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Unsymmetrical Functionalization of 1,3-Cyclohexadienes: Palladium-Catalyzed Stereoselective 1,4-Acyloxy-Alkoxylation

Eike Hupe, Kenichiro Itami#, Attila Aranyos, Kálmán J. Szabó* and Jan-E. Bäckvall*

University of Uppsala, Department of Organic Chemistry

Box 531, S-751 21 Uppsala, Sweden

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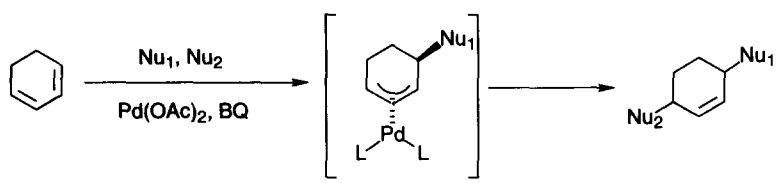
Summary. Palladium-catalyzed reaction of 1,3-cyclohexadiene with alcohols and acetic or benzoic acid under mild acidic conditions gives *trans*-1-acetoxy- or *trans*-1-benzyloxy-4-alkoxy-2-cyclohexenes, respectively, with high regio- and stereo-selectivity. The unsymmtrical 1,4-acyloxy-alkoxy products are obtained by fine tuning the reaction conditions in a narrow pH range.

The application of allylpalladium chemistry to organic synthesis has made remarkable progress in recent decades.[1-4] One of the most intriguing aspects of this type of chemistry is the possibility of controlling the selectivity of the nucleophilic attack on the allyl moiety by choosing the reaction conditions and the ancillary ligands on palladium.[3,5-9] A remarkably high control of regio-, stereo- and chemoselectivity can be accomplished in palladium-catalyzed 1,4-oxidation of conjugated dienes with benzoquinone (BQ) as oxidant.[10,11] Using this procedure a tandem functionalization by two different external nucleophiles (Nu_1 and Nu_2, eq 1) can be done leading to unsymmetrically substituted products from symmetrical substrates.[10-12]



(1)

Unsymmetrical bis-allylic compounds are useful building blocks in organic synthesis, since they can be selectively functionalized at either allylic position. In this respect, bis-allylic compounds bearing an acyloxy and an alkoxy functionality are particularly useful synthons, because of the markedly different reactivity of these functionalities in palladium-catalyzed allylic substitution and other nucleophilic substitution reactions.

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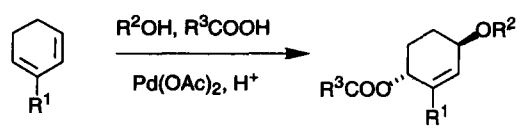
Preparation of bis-allylic compounds with an acyloxy and an ether functionality can be achieved by for example partial alkylation of 1,4-dihydroxy 2-alkenes followed by esterification,[13] however the yield of the alkylation reaction is rather low.[13] Selective ether formation by alkylation of one of the bis-allylic functionalities is rather difficult to achieve, since the basic reaction conditions employed can affect the other allylic functionality (e.g. OH, OAc, Cl) and/or the double bond. Introduction of a secondary or a tertiary ether functionality is even more complicated due to the bulkiness of the alkylating group. Therefore, an attractive approach is to introduce the acyloxy and alkoxy groups in one reaction step by tandem functionalization of conjugated dienes.

In a recent publication[12] on trifluoroacetoxylation of 1,3-dienes we described a new method for 1,4-alkoxy-trifluoroacetoxylation of cyclic conjugated dienes, which is suitable for the synthesis of bis-allylic compounds having a trifluoroacetoxy and a primary or secondary alkoxy functionality. Attempts to extend this method to carboxylic acids which form more stable esters failed and resulted in predominant 1,4-diacyloxylation. On the other hand, addition of a strong acid led only to 1,4-dialkoxylation. However, we have now found that by fine tuning the reaction conditions in a narrow pH range, a selective 1,4-alkoxy-acetoxylation of 1,3-cyclohexadienes can be obtained.

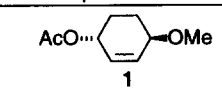
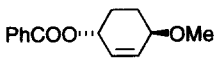
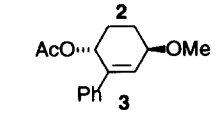
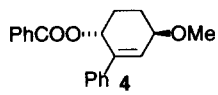
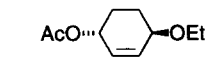
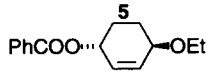
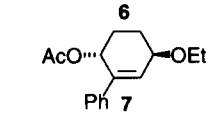
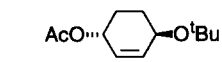
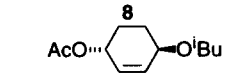
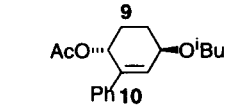
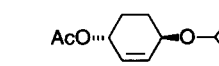
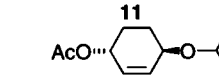
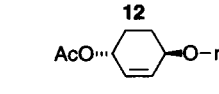
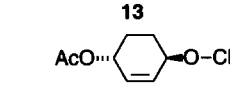
Catalytic Acyloxy-Alkoxylation of 1,3-Cyclohexadienes. Initial attempts to obtain 1,4-acetoxy-alkoxylation of 1,3-cyclohexadiene under the usual reaction conditions of 1,4-oxidation[14] in the presence of alcohols resulted mainly in formation of 1,4-diacetate. This can be explained by the fact that acetate is a relatively good nucleophile, and apparently competes in the first addition to the diene providing a 4-acetoxy-(η^3-allyl)palladium complex (Nu_1 = OAc, eq 1). Such a problem was not encountered in the alkoxy-trifluoroacetoxylation, where the trifluoroacetate ion employed is a very weak nucleophile, and, therefore it cannot compete with the alcohol nucleophile. An obvious solution to the problem with the acetate would be to reduce the concentration of free acetate ion by, for example, lowering the pH. However, attempted 1,4-acetoxy-alkoxylation in acetic acid in presence of an alcohol and a strong acid (H_2SO_4) in high concentration afforded mainly the 1,4-dialkoxy compound.

In order to obtain an unsymmetrical product instead of a symmetrical one, the usual reaction conditions of 1,4-oxidiation of dienes had to be changed: (1) RCOOLi salt was not employed in order to lower the concentration of the carboxylate nucleophile; (2) Catalytic amount of H_2SO_4 was added to the reaction mixture. Under these reaction conditions various alcohols and acetic (R^3 = CH_3) or benzoic (R^3 = Ph) acid were reacted with 1,3-cyclohexadiene (R_1 = H) as well as 2-phenyl-1,3-cyclohexadiene (R^1 = Ph) leading to *trans*-1-acetoxy-4-alkoxy-cyclohexenes in fairly good yields and very high stereoselectivities (eq 2, Table 1). In the case of 2-phenyl-1,3-cyclohexadiene a catalytic amount of 2-(*p*-tolylsulfinyl)-5-*tert*-butyl-1,4-benzoquinone (see method B in the experimental part) was employed as ligand, since this ligand gave asymmetric induction in the palladium catalysed 1,4-diacetoxylation.[15]

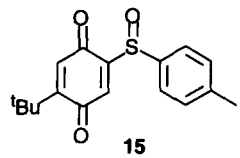


(2)

Table 1. Palladium-catalyzed 1,4-Acyloxy Alkoxylation

entry	R^1	R^2	R^3	method[a]	product	yield[b]	chemo-selectivity	stereo-selectiviy
1	H	Me	Me	A	 **1**	60 %	85 %	> 98%
2	H	Me	Me	A	 **2**	60 %	87 %	> 98%
3	Ph	Me	Me	B	 **3**	63 %	> 98 %	> 95%
4	Ph	Me	Ph	B	 **4**	65 %	> 98 %	> 95%
5	H	Et	Me	A	 **5**	56 %	85 %	> 98%
6	Ph	Et	Me	D	 **6**	60 %	87 %	> 98%
7	Ph	Et	Me	B	 **7**	58 %	> 98 %	> 98%
8	H	^{t}Bu	Me	C	 **8**	54 %	> 85 %	> 98%
9	H	^{i}Bu	Me	B	 **9**	68 %	90 %	> 98%
10	Ph	^{i}Bu	Me	B	 **10**	54 %	> 98 %	> 98%
11	H	cyclopentyl	Me	A	 **11**	56 %	90 %	> 98%
12	H	cyclohexyl	Me	A	 **12**	59 %	92 %	> 98%
13	H	2-menthyl	Me	A	 **13**	59 %	92 %	> 98%
14	H	$PhCH_2$	Me	A	 **14**	68 %	87 %	> 98%

[a] Method A: 5 mol% $Pd(OAc)_2$, 2.5 mol% H_2SO_4, 2.6 equiv. of acetic acid or benzoic acid, 4 equiv. of alcohol, 2 equiv. of BQ in 10 ml CH_2Cl_2 at r.t. Method B: 10 mol% of $Pd(OAc)_2$, 5 mol% of H_2SO_4, 10 equiv. of acetic acid or benzoic acid, 20 equiv. of alcohol, 10 mol% of **15** in 10 ml of CH_2Cl_2 at 40°C. Method C same as method A except that 10 mol% of $Pd(OAc)_2$ and 11 equiv. of ^{t}BuOH were employed. Method D: The same as method A, except that 3.9 equiv. of EtOH, 2.2 equiv. benzioc acid and 0.06 ml of stock solution was employed. [b] Isolated yields.



15

quinone used in Method B

Chemoselectivity. The chemoselectivity of the reaction could be controlled by the amount of H_2SO_4 added. The largest amount of the unsymmtrical product was obtained when the H_2SO_4 concentration was about half of the concentration of the palladium catalyst: 2.5 mol% in Method A and 5 mol% in method B. It is assumed that under these conditions $Pd(OAc)_2$ is converted to the cationic $[PdOAc]^+$, which is probably the active catalyst in the reaction.

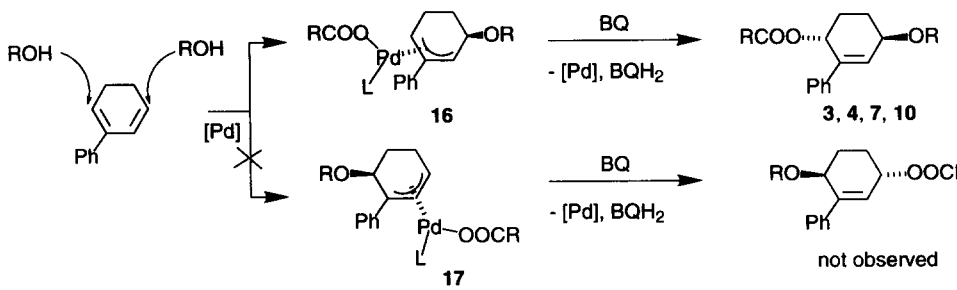
The best chemoselectivity (>98%) was accomplished for 2-phenyl-1,3-cyclohexadiene using method B (entries 3,4,7 and 10). Under these conditions, both acetoxy and benzoyloxy functionalities were introduced without formation of the symmetrical product. Using the appropriate reaction conditions a chemoselectivity of 85-92 % was accomplished for 1,3-cyclohexadiene employing method A (Table 1). The symmetrically substituted 1,4-dialkoxy- and 1,4-diacetoxycyclohexenyl side products were easily removed by silica-gel chromatography. The chemoselectivity was slightly better for secondary alcohols and benzyl alcohol (entries 9-14), than for methyl and ethyl alcohols (entries 1-2 and 5-6). The catalytic reaction was rather slow in the case of ^{t}BuOH (entry 8). In this reaction the diacetoxylation process was more extensive than for other substrates. The yield of unsymmetrical product was improved by the use of a high concentration of ^{t}BuOH (35 mmol) and 10 mol % $Pd(OAc)_2$ (Method C).

Stereoselectivity. The *trans* stereoselectivity of the present acyloxy-alkoxylation reaction is better than that of any other known palladium-catalyzed intermolecular 1,4-oxidation of conjugated dienes.[4] In the crude products only the *trans* isomer was observed by ^{1}H NMR spectroscopy. Due to the remarkably high stereoselectivity (Table 1) the isolated yields are relatively high even in such processes, where the chemoselectivity is somewhat lower (entries 1 and 4).

The very high stereoselectivity in the acyloxy-alkoxylation reactions is rather interesting in view of the fact that in palladium catalyzed *trans*-diacetoxylation of 1,3-cyclohexadiene, the *cis* isomer also forms up to 9%.[14] Furthermore, under the reaction conditions of acyloxy-alkoxylation in the absence of alcohol the *cis*- and *trans*-1,4-diacetoxy products are formed in a 1:1 ratio. Mechanistic studies on the variation of stereoselectivity as a function of nucleophiles in 1,4-oxidation reactions are in progress.

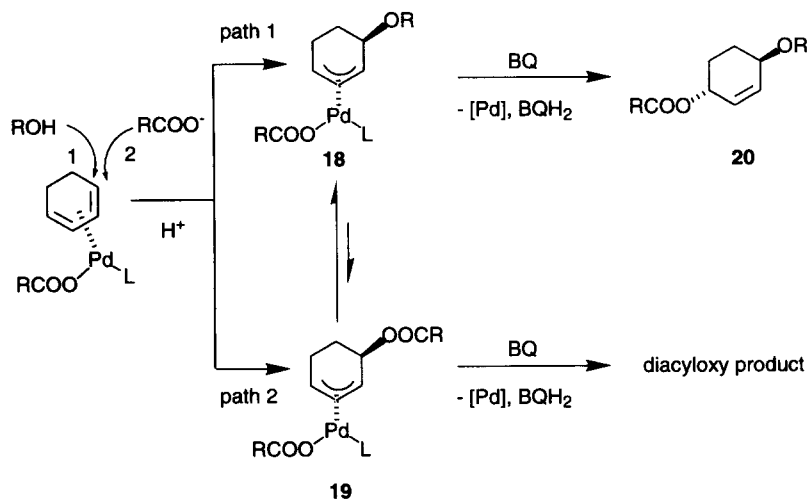
Regioselectivity. Similarly to other 1,4-oxidation reactions of conjugated dienes the 1,4-regioselectivity of the acyloxy-alkoxylation reaction is very high. Formation of 3-acetoxy-4-alkoxycyclohexenes expected from 1,2-addition to 1,3-cyclohexadiene was not observed. It is especially interesting that the reaction is regioselective even in the case of 2-phenyl-1,3-cyclohexadiene, since the acyloxy-alkoxylation may afford two 1,4-regioisomers. It is reasonable to assume that the first nucleophilic attack takes place at the less hindered terminal position of the diene to give the more stable (η^3-allyl)palladium complex **16** (eq 3).[10] Considering that the reactions gave only *trans*-1-acyloxy-2-phenyl-4-alkoxy-2-cyclohexene products (**3, 4, 7, 10**), it is reasonable to

assume that alcohol is the first nucleophile. A subsequent *cis*-migration by coordinated carboxylate would produce the regioisomer observed.



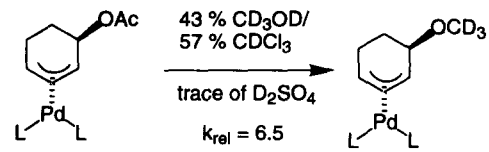
(3)

Mechanism. According to the accepted mechanistic scheme of the palladium catalyzed 1,4-oxidation of conjugated dienes, this reaction proceeds via coordination of the diene to the active palladium species, followed by a *trans* attack by the nucleophile at one of the double bonds.[14,16] In the presence of RCOO(H) and ROH nucleophiles two different allylpalladium complexes may form. Addition of catalytic amounts of the strong acid has two major effects: (1) The dissociation of the carboxylic acid employed is suppressed which reduces the concentration of the carboxylate ion; (2) The 4-acyloxy substituted (η^3-allyl)palladium complex is destabilized. The kinetic stability of 4-substituted (η^3-allyl)palladium complexes under mild acidic conditions were discussed in some recent theoretical and experimental studies.[17-19] The theoretical studies described and characterized a novel electronic effect, which occurs between the palladium atom and a polar 4-substituent in (η^3-allyl)palladium complexes. A particularly important consequence of the 4-substituent effects (ß-substituent effects) is the elongation and weakening of the C4-Nu_1 bond in the substituted allylpalladium intermediates. It has been shown[17-19] that the increase of polarity of the C4-Nu_1 bond leads to weakening of this bond, and, accordingly a decrease in the kinetic stability of the complex.

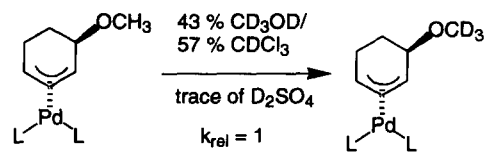


Scheme 1

Since the added H_2SO_4 suppresses the dissociation of RCOOH, the free carboxylate ion concentration is very low, and, therefore, path 2 is depressed (Scheme 1). As a consequence, formation of the 4-OR substituted allyl-palladium complex (**18**) will predominate (path 1, Scheme 1), and the subsequent second nucleophilic attack will mainly occur by rapid *cis*-migration of the carboxylate ion coordinated to palladium to produce **20**. However, under less acidic conditions path 2 is favoured and formation of allyl-palladium complex **19** will predominate. It is known that, the alkoxy complex **18** and the acyloxy complex **19** can be in equilibrium with one another.[18,19] This equilibrium is shifted towards the alkoxy complex (**18**) and its rate will increase when the acidity is increased. Therefore, the acyloxy-alkoxylation may also proceed trough path 2 via (η^3-allyl)palladium intermediates **19** and **18** to give the unsymmetrical product **20**. The faster exchange of an 4-acetoxy group compared to a 4-methoxy group in (η^3-allyl)palladium complexes was previously demonstrated.[18,19] For example, under mild acidic conditions, the 4-acetoxy functionality of [η^3-(1,2,3)-cyclohexenyl]palladium complex was replaced by a deuteromethoxy group 6.5 times faster, than the 4-functionality of the methoxy analog (eqs 4 and 5). Accordingly, under exactly the same reaction conditions the lifetime of the 4-methoxy substituted complex is substantially longer than that of its 4-acetoxy substituted counterpart.



(4)



(5)

The subtle interplay of steric and electronic effects, such as 4-substituent effects, leads to a remarkable high selectivity in the case of the 2-phenyl substituted substrates. In the acyloxy-alkoxylation reaction of 2-phenyl-1,3-cyclohexadiene two symmetrically substituted and two unsymmetrically substituted compounds as well as two stereo- and two regioisomers, i.e. 12 different isomeric products are possible, nevertheless only a single product was formed. The regio- and stereoselectivity is excellent for both dienes, however the chemoselectivity is somewhat lower for 1,3-cyclohexadiene compared to its 2-phenyl substituted analog. The chemoselectivity critically depends on the intensity of the 4-substituent effects in the 4-acyloxy and 4-alkoxy substituted (η^3-allyl)palladium complexes (c.f. eqs 4 and 5). We believe that the kinetic stability of the 4-acyloxy substituted (η^3-allyl)palladium complex is even lower in case of the 2-phenyl substituted species compared to the unsubstituted parent compound, which would explain the exclusive formation of the unsymmetrical product from the 2-phenyl dienes.

The reaction products. In this study we have described a new catalytic oxidation procedure, which is suitable for a one pot synthesis of *trans*-1-acyloxy-4-alkoxy-2-cyclohexenes from readily available starting materials. This procedure allows the employment of a wide variety of primary and secondary alcohols and, with

a slight modification, even the use of tertiary alcohols. Since the functionalities (OOCR and OR) of the products have different reactivities, subsequent nucleophilic substitution (either S_N2 or a metal-mediated process) permits regioselective functionalizations. In this respect, the benzyloxy compound (**14**) is particularly interesting, since it has a protected alcohol functionality. The reaction also offers a good opportunity to introduce bulky alkoxy functionalities, such as ^{t}Bu or menthyl groups (entries 8 and 13). Since the reaction shows a very high selectivity even in case of 2-phenyl-1,3-cyclohexadiene using catalytic amounts of BQ auxiliary, the alkoxy-acetoxylation reaction can be further developed to an asymmetric catalytic process.

Acknowledgement

This work was supported by the Swedish Natural Science Research Council (NFR). E. H. thanks for an Erasmus stipend. K. I. thanks the Japan Society for Promotion of Science for a predoctoral fellowship.

Experimental Part

NMR spectra were recorded for $CDCl_3$ solutions, (^{1}H at 400 MHz and ^{13}C at 100.5 MHz) using chloroform (7.26 ppm, ^{1}H, 77.0 ppm, ^{13}C) as internal standard. Coupling constants were evaluated using J-doubling procedure. Mass spectra were obtained by GC/MS technique (E.I., 70 eV). Dichloromethane was distilled over CaH_2 other solvents were used without further purification. All chemicals were purchased from Lancester or Aldrich. Cyclohexadiene was fresly destilled other chemicals were used without further purification. Merck silica gel 60 (240-400 mesh) was used for flash chromatography.

Method A: $Pd(OAc)_2$ (36 mg, 0.16 mmol), *p*-benzoquinone (670 mg, 6.2 mmol), acetic acid (0.45 ml, 8 mmol), the corresponding alcohol (12 mmol) and 0.12 ml stock solution (250 mg cc. H_2SO_4 in 4 ml acetic acid) were dissolved in 10 ml CH_2Cl_2. To this stirred solution, 1,3-cyclohexadiene (0.28 ml, 3.1 mmol) was added via a syringe pump over 4 hours. The reaction mixture was stirred for an additional 16 hours at room temperature. Thereafter, 100 ml of a 1:4 mixture of ether and pentane was added and the resulting mixture was extracted with water, brine and with 2M NaOH (2 x 10 ml) and brine. The organic phase was dried ($MgSO_4$) and then evaporated to give the crude product, which was purified by flash chromatography (silica) using pentane/ether 4:1 as eluent.

Method B: $Pd(OAc)_2$ (11 mg, 0.05 mmol), 2-(*p*-tolylsulfinyl)-5-*tert*-butyl-1,4-benzoquinone (15 mg, 0.05 mmol), iron phthalocyanine (9 mg, 0.02 mmol), acetic acid (0.29 ml, 5 mmol), the corresponding alcohol (10 mmol) and 0.24 ml stock solution (250 mg cc. H_2SO_4 in 4 ml acetic acid) were dissolved in 3 ml CH_2Cl_2. To this stirred solution, 2-phenyl-1,3-cyclohexadiene (78 mg, 0.5 mmol) was added and the reaction mixture was stirred at 40°C for 24 hours under an oxygen atmosphere. Thereafter, 30 ml of ether was added and filtered through celite and the filtrate was washed with 2M NaOH (10 x 10 ml). The organic phase was dried ($MgSO_4$) and then evaporated to give the crude product, which was purified by flash chromatography (silica) using pentane/ether 9:1 to 4:1 as eluent.

Method C: The same as method A, except that 10 % $Pd(OAc)_2$ and 11 equiv. ^{t}BuOH was employed.

Method D: The same as method A, except that 3.9 equiv. EtOH, 2.2 equiv. benzioc acid and 0.06 ml stock solution was used.

***trans*-1-Benzoyloxy-4-methoxy-2-cyclohexene** (**2**): ^{1}H NMR: 8.04 (app d, 2H, J = 7.8 Hz), 7.55 (app t, 1H, J = 7.4 Hz), 7.43 (app t, 2H, J = 7.6 Hz), 6.04 (dm, 1H, J = 10.1 Hz), 5.93 (dm, 1H, J = 10.1 Hz), 5.60-5.54 (m, 1H), 3.91-3.85 (m, 1H), 3.40 (s, 3H), 2.32-2.23 (m, 1H), 2.20-2.11 (m, 1H), 1.82-1.65 (m, 2H), ^{13}C NMR: 166.1, 132.9, 132.1, 130.5, 129.6, 128.9, 128.3, 73.9, 69.0, 55.9, 26.1, 25.8. IR (neat): 2932, 1715, 1315, 1269, 1103 cm^{-1}.

***trans*-1-Acetoxy-4-methoxy-2-phenyl-2-cyclohexene** (**3**): ^{1}H NMR: δ 7.40-7.20 (m, 5H), 6.30 (d, 1H, J = 4.0 Hz), 5.97 (t, 1H, J = 4.8 Hz), 4.00-3.94 (m, 1H), 3.41 (s, 3H), 2.30-2.15 (m, 1H), 2.10-1.97 (m, 1H), 1.90 (s, 3H), 1.86-1.77 (m, 2H). ^{13}C NMR: δ 170.6, 139.2, 138.7, 129.4, 128.3, 127.7, 126.0, 73.9, 67.8, 56.2, 25.6, 24.1, 21.1. IR (in $CDCl_3$ solution): 2932, 2820, 1734, 1364, 1237, 1085 cm^{-1}.

***trans*-1-Benzoyloxy-4-methoxy-2-phenyl-2-cyclohexene** (**4**): ^{1}H NMR: δ 7.88 (d, 2H, J = 8.4 Hz), 7.55-7.20 (m, 8H), 6.39 (d, 1H, J = 3.6 Hz), 6.20 (t, 1H, J = 4.8 Hz), 4.07-4.01 (m, 1H), 3.45 (s, 3H), 2.42-2.30 (m, 1H), 2.15-2.05 (m, 1H), 2.02-1.85 (m, 2H). ^{13}C NMR: δ 166.1, 139.3, 138.8, 132.8, 130.3, 129.5, 129.4, 128.3, 128.2, 127.7, 126.1, 73.9, 68.6, 56.2, 25.6, 24.1. IR (in $CDCl_3$ solution): 2932, 1711, 1270, 1096 cm^{-1}. MS *m/z* (%): 187 (M^+-121, 1), 186 (100), 154 (36), 105 (65), 91(6), 77 (30). Anal. Calcd.: C, 77.90; H, 6.54; Found: C, 77.87; H, 6.60.

***trans*-1-Acetoxy-4-ethoxy-2-cyclohexene** (**5**): ^{1}H NMR: δ 5.95 (dm, 1H, J = 10.1 Hz), 5.75 (dm, 1H, J = 10.1 Hz), 5.32-5.26 (m, 1H), 3.97-3.97 (m, 1H), 3.56 (dq, 1H J = 9.1, 7.0 Hz), 3.50 (dq, 1H, J = 9.1, 7.0 Hz), 2.18-2.01 (m, 2H), 2.03 (s, 3H), 1.68-1.51 (m, 2H), 1.19 (t, 3H, J = 7.0 Hz). ^{13}C NMR: δ 170.6, 132.6, 128.6, 72.4, 68.6, 63.7, 26.4, 26.1, 21.2, 15.6. MS *m/z* (%): 184 (M^+, <1), 124 (49), 96 (100), 79 (55). IR (in $CDCl_3$ solution): 3039, 2977, 1728, 1390, 1373, 1248, 1085, 918 cm^{-1}. Anal. Calcd.: C, 65.42; H, 8.91; Found: C, 65.19; H, 8.75.

***trans*-1-Benzoyloxy-4-ethoxy-2-cyclohexene** (**6**): ^{1}H NMR: 8.04 (app d, 2H, J = 7.8 Hz), 7.55 (app t, 1H, J = 7.5 Hz), 7.43 (app t, 2H, J = 7.6 Hz), 6.03 (dm, 1H, J = 10.2 Hz), 5.91 (dm, 1H, J = 10.2 Hz), 5.60-5.54 (m, 1H), 4.00-3.94 (m, 1H), 3.61 (dq, 1H, J = 9.0, 7.0 Hz), 3.54 (dq, 1H, J = 9.0, 7.0 Hz), 2.32-2.23 (m, 1H), 2.18-2.09 (m, 1H), 1.81-1.68 (m, 2H), ^{13}C NMR: 166.0, 132.8, 132.7, 130.4, 129.5, 128.6, 128.2, 72.4, 69.1, 63.7, 26.4, 26.2, 15.6. IR (neat): 2972, 1716, 1341, 1105 cm^{-1}.

***trans*-1-Acetoxy-4-ethoxy-2-phenyl-2-cyclohexene** (**7**): ^{1}H NMR: δ 7.38-7.20 (m, 5H), 6.29 (d, 1H, J = 4.0 Hz), 5.98 (t, 1H, J = 4.8 Hz), 4.10-4.05 (m, 1H), 3.68-3.50 (m, 2H), 2.30-2.20 (m, 1H), 2.06-1.95 (m, 1H), 1.89 (s, 3H), 1.86-1.75 (m, 2H), 1.22 (t, 3H, J = 6.8 Hz). ^{13}C NMR: δ 170.6, 139.0, 138.7, 130.1, 128.3, 127.6, 126.0, 72.4, 67.9, 63.9, 25.7, 24.7, 21.1, 15.6. MS *m/z* (%): 201 (M^+-59, 16), 200 (96), 172 (40), 154 (100), 77 (30). IR (in $CDCl_3$ solution): 2972, 2867, 1734, 1370, 1237, 1097 cm^{-1}.

***trans*-1-Acetoxy-4-*tert*-butoxy-2-cyclohexene** (**8**): ^{1}H NMR: δ 5.78 (dm, 1H, J = 10.3 Hz), 5.67 (dm, 1H, J = 10.3 Hz), 5.32-5.25 (m, 1H), 4.10-4.02 (m, 1H), 2.18-2.06 (m, 1H), 2.02 (s, 3H), 2.04-1.94 (m, 1H), 1.65-1.54 (m, 2H), 1.22 (br s, 9H). ^{13}C NMR: δ 170.6, 135.5, 127.8, 73.9, 68.9, 65.2, 29.7, 28.3, 27.0, 21.3. MS *m/z* (%): 212 (M^+, <1), 169 (<1), 156 (2), 138 (5), 96 (100), 79 (75). IR (in $CDCl_3$ solution): 2976, 1728, 1451, 1371, 1248, 1062, 955 cm^{-1}. Anal. Calcd.: C, 67.89; H 9.50; Found: C, 67.96; H, 9.68.

***trans*-1-Acetoxy-4-isobutoxy-2-cyclohexene** (**9**): ^{1}H NMR: δ 5.96 (dm, 1H, J = 10.2 Hz), 5.76 (dm, 1H, J = 10.2 Hz), 5.33-5.27 (m, 1H), 3.90-3.85 (m, 1H), 3.26 (dd, 1H, J = 8.7, 6.7 Hz), 3.20 (dd, 1H, J = 8.7, 6.7 Hz), 2.19-2.08 (m, 1H), 2.04 (s, 3H), 2.09-2.00 (m, 1H), 1.81 (hept, 1H, J = 6.7 Hz), 1.68-1.55 (m, 2H), 0.89 (d, 6H, J = 6.7 Hz); ^{13}C NMR: δ 170.6, 132.8, 128.5, 75.4, 72.7, 68.7, 28.8, 26.8,

26.2, 21.2, 19.4, 19.4. MS *m/z* (%): 153 (M^+-59, 3), 152 (15), 138 (3), 126 (2), 112 (3), 96 (100), 79 (60). IR (in $CDCl_3$ solution): 2958, 2872, 1727, 1391, 1372, 1248, 1082 cm^{-1}.

***trans*-1-Acetoxy-4-isobutoxy-2-phenyl-2-cyclohexene (10)**: ^1H NMR: δ 7.36-7.24 (m, 5H), 6.29 (d, 1H, *J* = 3.6 Hz), 6.02-5.95 (m, 1H), 4.07-4.00 (m, 1H), 3.35-3.24 (m, 2H), 2.30-2.17 (m, 1H), 2.10-1.95 (m, 1H), 1.90 (s, 3H), 1.87-1.77 (m, 3H), 0.92 (d, 3H, *J* = 6.8 Hz), 0.91 (d, 3H, *J* = 6.8 Hz). ^{13}C NMR: d 170.6, 138.8, 138.7, 130.3, 128.3, 127.6, 126.1, 75.7, 72.8, 67.9, 28.8, 25.7, 24.7, 21.1, 19.44, 19.41. MS *m/z* (%): 229 (M^+-59, 6), 228 (15), 172 (100), 154 (36), 128 (18), 115 (15), 91 (10), 77 (13). IR (in $CDCl_3$ solution): 2955, 2870, 1734, 1369, 1237, cm^{-1}.

***trans*-1-Acetoxy-4-cyclopentyloxy-2-cyclohexene (11)**: ^1H NMR: δ 5.91 (dm, 1H, *J* = 10.2 Hz), 5.73 (dm, 1H, *J* = 10.2 Hz), 5.34-5.26 (m, 1H), 4.09-4.01 (m, 1H), 3.97-3.90 (m, 1H), 2.18-2.09 (m, 1H), 2.03 (s, 3H), 2.09-2.0 (m, 1H), 1.80-1.44 (m, 10H). ^{13}C NMR: δ 170.6, 133.4, 128.25, 79.3, 70.8, 68.8, 33.0, 32.8, 27.1, 26.3, 23.4, 23.4, 21.4. MS *m/z* (%): 165 (M^+-59, 1), 164 (5), 139 (4), 96 (49), 79 (100). IR (in $CDCl_3$ solution): 3039, 2957, 1728, 1438, 1327, 1248, 960 cm^{-1}.

***trans*-1-Acetoxy-4-cyclohexyloxy-2-cyclohexene (12)**: ^1H NMR: δ 5.90 (dm, 1H, *J* = 10.3 Hz), 5.73 (dm, 1H, *J* = 10.3 Hz), 5.32-5.27 (m, 1H), 4.04-3.98 (m, 1H), 3.39-3.31 (m, 1H), 2.18-2.08 (m, 1H), 2.03 (s, 3H), 2.07-1.97 (m, 1H), 1.92-1.81 (m, 2H), 1.78-1.69 (m, 2H), 1.65-1.49 (m, 3H), 1.35-1.12 (m, 5H). ^{13}C NMR: δ 170.6, 133.6, 128.2, 75.8, 69.8, 68.7, 33.3, 32.9, 27.4, 26.3, 25.7, 24.4, 24.3, 21.3. MS *m/z* (%): 179 (M^+-59, 1), 178 (6), 139 (3), 99 (1), 96 (73), 79 (100). IR (in $CDCl_3$ solution): 3935, 1728, 1372, 1249, 1076 cm^{-1}. Anal. Calcd.: C, 70.56; H 9.45; Found: C, 70.40; H, 9.30.

***trans*-1-Acetoxy-4-menthyloxy-2-cyclohexene (13)** formed as a 1 : 1 mixture of diastereoisomers. ^1H NMR: δ 5.95 (dm, 1H, *J* = 10.3 Hz), 5.90 (dm, 1H, *J* = 10.3 Hz), 5.78-5.71 (m, 2x 1H), 5.33-5.26 (m, 2x 1H), 5.33-5.26 (m, 2x 1H), 4.04-3.94 (m, 2x 1H), 3.19-3.10 (m, 2x 1H), 2.27-2.09 (m, 2x 2H), 2.04 (s, 2x 3H), 2.09-1.94 (m, 2x 2H), 1.71-1.54 (m, 2x 5H), 1.40-1.28 (m, 2x 1H), 1.24-1.14 (m, 2x 1H), 0.96-0.86 (m, 2x 6H), 0.77 (d, 3H, *J* = 3.6 Hz), 0.75 (d, 3H, *J* = 3.6 Hz). ^{13}C NMR: δ 170.6, 134.1, 133.0, 128.2, 128.0, 78.1, 77.6, 71.1, 70.0, 68.7, 68.4, 48.6, 48.3, 42.2, 41.6, 34.4, 31.7, 31.6, 28.4, 26.5, 26.4, 26.0, 25.2, 25.1, 23.1, 23.0, 22.3, 21.3, 21.2, 21.1. MS *m/z* (%): 235 (M^+-60, <1), 139 (15), 96 (40), 79 (100). IR (in $CDCl_3$ solution): 2957, 2871, 1728, 1455, 1372, 1248, 1081, 1028 cm^{-1}.

***trans*-1-Acetoxy-4-benzyloxy-2-cyclohexene (14)**: ^1H NMR: δ 7.35 (br s, 2H), 7.34 (br s, 2H), 7.34-7.26 (m, 1H), 6.01 (dm, 1H, *J* = 10.3 Hz), 5.80 (dm, 1H, *J* = 10.3 Hz), 5.36-5.30 (m, 1H), 4.61 (d, 1H, *J* = 11.8 Hz), 4.55 (d, 1H, *J* = 11.8 Hz), 4.07-4.00 (m, 1H), 2.22-2.03 (m, 2H), 2.05 (s, 3H), 1.77-1.67 (m, 1H), 1.67-1.55 (m, 1H). ^{13}C NMR: δ 170.6, 138.5, 132.3, 128.9, 128.4, 127.6, 127.6, 72.0, 70.3, 68.6, 26.3, 26.1, 21.2; MS *m/z* (%): 187 (M^+-59, 3), 186 (3), 155 (<1), 142 (1), 131 (2), 91 (100), 77 (31). IR (in $CDCl_3$ solution): 3035, 2953, 1724, 1454, 1372, 1248, 1029, 945 cm^{-1}. Anal. Calcd.: C, 73.15; H 7.37; Found: C, 73.03; H, 7.42.

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Visiting student from Kyoto University Japan.

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