 1238	7.3 (br s, 5), 5.04 (m, 1, CH-O), 3.56, 3.48 (AB q, 2, $PhCH_2$), 2.4 (m, 2, CH_2), 2.24 (s, 3, CH_3-N), 2.07 (s, 3, CH_3), 1.6 (m, 2), 0.87 (br t, 3)
	2960, 1742, 1230	7.3 (br s, 5), 4.1 (2, AB part of ABX, CH-O) 3.72, 3.64 (AB q, 2, $PhCH_2$), 2.76 (m, 1, CH-N), 2.23 (s, 3, CH_3-N), 2.09 (s, 3, CH_3), 1.5 (m, 2), 1.0 (t, 3)
	1740, 1230	7.4-6.8 (m, 5), 5.28 (m, 1, CH-OAc), 4.1 (2, AB part of ABX, CH_2-O), 2.55 (d, 2, CH_2-N), 2.27 (s, 6, $(CH_3)_2N$), 2.05 (s, 3, CH_3)
	2965, 1740, 1225	7.4-6.8 (m, 5), 5.23 (m, 1, CH-OAc), 4.2 (AB part of ABX, CH_2-O), 2.9-2.3 (m, 6, CH_2-N), 2.06 (s, 3, CH_3), 1.03 (t, 6, CH_3)

[a] Further characterization beyond IR and NMR (in most cases as the alcohol) is noted. [b] Reference 33. [c] Alcohol; see text in Experimental Section. [d] Reference 34. [e] Reference 35. [f] Reference 36. [g] Anal. Calcd for $C_{16}H_{33}O_2N$: C, 70.80; H, 12.25. Found: C, 71.41; H, 12.20. [h] Reference 37. [i] Anal. Calcd for $C_{13}H_{19}O_3N$: C, 65.79; H, 8.06. Found: C, 66.22; H, 8.09 (see also ref 38). [k] Reference 39.

1-(Diethylamino)-2-hexanol was prepared from 1-hexene oxide and diethylamine: yield after distillation 46%; bp 98 °C (20 mm); NMR ($CDCl_3$) δ 3.7 (s, 1, OH), 3.7–3.4 (m, 1, CH–O), 2.8–2.1 (m, 6, 3 CH_2–N), 1.4 (m, 6, $(CH_2)_3$), 1.0 (t overlapping br t, 9, 3 CH_3). Anal. Calcd for $C_{10}H_{23}NO$: C, 69.31; H, 13.38; N, 8.08. Found: C, 68.90; H, 13.28; N, 7.89.

2-(Diethylamino)-1-phenylethanol was prepared from styrene oxide and diethylamine: yield 78% before distillation; bp 82–84 °C (1 mm) [lit.[29] 149 °C (22 mm)]; NMR ($CDCl_3$) δ 7.4–7.2 (m, 5, aromatic), 4.62 (dd, 1, CH–O), 4.1 (br s, 1, OH), 2.9–2.1 (m, 6, 3 CH_2–N), 1.07 (t, 6, 2 CH_3 in Et_2N).

***erythro*-3-(Dimethylamino)-2-butanol** was prepared from (*E*)-2-butene oxide and dimethylamine: bp 152 °C (lit.[30] 152.5–153.5 °C); NMR (acetone-d_6) δ 3.69 (m, 1, CH–O, J_{23} = 5.8 Hz), 2.18 (br, 7, CH–N and $(CH_3)_2N$), 1.12 (d, 3, CH_3), 0.92 (d, 3, CH_3).

***threo*-3-(Dimethylamino)-2-butanol** was prepared from (*Z*)-2-butene oxide and dimethylamine: bp 140 °C [lit.[30] 141–142

(29) Marvel, C. S.; Du Vigneand, V. *J. Am. Chem. Soc.* **1924**, *46*, 2098.

(30) Wilson, C. E.; Lucas, H. J. *J. Am. Chem. Soc.* **1936**, *58*, 2399.

°C]; NMR (acetone-d_6) δ 3.8 (s, 1, OH), 3.35 (m, 1, CH–O, J_{23} = 9.1 Hz), 2.2 (br 7, CH–N and $(CH_3)_2N$), 1.03 (d, 3, CH_3), 0.83 (d, 3, CH_3).

1-(Dimethylamino)-2-butanol[28] was prepared from 1-butene oxide and dimethylamine: NMR ($CDCl_3$) δ 4.3 (s, 1, OH), 3.54 (m, 1, CH–O), 2.4–2.0 (m, 2, CH_2–N), 2.24 (s, 6, $(CH_3)_2N$).

1-(Dimethylamino)-2-decanol[31] was prepared from 1-decene oxide and dimethylamine: NMR ($CDCl_3$) δ 3.5 (m, 1, CH–O), 3.2 (s, 1, OH), 2.3–2.1 (m, 2, CH_2–N), 2.24 (s, 6, $(CH_3)_2N$), 1.3 (m, 14), 0.9 (br t, 3, CH_3); IR (CCl_4) 3450 (br), 2920, 2850, 1245 cm^{-1}.

1-(Benzylmethylamino)-2-butanol was prepared from 1-butene oxide and *N*-methylbenzylamine: NMR ($CDCl_3$) δ 7.2 (m, 5, aromatic), 3.8–3.3 (m, 4, CH–O, OH, $PhCH_2$), 2.27 (m, 2, CH_2–N), 2.19 (s, 3, N–CH_3), 1.35 (br q, 2, CH_2), 0.95 (br t, 3, CH_3). Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.57; H, 9.93; N, 7.21.

Acetylation of Authentic Amino Alcohols. The appropriate amino alcohol was treated with acetyl chloride either neat or in ether. Spectral data for amino acetates are given in Table IV.

General Procedure for Oxyamination of Olefins. A solution of 0.5 mL of olefin in 5 mL of anhydrous THF was added to $(PhCN)_2PdCl_2$ (383 mg, 1 mmol) under a nitrogen atmosphere at 0 °C. After the mixture was stirred for 10 min, the temperature was decreased to −50 °C, and 4 mmol of amine in THF (2 mL) was added during 15 min. The temperature was kept at −50 °C for 50 min, and then 1 mmol of oxidant and 8 mmol of acetic acid in 1.5 mL of anhydrous THF were added [when $Pb(OAc)_4$ was used as the oxidant, the acetic acid adsorbed on the salt (~20% of the weight) was the only acetic acid used]. The solution was kept at −50 °C for an additional 5 min and then allowed to slowly warm to room temperature. After 2 h, 6 mL of 2 M NaOH, 6 mL of ether, and 0.1 g of KBH_4 were added, and the mixture was stirred for 20 min. The palladium black and other precipitates that formed were filtered off and washed with ether (2 × 3 mL). The organic layer was separated and extracted with 2 M HCl (3 × 2 mL). The aqueous phase was washed with ether (3 × 2 mL), made alkaline (pH >11), and extracted with ether (3 × 3 mL). The organic phase was washed with brine and dried over K_2CO_3. Purification of the products was accomplished by preparative GLC or preparative TLC. Spectral data for the amino acetates are given in Table IV.

***threo*-1-Deuterio-2-(diethylamino)-1-decanol (6b).** The amino acetate **6a** (27 mg) was treated with $LiAlH_4$ (25 mg) in dry ether (2 mL) for 1 h. The excess hydride was destroyed by adding wet ether (3 mL) and 1 drop of water. The mixture was filtered and the precipitate washed several times with ether. The organic phase was dried (K_2CO_3) and evaporated to give 19 mg of **6b** (85%) as identified by NMR ($CDCl_3$).

1-Acetoxy-2-(diethylamino)-1-phenylethane was prepared in a 10-mmol-scale experiment [3.83 g of $(PhCN)_2PdCl_2$, 5 mL of styrene, 4 mL of diethylamine] by following the general procedure with the following restrictions: it is important to have careful temperature control during the slow addition of acetic acid (added over a 10-min period).

After the reaction was complete (stirring for 2 h at room temperature) 40 mL of 3 M NaOH and 1 g of KBH_4 were added at 0 °C. After the mixture was stirred at room temperature for 30 min, palladium black was filtered off, and the organic layer was extracted with 2 M HCl (3 × 20 mL). For the avoidance of hydrolysis during the extraction it is recommended that the solution be kept cold (~10 °C). The acidic aqueous layer was washed with ether (2 × 20 mL), made alkaline (first with K_2CO_3 to avoid a temperature increase and finally with a few NaOH pellets), and extracted with ether (3 × 20 mL). After the extract was dried (K_2CO_3) and the solvent evaporated, the crude, but essentially pure, product (1.53 g) was bulb to bulb distilled to give 1.43 g (61%) of pure amino acetate. For the spectral data see Table IV.

2-(Dimethylamino)-3-phenoxybutane was prepared from (*E*)-2-butene in a manner analogous to the general procedure for oxyamination by using phenol instead of acetic acid. The oxidant used was NBS: yield 19%; NMR ($CDCl_3$) δ 7.4–6.7 (m, 5, aromatic), 4.44 (m, 1, CH–O), 2.68 (m, 1, CH–N), 2.33 (s, 6, $(CH_3)_2N$), 1.23 (d, 3, CH_3), 1.04 (d, 3, CH_3).

Debenzylation of *N*-Benzyl-*N*-methyl-1-amino-2-butanol. The amino alcohol (1 g, 5.1 mmol) and palladium on carbon (40 mg, 10% Pd) were mixed in 2 mL of ethanol. The air was removed, and the mixture was treated with hydrogen (1 atm) for 20 h. Then the solution was filtered, made acidic (5 mL of 2 M HCl), and concentrated (to remove ethanol). The aqueous layer was washed twice with ether, made alkaline (NaOH pellets), and extracted with ether (4 × 5 mL). The extract was dried (K_2CO_3) and the ether evaporated to give 0.51 g of *N*-methyl-1-amino-2-butanol (97%) that was identified by comparison with an authentic sample.[32]

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Registry No. *erythro*-**5**, 56990-39-7; *threo*-**5**, 56956-10-6; **6a**, 73687-80-6; **6b**, 73687-81-7; **7a**, 73687-82-8; 1-(dimethylamino)-2-hexanol, 56956-07-1; 1-hexene oxide, 1436-34-6; 1-(diethylamino)-2-hexanol, 56956-07-1; dimethylamine, 124-40-3; diethylamine, 109-89-7; 2-(diethylamino)-1-phenylethanol, 4249-64-3; styrene oxide, 96-09-3; (*E*)-2-butene oxide, 21490-63-1; (*Z*)-2-butene oxide, 1758-33-4; 1-(dimethylamino)-2-butanol, 3760-96-1; 1-butene oxide, 106-88-7; 1-(dimethylamino)-2-decanol, 20542-99-8; 1-decene oxide, 2404-44-6; 1-(benzylmethylamino)-2-butanol, 73687-83-9; *N*-methylbenzylamine, 103-67-3; 1-acetoxy-2-(diethylamino)-1-phenylethane, 4152-30-1; styrene, 100-42-5; 2-(dimethylamino)-3-phenoxybutane, 73687-84-0; (*E*)-2-butene, 624-64-6; *N*-methyl-1-amino-2-butanol, 42163-27-9; ethene, 74-85-1; 1-butene, 106-98-9; (*Z*)-2-butene, 590-18-1; 1-hexene, 592-41-6; 1-decene, 872-05-9; (*E*)-1-phenylpropene, 873-66-5; allyl phenyl ether, 27318-96-3; $Et_2NCH_2CH_2OAc$, 10369-82-1; $C_2H_5CH(NMe_2)CH_2OH$, 17199-17-6; $C_2H_5CH(OH)CH_2NMe_2$, 3760-96-1; $C_2H_5CH(MeNCH_2Ph)CH_2OAc$, 73687-85-1; $C_2H_5CH(OAc)CH_2N(CH_2Ph)Me$, 73687-86-2; *threo*-$MeCH(OAc)CH(NEt_2)Me$, 73687-87-3; *n*-$C_4H_9CH(NMe_2)CH_2OAc$, 56956-05-9; *n*-$C_4H_9CH(OAc)CH_2NMe_2$, 56955-97-6; *n*-$C_4H_9CH(NEt_2)CH_2OAc$, 73687-88-4; *n*-$C_4H_9CH(OAc)CH_2NEt_2$, 73687-89-5; *n*-$C_8H_{17}CH(NMe_2)CH_2OAc$, 56956-06-0; *n*-$C_8H_{17}CH(OAc)CH_2NMe_2$, 56955-98-7; $PhCH(OAc)CH_2NEt_2$, 4152-30-1; *erythro*-$PhCH(OAc)CH(NMe_2)Me$, 73744-65-7; *threo*-$PhCH(OAc)CH(NMe_2)Me$, 73744-66-8; $PhOCH_2CH(OAc)CH_2NMe_2$, 73687-90-8; $PhOCH_2CH(OAc)CH_2NEt_2$, 38302-63-5.

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