1, J = 10.0, 5.2), 3.56 (dd, 1, J = 10.0, 6.6), 2.57 (dddd, 1, J = 14.4, 7.3, 5.1, 1.5), 2.41 (br dtt, 1, J = 7.9, 5, 5), 2.31 (dddd, 1, J = 14.4, 7.3, 7.0, 1.5), 1.06 (s, 9); ^{13}C NMR δ 171.7, 150.4, 138.2, 135.6 (4 C), 133.5 (2 C), 129.6 (2 C), 127.7 (4 C), 122.0, 116.6, 66.4, 45.3, 33.8, 26.9 (3 C), 19.3; IR (neat) 3066, 2926, 2851, 1698, 1654, 1428, 1110, 736, 698 cm^{-1}.

***exo*- and *endo*-2-[[(*tert*-Butyldiphenylsilyl)oxy]-methyl]bicyclo[3.2.0]hept-3-en-6-one (49, 51).** Acid **47** (0.276 g, 0.700 mmol) was treated with oxalyl chloride (0.444 g, 3.50 mmol) in benzene (4 mL) to give the acid chloride, which was added dropwise to Et_3N in benzene as described above. The reaction solution was heated at reflux for 5 h followed by normal workup to give crude **49** and **51**. Flash chromatography on silica gel (92:8 pentane-ether) gave 91.5 mg (39%) of an inseparable mixture of **49** and **51** as a viscous oil. Analysis of NMR data showed a 5:1 mixture of **49** and **51**: IR (neat) 3070, 2924, 2854, 1783, 1428, 1111, 821, 734, 698 cm^{-1}. Anal. Calcd for $C_{24}H_{28}O_2Si$: 376.1859. Found: 376.1874.

The data for **49**: ^{1}H NMR δ 7.65 (dd, 4, J = 7.7, 1.6), 7.43-7.35 (m, 6), 5.86 (br ddd, 1, J = 5.5, 2, 2, H_4), 5.70 (ddd, 1, J = 5.5, 1.9, 2.9, H_3), 4.26-4.14 (m, 1, H_5), 3.65 (dd, 1, J = 10.0, 5.6), 3.48 (dd, 1, J = 10.0, 6.7), 3.23 (ddd, 1, J = 17.9, 9.0, 4.3, $H_{7\beta}$), 2.94-2.87 (m, 1, H_2), 2.82 (ddd, 1, J = 17.9, 5.7, 3.1, $H_{7\alpha}$), 2.71 (ddd, 1, J = 9.0, 5.7, 5.9, H_1), 1.05 (s, 9); ^{13}C NMR δ 207.6, 135.5 (4 C), 134.6 (C_4), 133.6 (2 C), 129.7 (2 C), 127.6 (4 C), 127.2 (C_3), 73.2 (C_5), 66.7 (CH_2O), 56.3 (C_2), 52.2 (C_7), 28.9 (C_1), 26.8 (3 C), 19.2.

The data for **51**: ^{1}H NMR δ 7.73-7.57 (m, 4), 7.43-7.35 (m, 6), 5.87-5.78 (m, 1, H_4), 5.76-5.62 (m, 1, H_3), 4.26-4.14 (m, 1, H_5), 3.91 (dd, 1, J = 10.1, 6.6), 3.77 (dd, 1, J = 10.1, 9.0), 3.70-2.66 (m, 4), 1.05 (s, 9); ^{13}C NMR δ 135.5 (4 C), 134.4 (C_4), 133.6 (2 C), 129.7 (2 C), 127.6 (4 C), 126.9 (C_3), 73.5 (C_5), 62.6 (CH_2O), 50.7 (C_2), 46.3 (C_7), 28.3 (C_1), 26.8 (3 C), 19.2 (the carbonyl carbon was not observed).

Acknowledgment. We are grateful to the National Institutes of Health for generous financial support.

Palladium-Catalyzed C-Alkylations of the Highly Acidic and Enolic Triacetic Acid Lactone. Mechanism and Stereochemistry[1]

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Received March 14, 1988

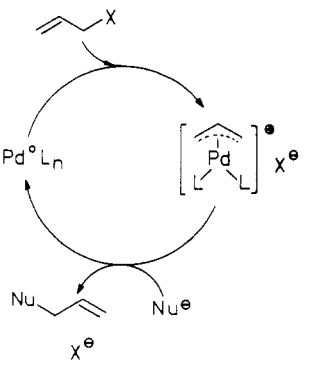
4-Hydroxy-6-methyl-2-pyrone (triacetic acid lactone) (**1**) is efficiently alkylated at C-3 with primary and secondary allylic substrates under thermodynamic control by using palladium(0) catalysts. Controlled hydrogenation of the resulting allylated derivatives affords pyrones with saturated chains at C-3. Allylic alkylations occur with retention of configuration at the allylic center, probably through a reversible kinetically favored O-alkylation.

Alylation of proton-active substrates with allylic systems under palladium catalysis is a well established synthetic methodology and some excellent reviews are available.[2] The acidities of the most frequently used proton-active compounds are in the range pK_a = 10-24. The mechanism involves nucleophilic attack of the conjugate bases of the proton-active substrates on a cationic (π-allyl)palladium complex formed in situ from an allylic derivative and zerovalent palladium stabilized by ligands, generally phosphines. The general features of the mechanism are represented in Scheme I. A great variety of leaving groups X have been used, although acetates and alkoxy carbonates have met with the most general acceptance.

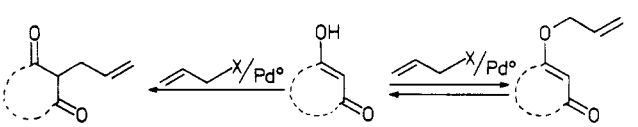
The situation is not so general when nucleophiles of high acidity (p$K_a \leq 10$) are considered. There are some examples of allylic alkylations of nitro acetates and nitro sulfones (p$K_a \sim 5.7$).[3] These nitro substrates do not contain appreciable quantities of alternative tautomers.

Cyclic β-diketones and β-keto esters are substrates having pK_a values around 5 and a high enol content (frequently >99%) which are particularly difficult to alkylate at the central carbon atom due to competition from O-alkylation. We reasoned that C-alkylation of these substrates could be achieved if the reactions were performed under reversibility conditions in order to permit the slow alkylation at carbon to predominate under thermodynamic control. Palladium-catalyzed alkylation with allylic reagents should fit the above conditions since the enol ether initially formed under kinetic control ought to act as an alkylating agent itself in which the leaving group, the enolate anion, is the conjugate base of an acid as strong as acetic acid. In other words, alkylation at oxygen must

Scheme I



Scheme II



(1) A preliminary report of the synthetic part of this work has been published: Moreno-Mañas, M.; Prat, M.; Ribas, J.; Virgili, A. *Tetrahedron Lett.* **1988**, *29*, 581.

(2) For recent reviews, see: (a) Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140. (b) Tsuji, J. *J. Organomet. Chem.* **1986**, *300*, 281. (c) Trost, B. M. *J. Organomet. Chem.* **1986**, *300*, 263. (d) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: New York, 1985.

(3) (a) Wade, P. A.; Hinney, H. R.; Amin, N. V.; Vail, P. D.; Morrow, S. D.; Hardinger, S. A.; Saft, M. S. *J. Org. Chem.* **1981**, *46*, 765. (b) Wade, P. A.; Morrow, S. D.; Hardinger, S. A. *J. Org. Chem.* **1982**, *47*, 365. (c) Genet, J. P.; Ferroud, D. *Tetrahedron Lett.* **1984**, *25*, 3579.

0022-3263/88/1953-5328$01.50/0

Table I.[a] Alkylations of Pyrone 1

run	allylyc derivative	T (°C)[d]	t (h)	2:1	solvent	DBU (equiv)	3 (%) and 4 (%)
1	(*E*)-$AcOCH_2CH$=$CHPh$ (**2a**)	74	2.5	1	toluene	0	**3a** (83)
2	**2a**	70	2	1	toluene	1	**3a** (66)
3	**2a**	r.t.	25	1	THF	0	**3a** (37); **4a** (49)
4	**2a**	40	69	2.5	THF	0	**4a** (73)
5	(*E*)-$AcOCH_2CH$=$CHCH_3$ (**2b**)	70	8	1	toluene	1	**3b** (63);[b] **3c** (23)
6	**2b**	40	71	2.5	THF	0	**4b** (51)
7	$AcOCH(CH_3)CH$=CH_2 (**2c**)	76	3	1	toluene	1	**3b** (59);[c] **3c** (20)
8	(*E*)-$AcOCH(CH_3)CH$=$CHCH_3$ (**2d**)	76	2	1	toluene	1	**3d** (47)
9	2-cyclohexen-1-yl acetate (**2e**)	72	2	1	toluene	1	**3e** (58)
10	$EtOCOOCH_2CH$=$C(CH_3)_2$ (**2f**)	r.t.	91	1	THF	0	**3f** (41); **3h** (9); **3i** (5)
		+65 °C	4				
11	**2f**	81	0.25	1	toluene	0	**3f** (28); **4f** (14); **3h** (3); **3i** (4); **3j** (5)
12	*cis*-**2g**	80	2.5	1	toluene	1	*cis*-**3g** (39.5); *trans*-**3g** (11.4)

[a] All yields are based on isolated pure compounds except for **3f** which could not be isolated pure. [b] As a (1:4) *Z*–*E* mixture. [c] Mixture of isomers. [d] r.t. = room temperature.

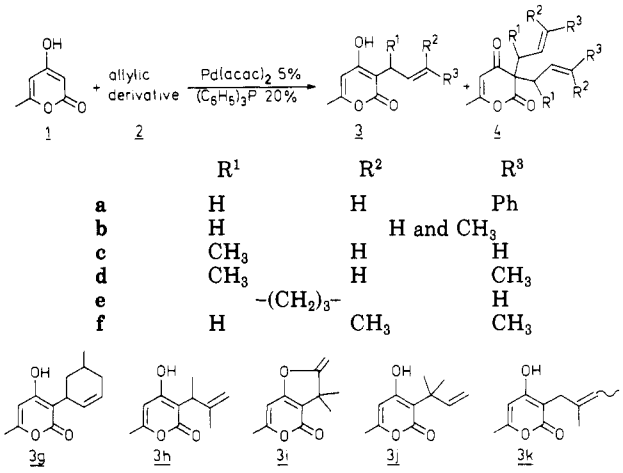
be reversible (Scheme II). A very limited number of cases of palladium-catalyzed carbon allylic alkylation of cyclopentane-1,3-diones, cyclohexane-1,3-diones, and Meldrum's acid, all of them with pK_a values around 5, have been reported[4] but the subject has not attracted general attention. With this idea in mind we achieved alkylations at the active carbon atom of a substrate as acidic as tetronic acid[1] (pK_a = 3.76).

Triacetic acid lactone (**1**) is a natural polyketide[5] which is also industrially available. It can be prepared by deacetylation of dehydroacetic acid.[6] Moreover, many related natural 2-pyrones have been described with biogenetically relevant substituents at C-3 and C-5. Therefore, methods to accomplish the regioselective alkylation of **1** at both C-3 and C-5 deserve some attention. A difficulty encountered when working with the pyrone **1** is that O-alkylation strongly competes with C-alkylation, thus rendering conventional C-alkylation methods useless. This is a direct consequence of its high enol content (>99%) and its low pK_a value: 4.94.[7] Our group has already reported some methodologies to indirectly achieve the above alkylations[8] based on sigmatropic rearrangements of sulfonium ylides[8a] (alkylation at C-5), regioselective alkylation of the cobalt(II)[8b] and copper(II)[8c] complexes of methyl 3,5-dioxohexanoate and subsequent cyclizations (alkylations at C-5 and C-3, respectively), and reaction of **1** with aldehydes and thiophenol followed by reductive desulfuration (alkylation at C-3).[8d]

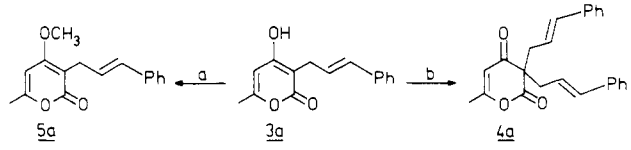
In this paper we want to present in detail (a) the alkylation of triacetic acid lactone at the central activated C-3 by a variety of allylic primary and secondary acetates, (b) the partial hydrogenation of the resulting pyrones at the allylic double bond, which results in an alkylation method to introduce fully saturated chains at C-3 of pyrone **1**, and (c) mechanistic experiments showing the overall retention of configuration at the allylic electrophilic center.

Alkylations of 1. Alkylations of pyrone **1** were performed as indicated in Scheme III and Table I with several primary and secondary allylic acetates. Palladium acetylacetonate and triphenylphosphine were added as catalyst precursors and blank experiments showed the reactions not to take place in their absence. With use of toluene as solvent, clean monoalkylations were accomplished and products **3a–g** were isolated in preparatively useful yields. When working in THF, mixtures of monoalkylation and dialkylation products **3a** and **4a** were produced (run 3). With use of an excess of allylic reagent in THF clean dialkylations took place (runs 4 and 6). Also, independent alkylation of 3-cinnamyl-4-hydroxy-6-methyl-2-pyrone, **3a**, produced 3,3-(dicinnamyl)-3,4-dihydro-6-methyl-4-oxo-2-pyrone (**4a**) in 43% yield (Scheme IV). Sometimes addition of 1 equiv of DBU proved to be beneficial although in other cases the yields were not improved (runs 1 and 2). The experimental conditions presented in Table I should be considered as optimal for each allylic substrate. Alkylations with the isomers 2-buten-1-yl acetate (**2b**) and 3-buten-2-yl acetate (**2c**) produced mixtures of 3-(2-buten-1-yl)-4-hydroxy-6-methyl-2-pyrone (**3b**) and 3-(3-buten-2-yl)-4-hydroxy-6-methyl-2-pyrone (**3c**) in the same >2:1 ratio within experimental error (the ratios of isomers were determined by chromatographic isolation and weighing). Clearly, the same mixture of intermediates is involved in each case. A

Scheme III



Scheme IV[a]



[a] (a) Me_2SO_4, K_2CO_3/acetone, reflux, 20 h; (b) **2a**, $Pd(acac)_2$ (10%), $(C_6H_5)_3P$ (40%)/THF, 46 °C, 44 h.

(4) (a) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6432. (b) Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699. (c) Schuda, P. F.; Bernstein, B. *Synth. Commun.* **1984**, *14*, 293. (d) Ferroud, D.; Genet, J. P.; Muzart, J. *Tetrahedron Lett.* **1984**, *25*, 4379.

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(6) Collie, J. N. *J. Chem. Soc.* **1891**, *59*, 607.

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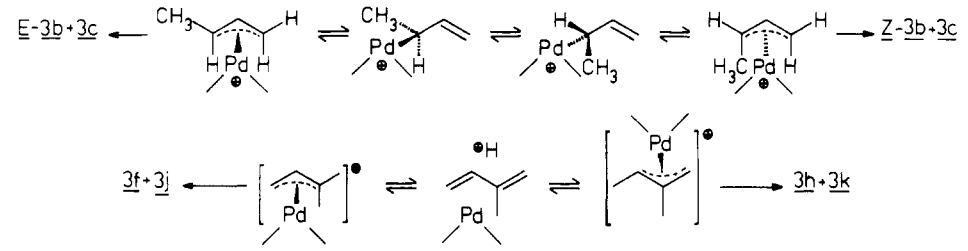
Scheme V. π-σ-π Isomerization Mechanism and Proton Elimination–Proton Addition Isomerization Mechanism



pathway through O-allylation and subsequent Claisen rearrangement would have produced more **3c** than **3b**. Product **3b** from run 5 was a mixture of *Z* and *E* isomers in a 1:4 ratio as determined by ^{1}H NMR with saturation of the olefinic region. The ratio was not determined for runs 6 and 7. An isomerization of the allylic system is responsible for these results, probably through a π-σ-π mechanism on the cationic (π-allyl)palladium species (Scheme V). However, the reaction with 3-penten-2-yl acetate (**2d**) afforded only one isomer of 4-hydroxy-6-methyl-3-(3-penten-2-yl)-2-pyrone, presumably with the *E* configuration (run 8).

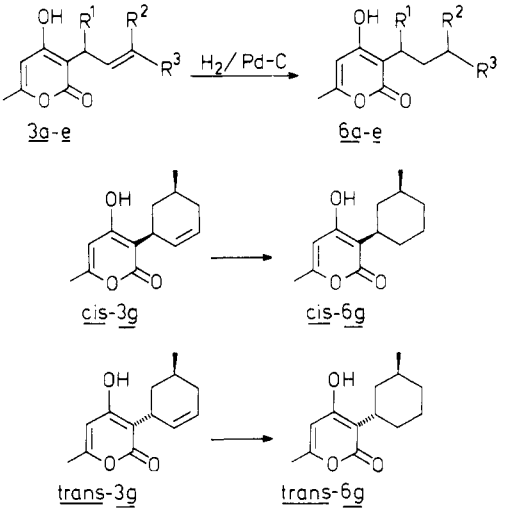
The reactions with dimethylallyl alkylating agents showed the scope of this method. No useful results were obtained with 3-methyl-2-buten-1-yl acetate. Instead, ethyl 3-methyl-2-buten-1-yl carbonate (**2f**) had to be used. However, 4-hydroxy-6-methyl-3-(3-methyl-2-buten-1-yl)-2-pyrone (**3f**) was never isolated in pure condition and the yields were only moderate (runs 10 and 11), several other products being produced as indicated in Scheme III. Thus, pyrone **3j** could arise by direct allylic reaction at the more substituted terminal carbon atom of the allylic system or through Claisen rearrangement from an initially formed *O*-allyl ether. Moreover, product **3h** requires the formation of a different (π-allyl)palladium complex as indicated in Scheme V via a proton elimination–proton addition isomerization mechanism.[9] This mechanism requires the formation of **3k** in addition to **3h** as observed for a different nucleophile.[9] We could not isolate **3k** but we believe it is the contaminant in **3f**. Finally, product **3i** could be formed by oxidation of **3j**.

Alkylations can be performed in good yields even with 2-cyclohexen-1-yl acetate (**2e**) (run 9). Reactions with **2g** will be discussed in the Stereochemistry and Mechanisms section.

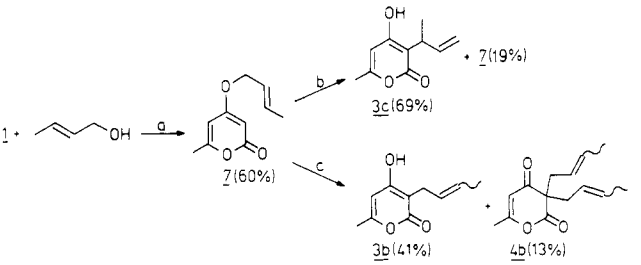
Controlled hydrogenation of pyrones **3a–e** and **3g** at the allylic double bond were carried out in practically quantitative yields by using palladium on charcoal catalyst and ethanol or ethyl acetate (Scheme VI). The overall outcome is a method to introduce saturated substituents, including secondary ones at the C-3 position of triacetic acid lactone.

Stereochemistry and Mechanism. First of all we performed rearrangement experiments on 4-(*E*-2-buten-1-yloxy)-6-methyl-2-pyrone **7** (Scheme VII). O- to C-rearrangements of allylic moieties have been performed intermolecularly under platinum catalysis[10] as well as intramolecularly under palladium catalysis.[11] Also a purely thermal Claisen rearrangement on an allylic ether of triacetic acid lactone has been reported.[12]

Scheme VI



Scheme VII[a]



[a] (a) $(C_6H_5)_3P$, $(EtOCON)_2$/benzene, room temperature, 9 h; (b) toluene, reflux, 18 h; (c) $Pd(acac)_2$ (5%), $(C_6H_5)_3P$ (20%)/toluene, 82 °C, 1 h.

We prepared the ether **7** by treating **1** with triphenylphosphine and diethyl azodicarboxylate, by a modification of an O-alkylation method described by Suzuki and coworkers.[13] When ether **7** was refluxed in toluene for 17 h the rearranged pyrone **3c** was the only isolated product beside a minor amount of starting material (Scheme VII). Pyrone **3c** clearly arises from a purely thermal Claisen rearrangement. However, when **7** was treated with the palladium catalyst, no **3c** could be isolated, but instead the nonbranched alkylpyrones **3b** and **4b** were isolated in 41% and 13% yields. Although these yields are not the same as those encountered in the direct alkylation of **1** (Table I, runs 5 and 7) these results do rule out Claisen rearrangement as the major pathway in the direct alkylation and support the intermolecular O- to C-rearrangement hypothesis.

Next, we wanted to know the stereochemistry of our alkylations. Four different cyclic model compounds have

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(10) (a) Balavoine, G.; Bram, G.; Guibe, F. *Nouv. J. Chim.* **1978**, *2*, 207. (b) Balavoine, G.; Guibe, F. *Tetrahedron Lett.* **1979**, 3949.
(11) Trost, B. M.; Runge, T. A.; Jungheim, L. N. *J. Am. Chem. Soc.* **1980**, *102*, 2840.
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(13) Suzuki, E.; Katsuragawa, B.; Inoue, S. *J. Chem. Res., Synop.* **1979**, 110.

Scheme VIII

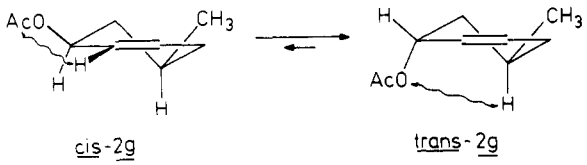


Table II.[a] Isomerization of Acetates 2g

	yield (%)		
t (h)	*cis*-**2g**	*trans*-**2g**	*trans*-**2g**/*cis*-**2g**
0.00	99.2	0.8	0.008
0.25	93.6	1.2	0.013
0.50	91.8	7.1	0.077
0.75	49.9	36.3	0.727
1.00	29.9	35.2	1.177
1.25	19.4	22.7	1.170
1.50	12.2	15.0	1.229
1.75	4.6	6.1	1.326
2.00	3.1	4.7	1.516
2.50	2.7	4.4	1.630
2.75	2.1	3.4	1.619
3.00	1.8	2.9	1.611
23.50	0.0	0.0	

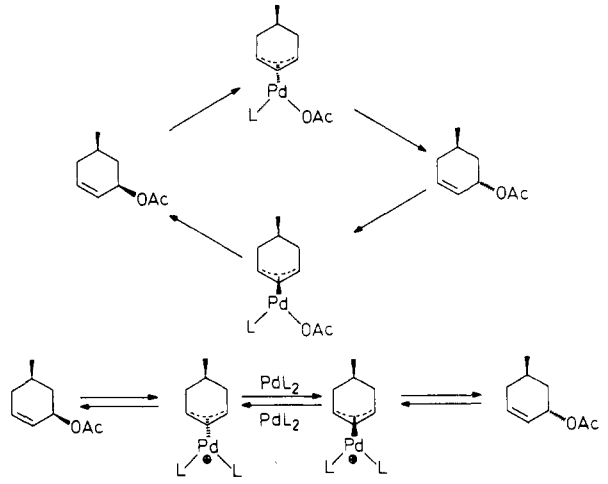
[a] $Pd(acac)_2$ (5%), $(C_6H_5)_3P$ (20%)/toluene, 81 °C, *t* (h). The starting material retained its stereochemical identity simply upon being heated in toluene (86 °C for 23.5 h).

been used to find out whether the palladium-catalyzed allylic alkylations occur with retention or inversion of configuration: *cis*-5-(methoxycarbonyl)-2-cyclohexen-1-yl acetate,[14a] *cis*-5-phenyl-2-cyclohexen-1-yl benzoate,[14b] *cis*-5-(acetoxymethyl)-2-cyclohexenyl acetate,[14c] and *cis*-5-methyl-2-cyclohexen-1-yl trimethylsilyl ether.[15] We reasoned that *cis*-5-methyl-2-cyclohexen-1-yl acetate (*cis*-**2g**) (Scheme VIII) could be a good probe since it is completely free from polar effects. We have prepared the 5-methyl-2-cyclohexenols 8 in a cis/trans ratio of 83:17 by a described procedure.[16] Pure *cis*-8 was prepared by hydrolysis of the 4-nitrobenzoate with alkaline alumina[17] and acetylated to afford *cis*-**2g** (Scheme VIII).

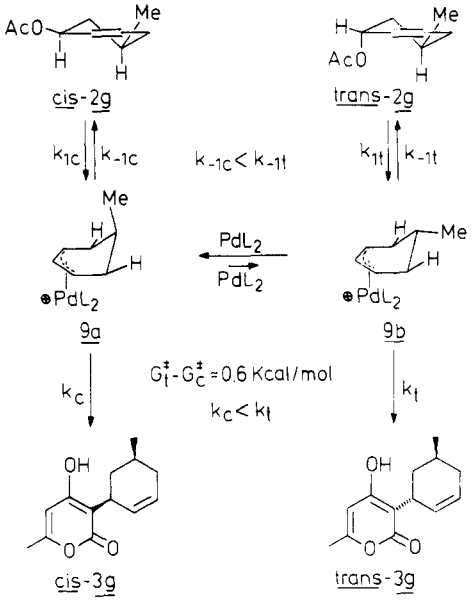
For any conclusion to be drawn concerning the stereochemistry of the alkylation procedure, an evaluation of the behaviour of the stereochemical probe toward the experimental conditions should be performed. Indeed, Trost and Verhoeven have found the two isomers of 5-(methoxycarbonyl)-2-cyclohexen-1-yl acetate to interconvert under palladium catalysis.[14]

Thus, when we treated *cis*-**2g** with palladium acetylacetonate and triphenylphosphine in toluene at 81 °C, it was converted into a mixture with its *trans*-**2g** isomer. The total amount of isomers **2g** decreased till complete disappearance, probably due to proton loss. However, at about 2.5 h the ratio *trans*-**2g**/*cis*-**2g** became constant and equal to 1.61 (Table II). An equilibrium constant of 1.61 at 354 K ($\Delta G°$ = ca. −0.33 Kcal/mol) (Scheme VIII) is in fair agreement with similar values reported in the literature for related interconvertions.[18] The higher stability of *trans*-3,5-disubstituted-cyclohexenes over their cis isomers

Scheme IX. Two Possible Mechanisms for the Isomerization of Acetates 2g (Above: through Pd-OAc Coordination and Reductive Elimination. Below: through PdL_2 Nucleophilic Displacement by PdL_2)



Scheme X. General Picture of the Alkylation of 1 with 2g



is related to the existence of only one 1,3 axial–pseudoaxial interaction in the trans isomer and a nearly eclipsed interaction in the cis isomer.

Two mechanisms for the interconversion of cyclic allylic acetates (for which the π-σ-π mechanism cannot operate) have been invoked in the chemical literature (Scheme IX). The first mechanism involves formation of a (π-allyl)-palladium intermediate and coordination of the leaving acetate to the palladium atom followed by internal return to the carbon framework.[14,19] The second mechanism also goes through a (π-allyl)palladium intermediate and nucleophilic substitution of PdL_n by another PdL_n molecule with inversion of configuration. Strong evidence in favor of this second mechanism has been contributed by Bosnich and co-workers.[20]

The two possible (π-allyl)palladium intermediates **9a** (from *cis*-**2g**) and **9b** (from *trans*-**2g**) do not have the same

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Table III. Stereochemistry of the Conversions 2g → 3g[a]

run	starting material cis-2g/trans-2g	phosphine	mol PR_3/mol Pd	T (°C)	t	final products cis-3g/trans-3g	yield (%)
1	99.2/0.8	$(C_6H_5)_3P$	2	77	38 min	77/23	26.5
2	99.2/0.8	$(C_6H_5)_3P$	4	80	2.25 h	77.6/22.4	50.9
3	83/17	$(C_6H_5)_3P$	4	83	1.25 h	78/22	39.7
4	83/17	$(C_6H_5)_3P$	4	80	1 h	70/30	42.4
5	99.2/0.8	$[(C_6H_5)_2PCH_2]_2$	2	76	1 h	89.8/10.2	33.7
6	99.2/0.8	$(C_6H_5)_3P$	20	77	24 h	91.7/8.3	54.6
7	99.2/0.8	$(C_6H_5)_3P$	30	80	43 h	90.6/9.4	60.9

[a] Reactions in toluene in the presence of DBU (1 equiv) (see run 12, Table I).

stability (Scheme X). Thus, other features being approximately equal, four gauche butane interactions are present in **9b** and only two are observed in **9a**. Consequently, **9a** is more stable by $\Delta H°$ ca. 1.6 kcal/mol. Neglecting the entropy contribution, an estimated value for $\Delta G°$ is also 1.6 kcal/mol. Since both acetates **2g** equilibrate under the usual reaction conditions we sought an improvement in order to ascertain the stereochemistry of the alkylation reaction. We have found that starting from both pure *cis*-**2g** and from *cis*-**2g**/*trans*-**2g** (83/17) mixtures the ratio of final products (*cis*-**3g**/*trans*-**3g**) was the same within experimental error (Table III, runs 1–4). In other words, the system is under Curtin–Hammett conditions and equilibration of **9a** and **9b** is faster than attack by the anion of **1**. From the values of the ratios of formed products ($\ln$ (*cis*-**3g**/*trans*-**3g**) = $(G_t^* - G_c^*)/RT$) a value $G_t^* - G_c^*$ of about 0.6 kcal/mol can be calculated (Table III, Scheme X).

A substantial improvement on the overall retention of configuration was achieved by using 1,2-bis(diphenylphosphino)ethane (Table III, run 5) and by using a large excess of triphenylphosphine (Table III, runs 6 and 7). Under the last conditions 90–91% retention of configuration was observed.

With all the available data already discussed we propose an overall mechanistic picture (Scheme X). In summary, our studies show that (a) both acetates isomerize under the usual reaction conditions and (b) nucleophilic substitution of **1** for acetate under palladium catalysis occurs with overall retention of configuration, presumably via double inversion (Scheme X).

A comment on the isomerization mechanism **9a** ⇄ **9b** is important. Upon increasing triphenylphosphine concentration, both allylic substitution and intermediate isomerization become slower, but isomerization is more sensitive and can be practically suppressed when substitution still occurs at an appreciable rate (Table III, runs 6 and 7). The effect of increasing triphenylphosphine concentration is to shift to the right side the equilibrium

$$Pd[(C_6H_5)_3P]_n + (4 - n)\ (C_6H_5)_3P \rightleftarrows Pd[(C_6H_5)_3P]_4$$

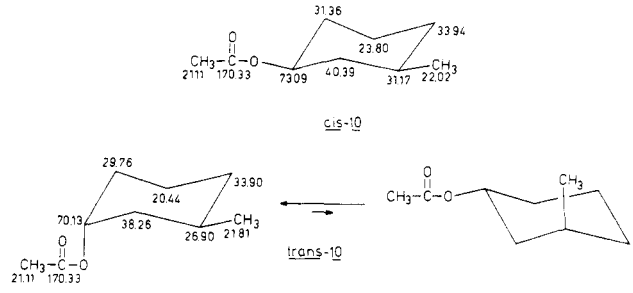
Since the actual catalytic species are PdL_n ($n < 4$, e.g., PdL_2), we can conclude that intermediate isomerization should exhibit a higher order kinetic law with respect to PdL_2 than the allylic substitution itself. Thus, the alkylation rate depends on the first power of $[PdL_2]$ whereas the isomerization rate is a function of the second power of $[PdL_2]$. Therefore, isomerization is expected to be more sensitive to the decrease of $[PdL_2]$ as is indeed observed. Our data are in agreement with Bosnich's isomerization mechanism.

Stereochemistry of 3g and 6g Isomers. The mechanistic conclusions that have been discussed rely upon the correct assignment of stereochemistry to *cis*- and *trans*-**3g** and -**6g**. The assignment of stereochemistry to *cis*- and *trans*-5-methyl-2-cyclohexen-1-ol (**8**) is well established.[16] Moreover, both *cis*-**2g** and a 1:1 mixture of *cis*- and *trans*-**2g** were hydrogenated to afford **10** (Scheme XI). By comparison of the ^{13}C NMR spectra of the pure isomer with that of the second isomer present in the 1:1 mixture, we could confirm the cis configuration for the pure isomer. The ^1H NMR chemical shifts are collected in Scheme XI. A conformational equilibrium for *trans*-**10** has been assumed. All the chemical shift differences between corresponding atoms of both isomers agree with the well-known α, β and gauche γ effects.[21]

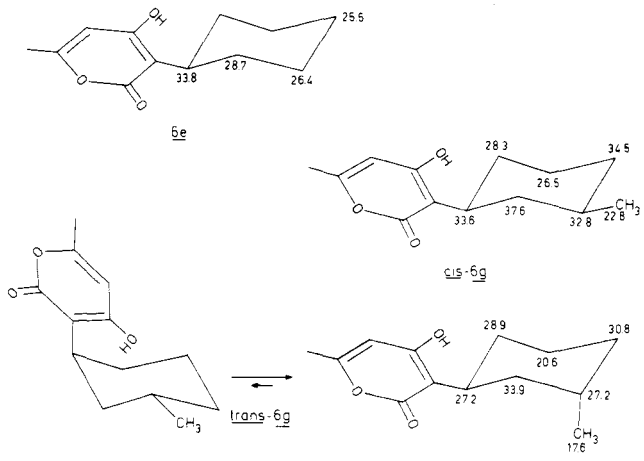
Finally, a sample of the major isomer alcohol **8** obtained as previously reported was converted into *cis*-3-methylcyclohexanol (**11**) which exhibited a ^{13}C NMR spectrum as previously described.[22]

Having confirmed the stereochemistry of the isomers **2g**, we performed a similar study on compounds **6g**, formed by hydrogenation of **3g**. Data for compound **6e** are also included in Scheme XII for comparison. Again a reasonable conformational assumption for *trans*-**6g** had to be made. The assignment of peaks to the corresponding carbon atoms (in DMSO-d_6 was accomplished by standard NOE, SEFT, and GATED techniques. Once again the

Scheme XI



Scheme XII



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differences in chemical shifts between corresponding carbon atoms of both isomers **6g** and **6e** agree well with the expected α, β and gauche γ effects.[21]

Experimental Section

General. All melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 80 and 20 MHz on a Brucker WP80SY spectrometer using TMS as internal standard. Mass spectra were registered on a Hewlett-Packard 5985B spectrometer. IR spectra were recorded on a Perkin-Elmer 1310 spectrophotometer.

The pyrone **1** was prepared by deacetylation of dehydroacetic acid as previously described.[6] Acetates **2a–e** were better prepared by treating equimolar amounts of the corresponding alcohols with acetic anhydride and pyridine in dichloromethane at room temperature followed by conventional workup and fractional distillation of the dichloromethane and **2**. Ethyl 3-methyl-2-buten-1-yl carbonate (**2f**) was prepared by reaction of equimolar amounts of ethyl chlorocarbonate, 3-methyl-2-buten-1-ol, and pyridine in ether at 4 °C.

***cis*-5-Methylcyclohex-2-en-1-ol (*cis*-8a).** A mixture ***cis*-8a/*trans*-8a** (83:17) was prepared as previously described.[16b] 4-Nitrobenzoyl chloride (81.4 g, 0.44 mol) was added portionwise during 1.25 h under stirring to a solution of the above cis/trans mixture (44.8 g, 0.4 mol) in pyridine (225 mL) at 0–4 °C. When the addition was finished, the stirring was maintained at 0 °C for 30 min. Water (15 mL) was then added and the precipitate was filtered, washed with cold water, and dried. The dried solid was treated twice with boiling hexane (250 and 100 mL) and filtered. The combined filtrates gave 81.6 g of a yellowish solid (mp 90–92 °C) upon standing in a refrigerator, which was twice recrystallized to afford 73 g (70%) of *cis*-5-methylcyclohex-2-en-1-ol 4-nitrobenzoate: mp 93–94 °C (lit.[16b] mp 93.6–94 °C).

A mixture of this 4-nitrobenzoate (60.03 g, 0.23 mol), benzene (200 mL), and alkaline alumina[17] (354 g) was shaken occasionally for 72 h. The mixture was filtered. The solid was washed with ether until TLC monitoring showed no solute was contained in the solvent (7 × 200 mL). The combined solutions were fractionally distilled to separate the solvents and the residue was distilled at 74 °C/12 mmHg to afford 23.18 g (90%) of *cis*-**8a**. GLC analysis showed it to be pure to an extent of more than 99%.

Its acetate *cis*-**2g** (bp 70.5–71 °C/10 mmHg, (lit.[16c] bp 84 °C/25 mmHg) was prepared by our general method previously described.

General Procedure To Prepare 3-Allyl-4-hydroxy-6-methyl-2-pyrones 3. 3-Cinnamyl-4-hydroxy-6-methyl-2-pyrone (3a) (Run 2, Table I). Palladium acetylacetonate (76 mg, 0.25 mmol), triphenylphosphine (262 mg, 1 mmol), and cinnamyl acetate (**2a**) (880 mg, 5 mmol) were added under an argon atmosphere to a stirred solution of pyrone **1** (630 mg, 5 mmol) and DBU (760 mg, 5 mmol) in anhydrous toluene (25 mL). The round-bottomed flask containing this mixture was inmersed in a bath at 70–71 °C for 2 h until **2a** was consumed (TLC monitoring). The mixture was partitioned between ethyl acetate and dilute hydrochloric acid. The organic layer was washed with water to neutrality, dried, and evaporated. The residue (1.59 g) was recrystallized from boiling ethanol to afford 723 mg (60%) of **3a**: mp 221–222.5 °C; IR (KBr) 3500–2000 (br), 1660, 1620, 990, 970 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 2.14 (d, J = 1 Hz, 3 H), 3.15 (d, J = 5 Hz, 2 H), 6.01 (q, J = 1 Hz, 1 H), 6.06–6.49 (m, 2 H), 7.03–7.47 (m, 5 H); MS, m/e (relative intensity) 243 (M + 1, 17), 242 (M, 80), 184 (20), 151 (100), 128 (25), 115 (24), 85 (23), 43 (27). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.25: H, 5.84.

3-(2-Buten-1-yl)-4-hydroxy-6-methyl-2-pyrone (3b) and 3-(3-Buten-2-yl)-4-hydroxy-6-methyl-2-pyrone (3c) (Runs 5 and 7, Table I). **3b** and **3c** were prepared from (*E*)-2-buten-1-yl acetate (**2b**) (run 5) and from 1-buten-3-yl acetate (**2c**) (run 7) by the same procedure as **3a** under the experimental conditions indicated in Table I. Both compounds were separated by column chromatography on silica gel. Using mixtures of hexane/EtOAc pyrone **3c** eluted first: mp 174–175 °C; IR (KBr) 3500–2500 (br), 1660, 1640, 995 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (d, J = 7.5 Hz, 3 H), 2.19 (d, J = 1 Hz, 3 H), 3.83 (m, 1 H), 5.21 (ddd, J = 2, 2, and 10 Hz, 1 H), 5.28 (ddd, J = 2, 2, and 17.5 Hz, 1 H), 5.96 (q, J = 1 Hz, 1 H), 6.25 (ddd, J = 5.3, 10, and 17.5 Hz, 1 H), 8.37 (br s, 1 H); ^{13}C NMR (CD_3OD) δ 18.08, 19.53, 34.60, 101.63, 106.25, 113.30, 142.25, 162.07, 167.35, 167.42; MS, m/e (relative intensity) 180 (M, 53), 165 (100), 137 (26), 53 (21), 43 (30). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.39; H, 6.66.

3b was eluted second as a mixture of *Z*–*E* isomers: IR (KBr) 3400–2400 (br), 1665, 1630, 995, 970 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.56–1.83 (m, 3 H), 2.21 (d, J = 1 Hz, 3 H), 3.06–3.34 (m, 2 H), 5.46–5.72 (m, 2 H), 6.09 (m, J = 1 Hz, 1 H). Irradiation at δ 5.5 collapsed the 1.56–1.83 region into two broad singlets at δ 1.61 and 1.71 of 4:1 intensity. The *E* isomer was previously reported.[23]

4-Hydroxy-6-methyl-3-(3-penten-2-yl)-2-pyrone (3d) (Run 8, Table I). This compound was prepared from 3-penten-2-yl acetate (**2d**) by the same procedure as **3a** under the experimental conditions indicated in Table I. **3d**: mp 131–132 °C; IR (KBr) 3500–2500 (br), 1650 (shoulder), 1635, 1000, 960 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30 (d, J = 7 Hz, 3 H), 1.74–1.85 (m, 3 H), 2.19 (d, J = 1 Hz, 3 H), 3.54–3.95 (m, 1 H), 5.75 (q, J = 1 Hz, 1 H), 5.79–5.94 (m, 2 H), 7.15 (br s, 1 H); ^{13}C NMR (CD_3OD) δ 17.91, 18.66, 19.51, 101.68, 107.00, 124.43,134.94, 161.80, 167.12, 167.42; MS, m/e (relative intensity) 194 (M, 69), 179 (32), 165 (57), 152 (20), 151 (34), 85 (28), 69 (33), 43 (100). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.89; H, 7.33.

3-(2-Cyclohexen-1-yl)-4-hydroxy-6-methyl-2-pyrone (3e) (Run 9, Table I). This compound was prepared from 2-cyclohexen-1-yl acetate (**2e**) by the same procedure as **3a** under the experimental conditions indicated in Table I. **3e**: mp 200–201 °C; IR (KBr) 3400–2800 (br), 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33–2.33 (m, 6 H), 2.20 (d, J = 1 Hz, 3 H), 3.52–3.87 (m, 1 H), 5.75 (q, J = 1 Hz, 1 H), 5.85–6.36 (m, 2 H), 7.37 (s, 1 H); ^{13}C NMR (Me_2SO-d_6) δ 19.05, 22.54, 24.08, 25.92, 31.53, 99.83, 103.79, 125.06, 130.61, 159.77, 163.50, 165.11; MS, m/e (relative intensity) 206 (M, 83), 152 (43), 85 (27), 69 (22), 43 (100). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.97; H, 6.79.

***cis*- and *trans*-4-Hydroxy-6-methyl-3-(5-methyl-2-cyclohexen-1-yl)-2-pyrone (*cis*- and *trans*-3g) (Run 12, Table I).** These compounds were prepared from *cis*-5-methyl-2-cyclohexen-1-yl acetate (*cis*-**2g**) by the same procedure as **3a** under the experimental conditions indicated in Table I. They were separated by column chromatography on silica gel with mixtures of hexane/EtOAc, the trans isomer being eluted first.

***trans*-3g**: mp 206–207 °C; IR (KBr) 3400–2600 (br), 1650 (shoulder), 1635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.99 (d, J = 5.5 Hz, 3 H), 1.50–2.50 (m, 5 H), 2.18 (d, 0.9 Hz, 3 H), 3.56–3.81 (m, 1 H), 5.70 (q, J = 0.9 Hz, 1 H), 5.93, 6.36 (m, 2 H), 7.84 (s, 1 H); ^{13}C NMR ($CDCl_3$–Me_2SO-d_6) δ 19.0, 20.0, 25.5, 30.0, 32.4, 34.3, 100.8, 104.3, 128.3, 129.7, 160.0, 165.8, 166.4; MS, m/e (relative intensity) 220 (M, 100), 205 (19), 177 (26), 152 (31), 135 (23), 91 (28), 85 (34), 69 (21), 43 (53). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.91; H, 7.41.

***cis*-3g**: mp 179–181 °C; IR (KBr) 3500–2500 (br), 1640, 1615 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.97 (d, J = 5.6 Hz, 3 H), 1.08–2.42 (m, 5 H), 2.15 (s, 3 H), 3.57–3.97 (m, 1 H), 5.68–5.92 (br d, J = 8.8 Hz, 1 H), 5.75 (s, 1 H), 6.00–6.29 (m, 1 H), 6.81 (s, 1 H); ^{13}C NMR ($CDCl_3$–Me_2SO-d_6) δ 19.2, 21.8, 29.1, 32.9, 33.3, 35.1, 100.8, 105.1, 127.9, 129.2, 160.0, 166.1; MS, m/e (relative intensity) 220 (M, 100), 205 (21), 177 (28), 152 (91), 139 (30), 135 (27), 121 (25), 85 (65), 43 (65). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.80; H, 7.07.

Reactions of Table III were performed by the same general method. The particular variations in the *cis*-**2g**:*trans*-**2g** ratio, phosphine, phosphine:palladium ratio, temperature, and time are indicated in the table.

Reaction between 1 and 2f (Run 11, Table I). This reaction was performed under the same general conditions as for products **3** but in the absence of DBU (see Table I). The following products were isolated by column chromatography.

4-Hydroxy-6-methyl-3-(3-methyl-2-buten-1-yl)-2-pyrone (3f): it could never be isolated in pure condition; ^{1}H NMR ($CDCl_3$) δ 1.85 (br s, 6 H), 2.2 (s, 3 H), 3.25 (d, J = ca. 7 Hz, 2 H), 5.35 (t, J = ca. 7 Hz, 1 H), 6.05 (s, 1 H).

6-Methyl-3,3-bis(3-methyl-2-buten-1-yl)-2,4-pyrandione (4f): low melting solid; ^{1}H NMR data agree with those previously described.[24]

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4-Hydroxy-6-methyl-3-(3-methyl-3-buten-2-yl)-2-pyrone (3h): mp 135–136 °C; IR (KBr) 3400–2500 (br), 1640, 995 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (d, J = 7 Hz, 3 H), 1.82 (m, 3 H), 2.19 (d, J = 0.9 Hz, 3 H), 3.49–3.83 (m, 1 H), 5.11–5.29 (m, 2 H), 5.72 (q, J = 0.9 Hz, 1 H); MS, m/e (relative intensity) 194 (M, 33), 179 (67), 151 (26), 43 (100). Anal. Calcd for $C_{11}H_{13}O_3$: C, 68.02; H, 7.27. Found: C, 67.66; H, 7.34.

3,3,6-Trimethyl-2-methylene-4-oxo-2,3-dihydrofuro[3,2-c]pyran (3i): mp 89.5–90.5 °C; IR (KBr) 1710, 980, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 6 H), 2.26 (d, J = 1 Hz, 3 H), 4.36, 4.40, 4.73, 4.77 (AB system, 2 H), 5.97 (q, J = 1 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.36, 27.28, 42.54, 85.90, 94.93, 107.76, 160.11, 165.62, 166.81, 171.18; MS, m/e (relative intensity) 192 (M, 12), 177 (100). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.65; H, 6.44.

4-Hydroxy-6-methyl-3-(2-methyl-3-buten-2-yl)-2-pyrone (3j): mp 129–130 °C (lit.[12] mp 131 °C); IR (KBr) 3300–2500 (br), 1670, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (s, 6 H), 2.15 (d, J = 0.9 Hz, 3 H), 5.39 (dd, J = 1.1 and 10.3 Hz, 1 H), 5.49 (dd, J = 1.1 and 18 Hz, 1 H), 5.65 (q, J = 0.9, 1 H), 6.40 (dd, J = 10.3 and 18 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.26, 25.62, 39.38, 101.05, 105.70, 113.82, 148.86, 160.20, 163.64, 165.33; MS, m/e (relative intensity) 194 (M, 2), 69 (24), 43 (100).

3,3-Dicinnamyl-6-methyl-2,4-pyrandione (4a) (Run 4, Table I). This product was prepared by the same general procedure as products **3** in THF and in the absence of base under the particular experimental conditions described in Table I. **4a**: mp 96–97 °C; IR (KBr) 1770, 1660, 1640, 990, 980, 965 cm^{-1}, ^1H NMR ($CDCl_3$) δ 2.03 (d, J = 1 Hz, 3 H), 2.67, 2.84, 2.87, 3.05 (inner part of the AB part of a ABX system, 4 H), 5.63 (q, J = 1 Hz, 1 H), 5.88 (dt, J = 7.3 and 16 Hz, 2 H), 6.50 (d, J = 16 Hz, 2 H), 7.10–7.39 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 19.77, 41.15, 61.37, 106.67, 122.01, 126.06, 127.38, 128.23, 134.90, 136.48, 167.27, 170.19, 193.81, MS, m/e (relative intensity) 358 (M, 0.5), 241 (24), 157 (41), 140 (57), 128 (25), 117 (100), 115 (82), 91 (69), 43 (32). Anal. Calcd for $C_{24}H_{22}O_3$: C, 80.42; H, 6.19. Found: C, 80.45; H, 6.29.

3,3-Di-2-buten-1-yl-6-methyl-2,4-pyrandione (4b) (Run 6, Table I). This product was prepared as a mixture of isomers by the same general procedure as **4a** under the experimental conditions indicated in Table I. **4b**: bp (oven temperature) 75 °C/0.05 mmHg; IR ($CHCl_3$) 1780, 1650, 1635, 990, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59 (br d, J = 6 Hz, 6 H), 2.14 (d, J = 1 Hz, 3 H), 2.40–2.83 (m, 4 H), 4.96–5.80 (m, 5 H); MS, m/e (relative intensity) 234 (M, 15), 179 (100), 178 (47).

3-Cinnamyl-4-methoxy-6-methyl-2-pyrone (5a). A mixture of **3a** (726 mg, 3 mmol), dimethyl sulfate (420 mg, 3.5 mmol), potassium carbonate (1.66 g, 12 mmol), and acetone (200 mL) was refluxed under stirring for 8 h (TLC monitoring). Additional methyl sulfate (1.65 mmol) was added and the refuxing continued for 12 h. After cooling, the mixture was filtered and the precipitate was washed with acetone. The combined liquids were evaporated to give 1.046 g of a solid which was recrystallized from THF/pentane to afford 323 mg (42%) of **5a**: mp 108–110.5 °C; IR (KBr) 1685, 990, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.26 (d, J = 1 Hz, 3 H), 3.29 (d, J = 5.5 Hz, 2 H), 3.86 (s, 3 H), 6.00 (q, J = 1 Hz, 1 H), 6.1–6.6 (m, 2 H), 7.07–7.42 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 19.75, 26.18, 55.99, 94.80, 102.32, 125.60, 126.43, 127.94, 130.10, 137.35, 161.25, 164.62, 166.03; MS, m/e (relative intensity) 257 (M + 1, 26), 256 (M, 40), 165 (93), 153 (42), 115 (31), 91 (21), 43 (100). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.86; H, 6.31.

General Procedure for Preparation of Compounds 6a–e and 6g. Shaken mixtures of compounds **3a–e** and **3g** (1–2 mmol) and catalytic amounts of 10% Pd–C in ethanol or in ethyl acetate were hydrogenated at atmospheric pressure until absortion of the theoretical volume of hydrogen. Hydrogenations in ethanol (5–15 min) were faster than those in ethyl acetate (180–900 min). Yields were higher than 99%.

4-Hydroxy-6-methyl-3-(3-phenylpropyl)-2-pyrone (6a): mp 129–131 °C; IR (KBr) 3300–2400 (br), 1665, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.61–2.14 (m, 2 H), 2.19 (d, J = 0.9 Hz, 3 H), 2.36–2.82 (m, 4 H), 6.12 (q, J = 0.9 Hz, 1 H), 7.05–7.26 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 19.39, 22.84, 29.44, 35.64, 101.74, 102.72, 125.40, 128.00, 128.10, 142.30, 159.84, 167.77, 168.34; MS, m/e (relative intensity) 245 (M + 1, 12), 244 (M, 22), 140 (64), 139 (24), 112 (78), 104 (25), 91 (43), 85 (34), 77 (26), 65 (30), 55 (22), 43 (100). Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.94; H, 7.01.

3-Butyl-4-hydroxy-6-methyl-2-pyrone (6b): mp 130–132 °C (lit.[8d] mp 132–133 °C); IR (KBr) 3400–2500 (br), 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.72–1.32 (m, 7 H), 2.20 (s, 3 H), 2.27–2.85 (m, 2 H), 6.18 (s, 1 H).

3-(2-Butyl)-4-hydroxy-6-methyl-2-pyrone (6c): mp 178–179 °C; IR (KBr) 3500–2500 (br), 1650 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OD) δ 0.85 (t, J = 7.4 Hz, 3 H), 1.21 (d, J = 7.4 Hz, 3 H), 1.37–1.93 (m, 2 H), 2.20 (d, J = 1 Hz, 3 H), 2.68–3.22 (m, 1 H), 5.88 (q, J = 1 Hz, 1 H); ^{13}C NMR (CD_3OD) δ 12.89, 18.18, 19.47, 27.74, 32.37, 101.66, 106.82, 161.63, 167.69, 167.87; MS, m/e (relative intensity) 182 (M, 26), 153 (100), 85 (20), 69 (32), 43 (22). Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.92; H, 7.74. Found: C, 65.94; H, 7.93.

4-Hydroxy-6-methyl-3-(2-pentyl)-2-pyrone (6d): mp 123–125 °C; IR (KBr) 3500–2500 (br), 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76–2.14 (m, 10 H), 2.21 (s, 3 H), 2.80–3.29 (m, 1 H), 6.06 (s, 1 H), 8.57 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.07, 17.98, 19.48, 21.21, 29.10, 36.15, 102.07, 106.69, 159.69, 167.74; MS, m/e (relative intensity) 196 (M, 23), 153 (100), 139 (20), 69 (28). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.33; H, 8.22. Found: C, 67.40; H, 8.43.

3-Cyclohexyl-4-hydroxy-6-methyl-2-pyrone (6e): mp 264–265 °C; IR (KBr) 3500–2500 (br), 1630 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.8–2.5 (m, 10 H), 2.11 (s, 3 H), 2.46–2.95 (m, 1 H), 5.92 (s, 1 H); ^{13}C NMR (Me_2SO-d_6) δ 18.99, 25.54, 26.46, 28.73, 33.78, 99.88, 105.18, 159.44, 163.73, 164.54; MS, m/e (relative intensity) 209 (M + 1, 21), 208 (M, 45), 165 (20), 139 (39), 137 (38), 127 (53), 98 (26), 85 (57), 81 (34), 69 (27), 55 (42), 43 (100). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.07; H, 8.01.

***cis*-4-Hydroxy-6-methyl-3-(3-methylcyclohexyl)-2-pyrone (*cis*-6g)**: mp 203–204 °C; IR (KBr) 3400–2500 (br), 1655, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (d, J = 4.6 Hz, 3 H), 1.00–2.11 (m, 9 H), 2.19 (s, 3 H), 2.61–3.09 (m, 1 H), 6.07 (s, 1 H), 8.86 (s, 1 H); ^{13}C NMR (Me_2SO-d_6) δ 19.2, 22.8, 26.3, 28.3, 32.8, 33.6, 34.5, 37.6, 100.1, 105.1, 159.6, 163.9, 164.8; MS, m/e (relative intensity) 223 (M + 1, 16), 222 (M, 28), 179 (31), 165 (20), 153 (35), 139 (54), 127 (87), 85 (100), 69 (64), 55 (59), 43 (86). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 70.34; H, 8.14.

***trans*-4-Hydroxy-6-methyl-3-(3-methylcyclohexyl)-2-pyrone (*trans*-6g)**: mp 258–259 °C; IR (KBr) 3500–2500 (br), 1660, 1630 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OD) δ 0.96 (d, J = 7.3 Hz, 3 H), 1.02–2.38 (m, 9 H), 2.05 (d, J = 1 Hz, 3 H), 2.78–3.18 (m, 1 H), 5.75 (q, J = 1 Hz, 1 H); ^{13}C NMR (Me_2SO-d_6) δ 17.6, 19.1, 20.6, 27.2, 28.9, 30.8, 33.9, 100.0, 105.1, 159.5, 163.9, 164.8; MS, m/e (relative intensity) 223 (M + 1, 8), 222 (M, 15), 153 (34), 139 (30), 127 (64), 85 (80), 69 (83), 55 (67), 43 (84), 41 (100). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 70.06; H, 8.08.

4-(2-Buten-1-yloxy)-6-methyl-2-pyrone (7). Diethyl azodicarboxylate (2.61 g, 15 mmol) was dropwise added to a stirred solution of **1** (1.26 g, 10 mmol), triphenylphosphine (3.93 g, 15 mmol), and (*E*)-2-buten-1-ol (1.08 g, 15 mmol) in anhydrous benzene (25 mL). The mixture was stirred for 9 h (TLC monitoring), the solvent was evaporated, and the residue was chromatographed through a silica gel column to afford 351 mg (20%) of **4b** and 1.08 g (60%) of **7** as an oil which crystallized spontaneously, mp 64–66 °C (lit.[24] mp 65–66 °C): IR ($CHCl_3$) 1710, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77 (d, J = 5.3 Hz, 3 H), 2.21 (s, 3 H), 4.43 (d, J = 5.3 Hz, 2 H), 5.40–6.13 (m, 3 H); MS, m/e (relative intensity) 180 (M, 7), 98 (29), 69 (24), 55 (100), 43 (53).

Thermal Isomerization of 7. A solution of **7** (360 mg, 2.0 mmol) and anhydrous toluene (10 mL) was heated at 85 °C for 3 h and finally refluxed for 18 h. The solvent was evaporated and the white solid residue (318 mg) was monitored by ^1H NMR spectroscopy. It contained only 19% of recovered **7** and 69% of pyrone **3c**.

Palladium-Catalyzed Isomerization of 7. A solution of **7** (360 mg, 2.0 mmol), palladium acetylacetonate (30 mg, 0.1 mmol), and triphenylphosphine (105 mg, 0.4 mmol) in anhydrous toluene (10 mL) was heated at 85 °C for 1 h (TLC monitoring). The solvent was evaporated and the residue chromatographed through a silica gel column to afford 146 mg (41%) of **3b** and 30 mg (19%) of **4b**.

Isomerization of *cis*-2g. Acetate ***cis*-2g** (1.54 g, 10 mmol) was introduced by means of a syringe into a stirred solution containing palladium acetylacetonate (152 mg, 0.5 mmol), tri-

phenylphosphine (526 mg, 20 mmol), and anhydrous toluene (25 mL) which was previously purged with argon and heated for 45 min at 80–81.5 °C. Aliquots were taken at the intervals indicated in Table II. Each aliquot was quenched by being poured into a mixture of 3 mL of solution A (0.77 g of 1-chloronaphthalene in 100 mL of pentane) and 2 mL of solution B (HCl, 1.2 N) and shaken for 30 s. The organic layers were washed and dried and analyzed by GLC to give the results indicated in Table II. A blank experiment was performed without palladium acetylacetonate and triphenylphosphine. After 24 h *cis*-**2g** remained unchanged.

***cis*-3-Methylcyclohexanol Acetate (10).** A shaken mixture of *cis*-**2g** (2.92 g, 20 mmol), a catalytic amount of Ra–Ni W2, and ethanol (50 mL) was hydrogenated at atmospheric pressure for 2 h until no more uptake of hydrogen was observed. The mixture was filtered through a short column of Celite and the solvent was fractionally distilled. The residue afforded 2.06 g (66%) of **10**: bp 69 °C/10 mmHg; IR ($CHCl_3$) 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.53–2.10 (m, 9 H), 0.93 (d, J = 5.3 Hz, 3 H), 2.02 (s, 3 H), 4.46–4.91 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.78, 21.81, 23.61, 30.98, 31.16, 37.72, 40.21, 72.67, 169.66.

Acknowledgment. Financial support from CAICYT (Ministerio de Educación y Ciencia of Spain) through Grant no. 2014/83 is gratefully acknowledged.

Registry No. 1, 675-10-5; **2a**, 21040-45-9; **2b**, 7204-29-7; **2c**, 6737-11-7; **2d**, 31001-80-6; **2e**, 14447-34-8; **2f**, 116504-03-1; *cis*-**2g**, 61221-47-4; *trans*-**2g**, 61221-48-5; **3a**, 115580-35-3; (*E*)-**3b**, 115580-47-7; (*Z*)-**3b**, 115580-49-9; **3c**, 115580-46-6; **3d**, 115580-36-4; **3e**, 115580-37-5; **3f**, 16266-64-1; *cis*-**3g**, 116503-95-8; *trans*-**3g**, 116503-96-9; **3h**, 116503-97-0; **3i**, 116503-98-1; **3j**, 16266-65-2; **4a**, 116503-99-2; **4b**, 115580-48-8; **4f**, 16266-55-0; **5a**, 116504-04-2; **6a**, 115580-42-2; **6b**, 39849-74-6; **6c**, 116504-00-8; **6d**, 115580-43-3; **6e**, 115580-44-4; *cis*-**6g**, 116504-01-9; *trans*-**6g**, 116504-02-0; **7**, 115580-45-5; *cis*-**8a**, 22049-46-3; *trans*-**8a**, 22031-97-6; *cis*-**10**, 116531-33-0; *trans*-**10**, 66922-08-5; (*E*)-$H_3CCH{=}CHCH_2OH$, 504-61-0; (*E*)-$HOCH_2CH{=}CHPh$, 4407-36-7; $H_3CCH(OH)CH{=}CH_2$, 598-32-3; (*E*)-$H_3CCH(OH)CH{=}CHCH_3$, 3899-34-1; palladium acetylacetonate, 14024-61-4; 2-cyclohexen-1-ol, 822-67-3; 3-methyl-2-buten-1-ol, 556-82-1; 4-nitrobenzoyl chloride, 122-04-3; *cis*-5-methylcyclohex-2-en-1-ol 4-nitrobenzoate, 52393-62-1.

Use of Carboxylic Acids as Chiral Solvating Agents for the Determination of Optical Purity of Chiral Amines by NMR Spectroscopy

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Received July 27, 1987

Optically pure mandelic acid, Mosher's acid, and *N*-(3,5-dinitrobenzoyl)phenylglycine have been used as chiral solvating agents to induce nonequivalence in the ^1H NMR spectra of several diamines, amino acid esters, amino alcohols, and other amines. The identity of the chiral solvating agent and the stoichiometry of the solvation complexes that yield the greatest nonequivalence varies with the nature of the substrate.

The increasing number of efforts devoted to the design of chiral ligands for metal-promoted reactions in organic synthesis have necessitated the development of methods for measuring the optical purity of both the ligands and the reaction products. The use of specific rotations to determine optical purity can be problematic since rotations vary significantly with the conditions of the measurement, particularly for polar molecules.[1] We were recently faced with the problem of determining the optical purity of several amino acid esters, β-amino alcohols and vicinal diamines of general structures **1–5** for use as potential chiral ligands in the asymmetric osmium tetroxide oxidation of olefins to vicinal diols.[2] Our initial efforts using the chiral shift reagent $Eu(tfc)_3$ were abandoned due to the immediate onset of severe line broadening when the shift reagent was added, even in trace amounts.[3] We subsequently found that mandelic acid and other readily available, optically pure carboxylic acids (**6–8**) can be successfully utilized as chiral solvating agents (CSA's) with ^1H NMR spectroscopy.[4] Nonequivalence in the ^1H NMR spectrum suitable for integration was achieved under ambient conditions, enabling the measurement of the optical purity.

Results and Discussion

Induced Nonequivalence. Nonequivalence[5] was observed in the ^1H NMR spectra of the racemic substrate amines **1–5**, usually in the signals of the protons adjacent to the amino group, with mandelic acid (**6**),[6] Mosher's acid

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