Palladium-Catalyzed 1,4-Acetoxy-Trifluoroacetoxylation and 1,4-Alkoxy-Trifluoroacetoxylation of Cyclic 1,3-Dienes. Scope and Mechanism

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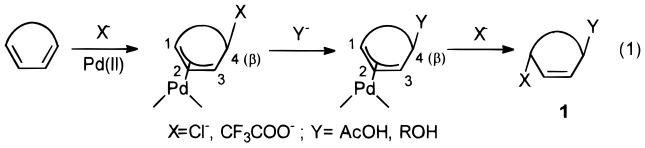
Palladium-catalyzed unsymmetrical 1,4-functionalizations of cyclic 1,3-dienes are described. Trifluoroacetate in combination with acetate or alcohols is utilized to obtain 1-acetoxy-4-(trifluoroacetoxy)-2-cycloalkenes and 1-alkoxy-4-(trifluoroacetoxy)-2-cycloalkenes, respectively, with good regio- and stereoselectivities. The chemoselectivity of these reactions relies on the different kinetic stability of the intermediate 4-(trifluoroacetoxy)-, 4-acetoxy-, and 4-methoxy-[η^3-(1,2,3)-cycloalkenyl]palladium complexes. Under the acidic reaction conditions employed, the 4-trifluoroacetoxy π-allyl intermediate is the least stable of the three. Certain mechanistic aspects of the reactions are discussed in the light of DFT calculations.

Introduction

Electrophilic addition to conjugated dienes have found limited use in organic synthesis, mainly due to problems with regio- and stereoselectivity.[1] Until recently, the major use of conjugated dienes has been in cycloadditions of different types.[2] During the last two decades, however, metal-mediated additions to conjugated dienes have attracted considerable interest,[3,4] and in particular, transition metal-catalyzed reactions via π-allyl complexes have evolved as viable processes.[4,5] These reactions often offer useful levels of regio- and stereocontrol.

We have previously reported on several different palladium(II)-catalyzed 1,4-oxidations of conjugated dienes.[6] These reactions, which proceed via (π-allyl)-palladium intermediates, are highly regio- and stereoselective and can be performed with a number of different hetero[7] and carbon nucleophiles[8] under mild conditions. The synthetic utility of these processes has been successfully demonstrated in natural product synthesis.[9] An intriguing feature of these reactions is that under the appropriate conditions two different nucleophiles can be added to the diene leading to unsymmetrical products **1** (X ≠ Y, eq 1). Examples of such reactions are the palladium-catalyzed 1,4-chloroacetoxylation[10] and the 1,4-acetoxy-trifuoroacetoxylation.[11] The success of these unsymmetrical additions relies on the fact that one of the two nucleophiles employed forms a kinetically unstable 4-substituted (π-allyl)palladium intermediate. The kinetic stability of the (π-allyl)palladium intermediate depends on the polarity of the C4−X(Y) bond. In the case of a polar C4−X(Y) bond the functionality at the 4-position can be readily exchanged to another group in a palladium-assisted process.[10,12]



(1)

This exchange involves an anchimeric assistance by palladium via a (π-diene)palladium complex and proceeds with retention of configuration.

Unsymmetrical bis-allylic compounds **1** are useful building blocks in organic synthesis[4−6,10,13] since they can be selectively functionalized at either allylic position. In

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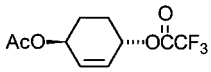
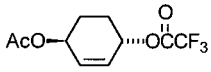
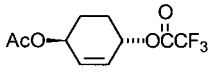
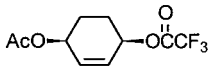
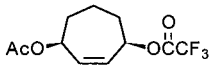
Table 1. Palladium(II)-Catalyzed 1,4-Acetoxy-Trifluoroacetoxylation

entry	diene	solvent	additives (equiv.)	yield (%)[a]	product[c]
1		CH_2Cl_2/ HOAc	CF_3COOLi, (1) CF_3COOH, (2) $(CF_3CO)_2O$ (1.5)	74	 **2** (93 % *trans*)
2		CH_2Cl_2/ HOAc	CF_3COOLi, (1) CF_3COOH, (2)	n.d.[b]	Mixture of products; low yield and selectivity
3		CH_2Cl_2/ HOAc	CF_3COOLi, (2) CF_3COOH, (5) $(CF_3CO)_2O$ (1.5)	n.d.[b]	 **2** (80 % *trans*)
4		CH_2Cl_2/ HOAc	CF_3COOLi, (2) CF_3COOH, (2) $(CF_3CO)_2O$ (1.5)	78	 **2** (88 % *trans*)
5		Acetone/ HOAc	CF_3COOLi, (5) CF_3COOH, (2) $(CF_3CO)_2O$ (2) CH_3CN (2)	40	 **3** (83% *cis*)
6		HOAc	CF_3COOLi, (4) CF_3COOH, (5)	58	 **4** (96% *cis*)

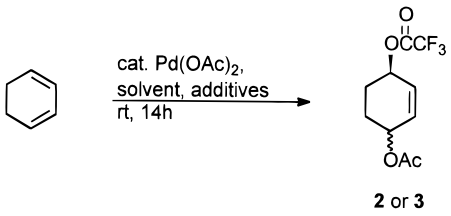
[a] Isolated yields. [b] Not determined. [c] Determined by ^1H NMR spectroscopy.

particular when X and Y are leaving groups of different reactivity, sequential nucleophilic substitution (either S_N2 or metal-mediated) offers unique opportunities for regioselective functionalizations. In view of the synthetic versatility of these unsymmetrical compounds, further studies on the palladium-catalyzed 1,4-oxidation of 1,3-dienes leading to their formation were desirable.

In this paper we report on the use of trifluoroacetate as an exchangeable nucleophile and the application to 1,4-acetoxy-trifluoroacetoxylation[14] and 1,4-alkoxy-trifluoroacetoxylation of cyclic 1,3-dienes. An important observation is that the stereoselectivity of the 1,4-acetoxy-trifluoroacetoxylation reaction can be reversed by addition of acetonitrile. The mechanism of the reactions is discussed in the light of density functional calculations.

Results and Discussion

1,4-Acetoxy-Trifluoroacetoxylation. Palladium-catalyzed oxidation of 1,3-dienes was performed in dichloromethane/acetic acid or acetone/acetic acid solvent mixtures in the presence of lithium trifluoroacetate, trifluoroacetic acid, and trifluoroacetic anhydride using palladium acetate as the catalyst (eq 2). The reoxidation system manganese dioxide with catalytic amounts of *p*-benzoquinone (BQ) was employed.[15]



2 or **3** (2)

High chemoselectivities were obtained in the case of 1,3-cyclohexadiene and 1,3-cycloheptadiene, the 1-acetoxy-4-(trifluoroacetoxy)-2-alkenes being the main product.[16] Formation of the two symmetric side products (diacetate and bis-trifluoroacetate) was also observed but the relative amounts of these can be kept low by carefully tuned reaction conditions. The influence of some additives were studied in the oxidation of 1,3-cyclohexadiene, and the results are summarized in Table 1.

Trifluoroacetic anhydride proved to be an essential additive (cf. entries 1 and 2). Its role is to trap the water formed from manganese dioxide in the reaction. The presence of water would result in substantial hydrolysis of the trifluoroacetate group in the products under the strong acidic conditions employed. The optimum amount of lithium trifluoroacetate is between 1 and 2 equiv. One equivalent gave slightly better selectivity but lower yield, while 2 equiv gave slightly higher yield but lower stereo-

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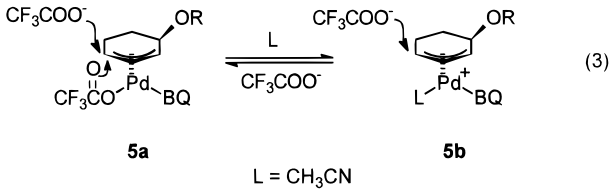
(14) A correction to the previously published procedure[11] is given in the Experimental Section.
(15) The oxidation system MnO_2/cat. BQ was developed in our laboratory in 1983: Bäckvall, J. E. *Pure Appl. Chem.* **1983**, *55*, 1669. Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619.
(16) Cyclooctadiene as well as acyclic dienes gave worse chemoselectivity and in some of the cases bad regioselectivity.[11]

selectivity (cf. entries 1 and 4). Further increase of this additive led to increase in the bis-trifluoroacetoxy side product. High trifluoroacetic acid concentration reduces the relative amount of the diacetates formed, but as a side effect the stereoselectivity drops as well. Thus, the use of 5 equiv of trifluoroacetic acid afforded **2** with a *trans*:*cis* ratio of 80:20 (entry 3). With addition of acetonitrile, and changing the solvent from dichloromethane to acetone−acetic acid (1:1), the stereochemistry of the 1,4-addition could be reversed providing predominantly the *cis*-product. Accordingly, with the use of 2 equiv of acetonitrile, compound **3** was obtained with a *cis*:*trans* selectivity of 83:17, however, only in a moderate yield (40%, entry 5).

The effect of acetonitrile on the stereoselectivity can be explained by its coordination to palladium leading to the displacement of the coordinated trifluoroacetate. In this way the migration pathway is blocked, and the external attack is favored. Nitriles are known to coordinate well to Pd(II) and form stable isolable complexes.[17]

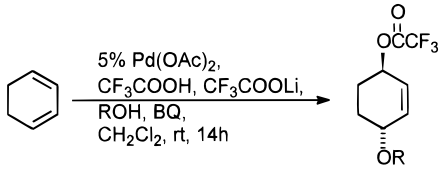


(3)

Acetonitrile also increases the polarity of the reaction medium which is expected to favor the ionic dissociation of trifluoroacetate from the (π-allyl)palladium trifluoroacetate. Even though, the cationic (π-allyl)palladium intermediate **5b** (eq 3) is expected to be more reactive than the neutral one (**5a**), trifluoroacetate is a very weak nucleophile, and therefore high yields from external attack are difficult to obtain.

When 1,3-cycloheptadiene was used as substrate, predominantly the *cis*-product **4** was formed. This result is in line with previous studies,[6b,11] where it was suggested that the geometry required for the *cis*-migration is unfavorable in the case of the seven-membered ring (entry 6).

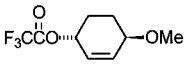
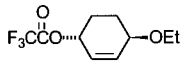
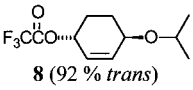
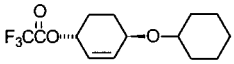
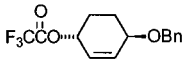
1,4-Alkoxy-Trifluoroacetoxylation. In the presence of various alcohols, trifluoroacetic acid, lithium trifluoroacetate and a stoichiometric amount of BQ, unsymmetrical alkoxy-trifluoroacetoxy compounds were obtained in fairly good yields and good stereoselectivities in a palladium-catalyzed oxidation (eq 4, Table 2).



(4)

Palladium acetate and palladium trifluoroacetate were tested as catalysts, and the former was found to give cleaner reactions and higher yields. To achieve a maximum amount of the unsymmetrical product, the relative amounts of the acid, the alcohol, and the lithium trifluoroacetate had to be optimized. Thus, 8.2 equiv of the alcohol, 4 equiv of trifluoroacetic acid, and 1 equiv of lithium trifluoroacetate gave the best results.

Table 2. Palladium(II)-Catalyzed 1,4-Alkoxy-Trifluoroacetoxylation[a]

entry	alcohol	yield (%)[b]	product[c]
1	methanol	61	 **6** (92 % *trans*)
2	ethanol	67	 **7** (93 % *trans*)
3	isopropanol	55	 **8** (92 % *trans*)
4	cyclohexyl-alcohol	63	 **9** (92 % *trans*)
5	benzyl alcohol	68	 **10** (93 % *trans*)

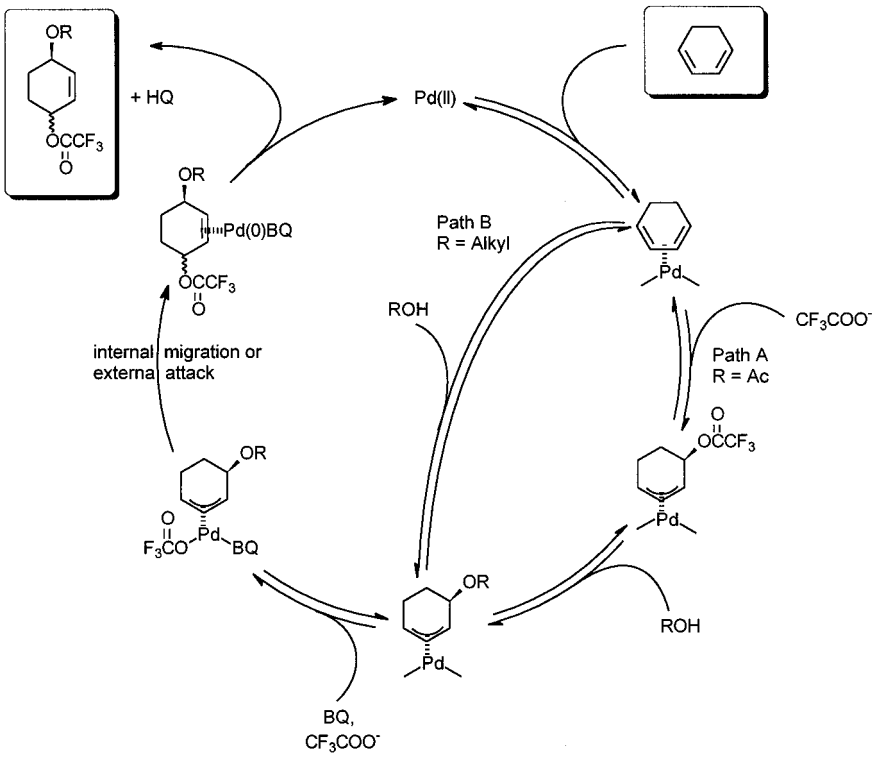
[a] The reactions were performed using 5% $Pd(OAc)_2$, 1 equiv of CF_3COOLi, 4 equiv of CF_3COOH, 8.2 equiv of ROH, and 1.5 equiv of BQ in 6 mL of CH_2Cl_2. [b] Isolated yields. [c] Determined by ^1H NMR spectroscopy.

Mechanism. According to the accepted mechanistic scheme of the palladium-catalyzed 1,4-oxidation of conjugated dienes (Scheme 1),[6] this reaction proceeds via coordination of the diene to the active palladium species, followed by *trans* attack of the nucleophile on one of the double bonds. In the 1,4-acetoxy-trifluoroacetoxylation, under the acidic reaction conditions employed, the trifluoroacetate is the strongest nucleophile available. The initial formation of the 4-trifluoroacetoxy-[η^3-(1,2,3)-allyl]-palladium complex is also indicated by the presence of a small amount of the bis-trifluoroacetate product in the final reaction mixture. However, this 4-trifluoroacetoxy substituted (π-allyl)palladium intermediate (eq 1) is kinetically unstable under the reaction conditions (vide infra), and therefore, the trifluoroacetoxy group can readily be displaced by another functionality, such as alkoxy or acetoxy, which forms a more stable C4−O bond (path A). In the case of the 1,4-alkoxy-trifluoroacetoxylations a direct nucleophilic attack on the palladium−diene complex is a likely competing pathway (path B).

The kinetically stable (π-allyl)palladium complex can subsequently react with a second nucleophile. Coordination of BQ activates the π-allyl intermediate which then will be attacked by the best nucleophile available. Addition of lithium trifluoroacetate ensures a high trifluoroacetate concentration, and therefore, the second nu-

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

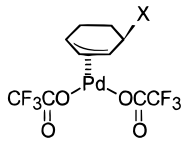
Scheme 1



cleophilic attack will be performed by trifluoroacetate, either by *cis*-migration or external attack. Internal attack via *cis*-migration leads to a *trans*-product (entries 1, 3, and 4 in Tables 1 and 1−5 in Table 2), whereas external attack by trifluoroacetate furnishes a *cis*-product (entries 5 and 6, Table 1). With 1,3-cyclohexadiene as a substrate, the stereochemistry of the nucleophilic attack can be reversed from *trans* to *cis* (entry 5 in Table 1). Trifluoroacetate is a weakly coordinated ligand on palladium(II), and in the presence of acetonitrile in an acetone/acetic acid solvent mixture it can be displaced, giving rise to more external attack.

Theoretical Results. The palladium-assisted exchange of the 4-functionality in the [η^3-(1,2,3)-allyl]-palladium intermediates is a mechanistically interesting process of the 1,4-alkoxy-trifluoroacetoxylation and 1,4-acetoxy-trifluoroacetoxylation reactions, and it is also responsible for the chemoselective formation of the unsymmetrical products. Functional groups in the 4-position (X or Y in eq 1) of (π-allyl)palladium complexes may interact with the palladium atom. The intensity of this 4-substituent effect (β-substituent effect) depends on the conformation of the X(Y) functionality, the polarity of the C4−X(Y) bond, and the σ-donor π-acceptor property of the ancillary ligands on palladium.[12] Various aspects of these substituent effects have been discussed in three recent publications,[12] and therefore, in this theoretical section we discuss only those features, which are of relevance for the present catalytic reactions.

A particularly important consequence of the 4-substituent effect is the elongation and weakening of the C4−X(Y) bond in the substituted (π-allyl)palladium intermediates. It has been shown[12] that increase of the polarity of the C4−X(Y) bond leads to weakening of this bond and, accordingly, decrease of the kinetic stability of the complex. In the investigated catalytic 1,4-oxidation reactions three different π-allyl complexes (Figure 1, **11a**−**13a**) are involved as a result of the first nucleophilic attack. Density functional calculations on these complexes show[18] (Figure 1) that the C4−O bond in the trifluoroacetoxy complex **13a** is longer (1.542 Å) than the corresponding distance in the acetoxy (**12a**, 1.514 Å), or methoxy complexes (**11a**, 1.483 Å). Other structural parameters, such as C3−C4 and Pd−C3 bond lengths, also suggest a more intensive 4-substituent effect[12] in compound **13a** than in **11a** or **12a**.



11-13
(for a definition of X, see Figure 1)

In the presence of trifluoroacetic acid the 4-functionality (OMe, OAc, $OCOCF_3$) can be protonated. Protonation of the O4 atom further increases the polarity of the C4−O bonds thereby amplifying the 4-substituent effect. We also attempted to optimize the O-protonated structures, but these complexes did not represent a minimum on the potential energy surface, since during the optimization dissociation of the C4−O bond occurred. Therefore, the properties of the protonated species could only be studied by freezing the C4−O bond lengths at various distances, while optimizing the rest of the geometrical parameters.

In the protonated complexes **11b**−**13b**[19] the C4−O distance is constrained at 1.6 Å, which would be conceiv-

(18) In all these compounds there are two conformations the boat and the chair, which have about the same energy. As the β-substituent effect is stronger in the chair conformation than in the boat one, only the former was considered here. For the different conformers of similar compounds see ref 12.

(19) In the case of the acetate and trifluoroacetate, protonation at the carbonyl oxygen is energetically more favorable. However, protonation of O4 allows direct comparison with the methoxy group. See ref 12c.

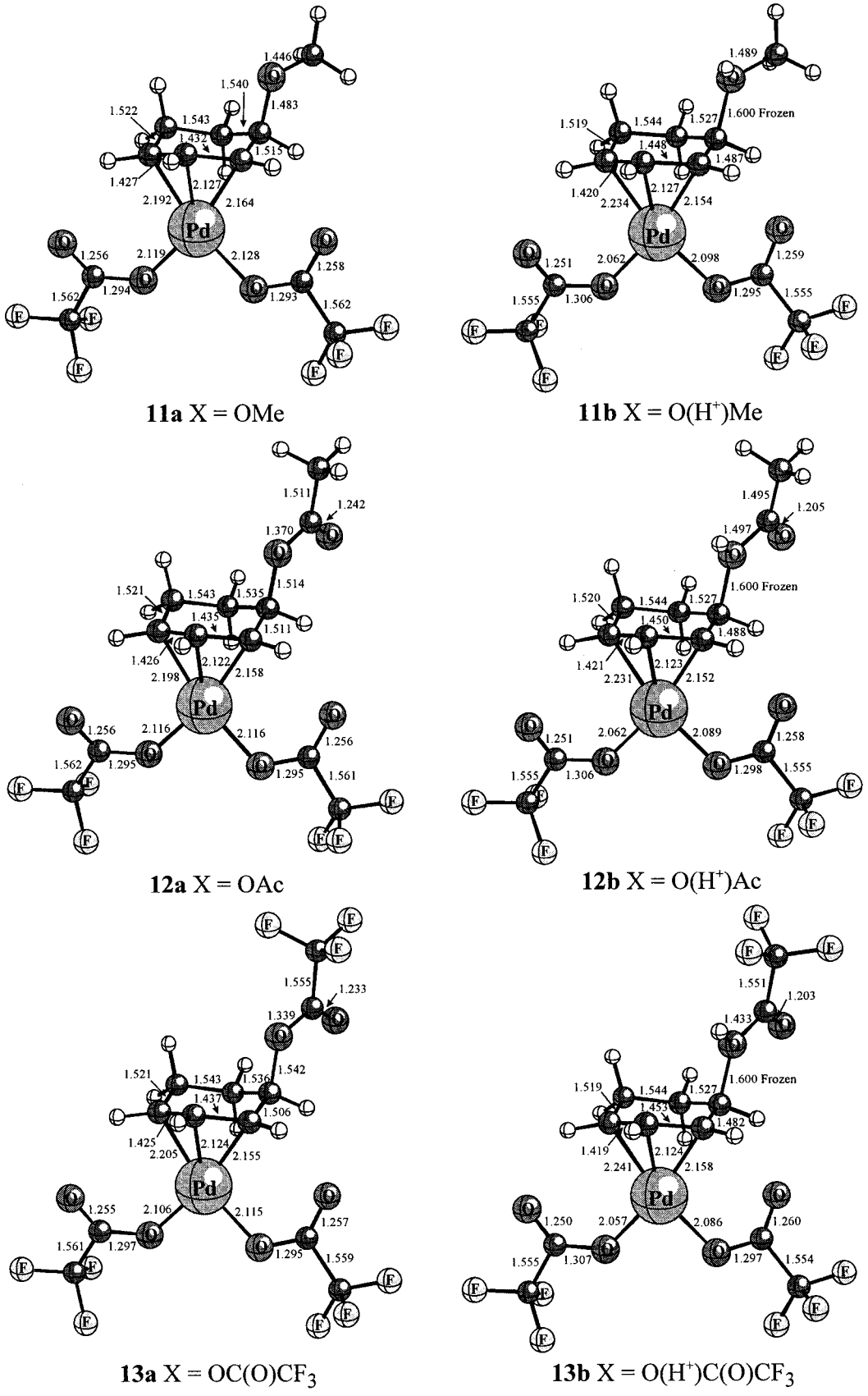


Figure 1. B3PW91/LANL2DZ-optimized geometries of **11a,b**−**13a,b**.

able for the equilibrium bond length in an O-protonated C−O(H)−C structure (Figure 1). Comparison of the geometry of **11a**−**13a** with **11b**−**13b** reveals some typical structural effects of the enhanced β-substituent effects: (a) increased difference between the Pd−C1 and Pd−C3 bond lengths; (b) shortening of the C3−C4 bond indicating the enhanced π-character of the C3−C4 bond.[20] The stability of the protonated complexes was investigated

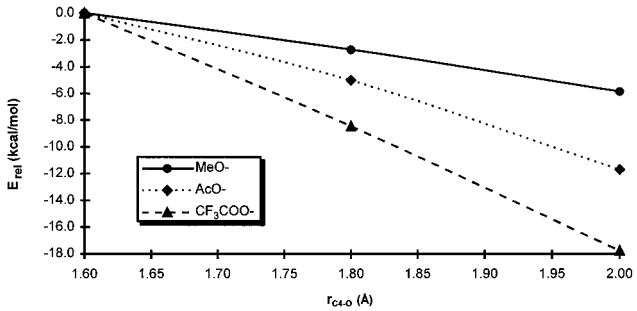


Figure 2. Calculated relative B3PW91/LAN2DZ+P//B3PW91/LAN2DZ energies of complexes **11b**−**13b** as a function of C4−O bond distances.

in two additional points of the potential energy surface. Freezing the C4−O distance at 1.8 Å led to a sharp decrease of total energies (Figure 2). When the C4−O bond was constrained at 2.0 Å, which would be expected for the transition state of a C−O bond cleavage, a further decrease of the total energy occurred for all three complexes. The energy decrease was considerably greater for the trifluoroacetoxy substituted complex (17.8 kcal/mol) than the acetoxy (11.7 kcal/mol) or methoxy (5.8 kcal/mol) substituted ones.

The results clearly show the expected trend, namely that the reactivity order of these groups in the acid-catalyzed C4−O bond cleavage is the following: $CF_3COO^- > AcO^- > MeO^-$.[21] This means that in any combination of these nucleophiles, the more reactive[22] will form a kinetically less stable 4-substituted [η^3-(1,2,3)-allyl]palladium intermediate, and under sufficiently acidic reaction conditions, unsymmetrical functionalization is possible.

Concluding Remarks

In the above study we have described a new method for preparation of some unsymmetrically substituted cycloalkenes. These products can be further functionalized selectively by for example Pd(0)-catalyzed allylic substitutions.[23] A mechanism for the alkoxy- and acetoxy-trifluoroacetoxylations has been suggested, which is supported by theoretical calculations performed on the proposed allylpalladium intermediates.

Computational Details. The geometries were optimized employing Density Functional Theory using a Becke[24] type three-parameter model B3PW91[25−27] in connection with the LANL2DZ basis set[28] (denoted as B3PW91/LANL2DZ). For single-point energy calculations of the protonated species the LANL2DZ basis set was augmented with one set of d polarization functions on the heavy atoms (LANL2DZ+P)[29] leading to a theoretical model, which is denoted as B3PW91/LANL2DZ+P//B3PW91/LANL2DZ. All calculations were performed on a Digital Alphastation 500 using Gaussian94 software package.[30]

Experimental Section

NMR spectra were recorded for $CDCl_3$ solutions (^{1}H at 400 MHz and ^{13}C at 100.5 MHz) using chloroform-*d* (7.26 ppm, ^{1}H, 77.0 ppm, ^{13}C) as internal standard. Coupling constants were evaluated using *J*-doubling[31] technique. Mass spectra were obtained in GC/MS mode (EI, 70 eV). Dichloromethane was distilled over CaH_2. Other solvents were used without further purification. $Pd(OAc)_2$ was purchased from Fluorochem. All other chemicals were bought from Lancaster or Aldrich and were used without further purification. Merck silica gel 60 (240−400 mesh) was used for flash chromatography.

***trans*-1-Acetoxy-4-(trifluoroacetoxy)-2-cyclohexene (2).** $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), lithium trifluoroacetate (180 mg, 1.5 mmol), CF_3COOH (230 μL, 3 mmol), $(CF_3CO)_2O$ (320 μL, 2.25 mmol), MnO_2 (157 mg 1.65 mmol), and *p*-benzoquinone (24 mg, 0.225 mmol) were dissolved in a mixture of 5 mL of CH_2Cl_2 and 2 mL of acetic acid. To this stirred solution freshly distilled 1,3-cyclohexadiene (147 μL, 1.5 mmol) was added via a syringe pump during 6−8 h. The reaction mixture was stirred for another 8 h at room temperature and then diluted with 50 mL pentane/ether (50/50). The resulting mixture was extracted with water (2 × 15 mL), brine (2 × 15 mL), saturated aqueous Na_2CO_3 (3 × 15 mL), and brine. The organic phase was dried over $MgSO_4$ and concentrated in vacuo. Rapid flash chromatography using an 85:15 mixture of pentane and ether as eluent gave 0.278 g (74%) of compound **2** as a colorless oil (93% *trans*). ^{1}H NMR: δ 6.05 (ddd, 1H, J = 10.0, 3.4, 1.5 Hz), 5.94 (ddd, 1H, J = 10.0, 3.7, 1.4 Hz), 5.52−5.47 (m, 1H), 5.36−5.30 (m, 1H), 2.27−2.11 (m, 2H), 2.06 (s, 3H), 1.92−1.82 (m, 1H), 1.82−1.72 (m, 1H); ^{13}C NMR: δ 170.3, 157.1 (q $^2J_{C-F}$ = 41.9 Hz), 132.5, 127.5, 114.4 (q $^1J_{C-F}$ = 286.1 Hz), 72.0, 66.6, 25.1, 25.0, 21.1; IR (in $CDCl_3$ solution): 3048, 2963, 2942, 1779, 1729, 1373, 1225, 1157, 1032, 1010 cm^{-1}; MS *m*/*z* (%): 252 (M^+, <1), 219 (<1), 209 (1) 192 (1), 139 (6), 96 (100), 79 (63), 69 (30). Anal. Calcd: C, 47.62; H 4.39. Found: C, 47.52; H, 4.32.

***cis*-1-Acetoxy-4-(trifluoroacetoxy)-2-cyclohexene (3).** $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), CF_3COOLi (900 mg, 7.5 mmol), CF_3COOH (230 μL, 3 mmol), MnO_2 (157 mg, 1.65 mmol), *p*-benzoquinone (35 mg, 0.33 mmol), $(CF_3CO)_2O$ (420 μL, 3 mmol), and acetonitrile (160 μL, 3 mmol) were dissolved in 5 mL of acetone/acetic acid (1:1). To this stirred solution was added 1,3-cyclohexadiene (147 μL, 1.5 mmol) via a syringe pump during 10 h. The reaction mixture was stirred for additional 12 h at room temperature, and then it was diluted with 50 mL of ether/pentane (50:50). The resulting mixture was worked up the same way as in the case of compound **2**, giving 0.148 g (40%) of colorless oil **2** (83% *cis*). ^{1}H NMR: δ 6.03 (dm, 1H, J = 10.1 Hz), 5.93 (dm, 1H, J = 10.1 Hz), 5.47−5.37 (m, 1H), 5.29−5.23 (m, 1H), 2.08 (s, 3H), 2.05−1.84 (m, 4H). ^{13}C NMR: δ 170.5, 157.1 (q $^2J_{C-F}$ = 42.7 Hz), 133.0, 127.1, 114.5 (q $^1J_{C-F}$ = 285.8 Hz), 71.7, 67.0, 24.5, 24.3, 21.1; IR (in $CDCl_3$ solution): 2962, 1780, 1727, 1374, 126, 1161, 1036 cm^{-1}; MS *m*/*z* (%): 192 (M^+ − 60, 1), 139 (12), 96 (100), 79 (56), 69 (34).

(20) The relationship between the geometrical parameters and the intensity of the β-substituent effects is discussed in ref 12.

(21) Even if the solvation effects raise an activation barrier to the C4−O bond cleavage, the intrinsic stabilization by the 4-substituent effect will lower most effectively the activation energy in case of the trifluoroacetoxy substituted complex **12b**.

(22) In the sense of the cleavage reaction.

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***cis*-1-Acetoxy-4-(trifluoroacetoxy)-2-cycloheptene (4).** $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), CF_3COOLi (720 mg, 6 mmol), CF_3COOH (580 μL, 7.5 mmol), *p*-benzoquinone (162 mg, 1.5 mmol), and MnO_2 (130 mg 1.5 mmol) were dissolved in 5 mL of acetic acid. To this stirred solution was added 1,3-cycloheptadiene (163 μL, 1.5 mmol) via a syringe pump over 6−8 h. The reaction mixture was stirred for further 16 h at room temperature, and then it was diluted with ether/pentane (50:50). The resulting mixture was worked up as in the case of compound **2**, resulting in 0.215 g of **4** as a colorless oil (96% *cis*).

***trans*-1-Methoxy-4-(trifluoroacetoxy)-2-cyclohexene (6).** $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), CF_3COOLi (180 mg, 1.5 mmol), CF_3COOH (430 μL, 6 mmol), *p*-benzoquinone (243 mg, 2.25 mmol), and methanol (0.5 mL 12.3 mmol) were dissolved in 6 mL of CH_2Cl_2. To this stirred solution was added 1,3-cyclohexadiene (147 μL, 1.5 mmol) via a syringe pump during 6−8 h. The reaction mixture was stirred for additional 16 h at room temperature. Then 50 mL of 50:50 mixture of ether and pentane was added, and the resulting mixture was extracted with water, brine, 2 M NaOH (2×) and brine. The organic phase was dried ($MgSO_4$) and then concentrated to give the crude product. Rapid flash chromatography with pentane/ether (90:10) as an eluent was used to separate the excess of the alcohol, and partially the quinone. The fractions containing the product were combined and concentrated, and the resulting mixture was subjected to a second flash chromatography using pentane/ether = 97:3 as eluent, which gave 0.230 g (61%) of **4** as a colorless oil (92% *trans*). The spectral data of this compound were identical with those previously reported.[32] This procedure is representative for the preparation of all the other *trans*-1-alkoxy-4-(trifluoroacetoxy)-2-cyclohexenes, using 8.2 equiv of the corresponding alcohols.

Correction of the Previously Published Procedure[11] for Preparation of Compound 2. To a stirred solution of $Pd(OAc)_2$ (700 mg, 3.12 mmol), CF_3COOH (9.5 mL, 125 mmol), $LiOOCCF_3$ (3.48 g, 32 mmol), MnO_2 (6.5 g, 75 mmol), $(CF_3CO)_2O$ (17.3 mL, 123 mmol), and *p*-benzoquinone (1.35 g, 12.5 mmol) in acetic acid (200 mL) at room temperature was added 1,3-cyclohexadiene (4.9 g, 61.3 mmol) over a period of 4 h. The reaction mixture was stirred for another 6 h and thereafter was poured into pentane/ether (9:1; 1500 mL). The resulting solution was washed with brine (150 mL), water (2 × 200 mL), sat. Na_2CO_3 (2 × 100 mL), 2 M NaOH (100 mL), water (100 mL), and brine (150 mL). The organic phase was dried and concentrated to give 11.3 g of crude product. Fractional bulb-to-bulb distillation afforded 10.3 g (67%) of compound **2** (92% *trans*) as a colorless oil, which contained traces of the bis-trifluoroacetate side product.

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Supporting Information Available: Experimental and characterization data for compounds **4**, **7**−**10**. Copies of ^1H and ^{13}C NMR spectra for compound **8** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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