Stereoselective Synthesis of Pyrano[3,2-*c*]benzopyrans via Intramolecular Cycloaddition of *o*-Quinonemethides Generated from Salicylaldehydes and Unsaturated Alcohols under Very Mild Conditions

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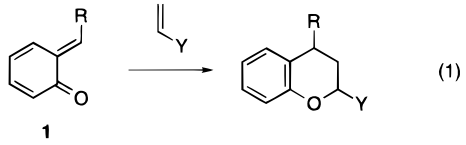
Received July 15, 1999

Intramolecular [4 + 2] cycloaddition reaction of 6-(4-alkenyloxymethylene)-2,4-cyclohexadien-1-ones generated from the reaction between substituted salicylaldehydes and unsaturated alcohols under mild conditions was investigated. In general, the reaction furnished tricyclic compounds containing the pyranobenzopyran skeleton with trans-fused B/C ring in very good yields (Tables 1 and 2). Furthermore, geometry of the olefinic bond of the starting material is retained during the reaction.

Introduction

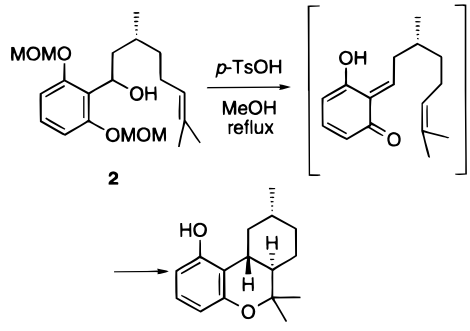
o-Quinonemethides[1] **1** are very reactive intermediates in organic synthesis, and some natural products have been synthesized using [4 + 2] cycloaddition of these species as the key step (eq 1).[2] We have been investigating the generation and reaction of *o*-quinonemethides under mild conditions in order to widen the application of *o*-quinonemethides in organic synthesis.[3] Previously, we reported that treatment of the phenol derivative **2** with a catalytic amount of an acid in methanol at reflux gave the tricyclic compound **3** in high yield as the sole stereoisomer (Scheme 1).



1 (1)

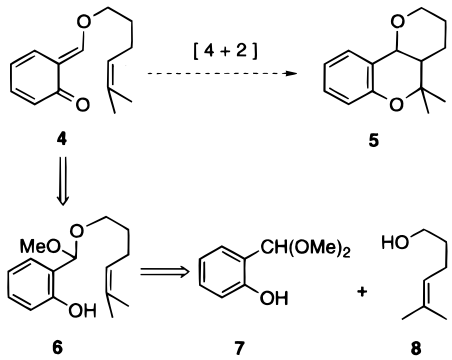
This fact indicates that *o*-quinonemethides can be generated even in a protic solvent under milder conditions than what have been known in the past syntheses.[2] Here, we were interested in the formation and reactivity of *o*-quinonemethides **4**, carrying an alkoxy group on the methylene carbon.[4] The intramolecular [4 + 2] cyclization of **4** would furnish directly tricyclic pyranobenzopyrans **5**, which contain two oxygen atoms in the adjacent two rings; hence, *o*-quinonemethides **4** would serve as the key reactive intermediates for the natural product synthesis (Scheme 2).

Scheme 1



2 **3** : 96%

Scheme 2



4 **5** **6** **7** **8**

o-Quinonemethides **4** were thought to be generated by elimination of methanol from **6**, which in turn, could be formed by acetal-exchange reaction between salicylaldehyde dimethyl acetal (**7**) and the unsaturated alcohol **8**. It is also of great interest to see whether *o*-quinonemethides **4** have enough reactivity toward electron-rich di-

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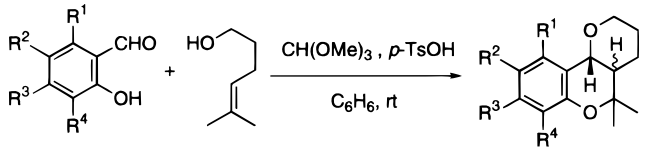
(4) Merten and Müller reported the reaction of salicylaldehyde diethyl acetal with styrene, isoprene, and isobutene in low yields: Merten, R.; Müller, G. *Chem. Ber.* **1964**, *97*, 682.

10.1021/jo991132h CCC: $18.00
Published on Web 12/02/1999

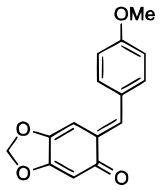
Table 1. Reaction of Substituted Salicylaldehydes with 5-Methyl-4-hexen-1-ol



10 **8** **5**

entry	aldehyde	R^1	R^2	R^3	R^4	time (h)	product	yield (%)	trans/cis
1	**10a**	H	H	H	H	1	**5a**	86	100:0
2	**10b**	H	Br	H	H	1.5	**5b**	81	100:0
3	**10c**	H	NO_2	H	H	8	**5c**	60	100:0
4	**10d**	Me	H	Me	H	4.5	**5d**	96	100:0
5	**10e**	Me	H	H	Me	7	**5e**	79	100:0
6	**10f**	−CH=CHCH=CH−		H	H	4	**5f**	79	100:0
7	**10g**	OMe	H	H	H	15	**5g**	8	100:0
8	**10h**	H	OMe	H	H	14	**5h**	93	100:0
9	**10i**	H	H	OMe	H	4	**5i**	60	100:0
10	**10j**	H	H	H	OMe	4.5	**5j**	81	100:0
11	**10k**	OH	H	H	H	8	**5k**	31	62:38
12	**10l**	H	OH	H	H	24	**5l**	84	99:1
13	**10m**	H	H	OH	H	3	**5m**	54	73:27
14	**10n**	H	H	H	OH	3	**5n**	90	100:0
15	**10o**	OH	H	OH	H	48		0	

enophiles or show rather weak reactivity like 6-*p*-methoxybenzylidene-3,4-methylenedioxy-2,4-cyclohexadien-1-one (**9**),[1f,3d] which is known as a stable and isolable *o*-quinonemethide.

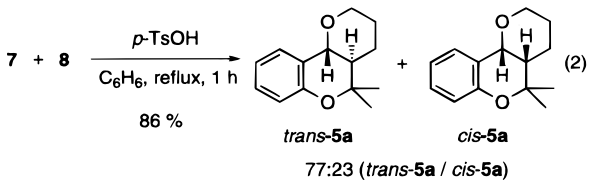


9

In this paper, we report the reaction of various substituted salicylaldehydes and unsaturated alcohols in detail.[5]

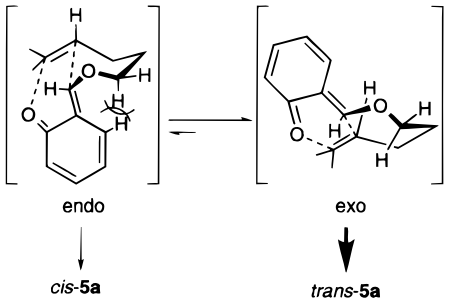
Results and Discussion

On the basis of the above concept, salicylaldehyde dimethyl acetal (**7**) and 5-methyl-4-hexen-1-ol (**8**) were reacted in benzene in the presence of *p*-toluenesulfonic acid (*p*-TsOH) at reflux to give pyranobenzopyran **5a** as a mixture of trans and cis stereoisomers (eq 2).



This fact strongly suggests that the reaction proceeds through alkoxy-substituted *o*-quinonemethide **4** with concurrent elimination of 2 mol of methanol. To improve the stereoselectivity of [4 + 2] cycloaddition and to avoid handling thermally labile and moisture-sensitive salicylaldehyde acetal, salicylaldehyde (**10a**) was reacted with trimethyl orthoformate in benzene in the presence of *p*-TsOH. To this solution was added alcohol **8** at room temperature, and the resulting solution was stirred for 1 h. The reaction gave *trans*-**5a** as a single stereoisomer (entry 1, Table 1).

Scheme 3



Reaction of Substituted Salicylaldehydes 10 with Alcohol 8. Then we investigated the reaction between various substituted salicylaldehydes and unsaturated alcohols to understand the reactivity and stereoselectivity of this reaction. The reactions were carried out by stirring a solution of alcohol **8** (1 mmol), aldehyde **10** (1.2 mmol), trimethyl orthoformate (1.2 mmol), and *p*-TsOH (0.2 mmol) in benzene (5 mL) at room temperature. The results are summarized in Table 1.

The formation of tricyclic compounds **5** took place in good yields with both salicylaldehydes carrying electron-withdrawing groups and those substituted by weekly electron-donating groups, and the products had B/C-trans ring junction in high stereoselectivity. The stereoselectivity of this reaction can be explained on the basis of steric repulsion illustrated in Scheme 3.[6]

The reaction of methoxy- or hydroxy-substituted salicylaldehydes merits some comments. In contrast to sterically hindered 2-hydroxy-1-naphthaldehyde (**10f**), which gave **5f** in 79% yield, salicylaldehydes substituted by methoxy or hydroxy groups at R^1 or R^3 positions gave very low yields of the tricyclic products, with a lack of stereoselectivity in the case of hydroxy-substituted ones. Obviously, the decrease of reactivity of these salicylaldehydes is not due to steric effects but seems to arise from electronic effects; that is, *o*-quinonemethides derived

(5) Inoue, S.; Asami, M.; Honda, K.; Miyazaki, H. *Chem. Lett.* **1996**, 889.

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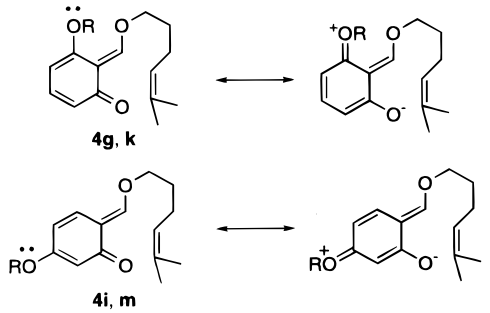
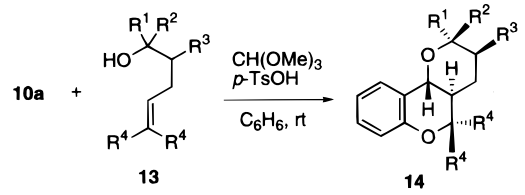


Figure 1.

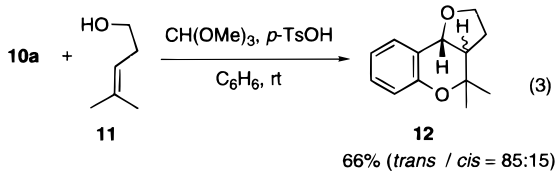
Table 2. Reaction of Salicylaldehyde and Substituted Unsaturated Alcohols



alcohol	R^1	R^2	R^3	R^4	time (h)	product	yield(%)	trans/cis
13a	H	H	H	H	5 days		0	
13b	Me	H	H	Me	4	**14b**	96	100:0
13c	Me	Me	H	Me	6	**14c**	64	100:0
13d	H	H	Me	Me	1.5	**14d**	95	100:0

from these salicylaldehydes are stabilized by resonance as shown in Figure 1 and hence have diminished reactivity as electron-deficient dienes.

Reaction with Alcohols of Different Carbon Length. Next, we investigated the reaction between salicylaldehyde and unsaturated alcohols of different numbers of carbon atoms, to clarify the possibility of formation of a tricyclic system of different ring size. When 3-methyl-2-buten-1-ol or 6-methyl-5-hepten-1-ol was treated with salicylaldehyde and trimethyl orthoformate as before at room temperature or at reflux, none of tricyclic products were obtained at all. On the contrary, reaction of salicylaldehyde with 4-methyl-3-penten-1-ol (**11**) afforded a stereoisomeric mixture of tricyclic compounds **12** at room temperature, and the ratio of trans/cis was 85:15 (eq 3).



(3)

Reaction of Salicylaldehyde with Substituted Alcohols. To clarify reactivity of substituted unsaturated alcohols, we next investigated the reaction between salicylaldehyde and methyl-substituted alcohols (Table 2).

The reaction between salicylaldehyde and 4-penten-1-ol (**13a**) was carried out at room temperature to refluxing conditions for 5 days, but tricyclic compound could not be obtained. The failure of the reaction may be attributed to the low electron density at the olefinic moiety. Therefore, it can be suggested that the present formation of pyranobenzopyran skeleton proceeded via inverse electron demand [4 + 2] cycloaddition.[1]

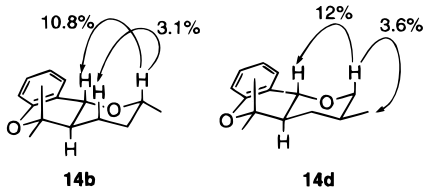


Figure 2.

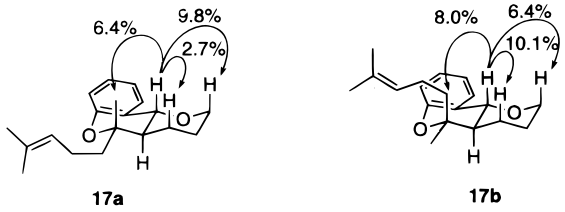
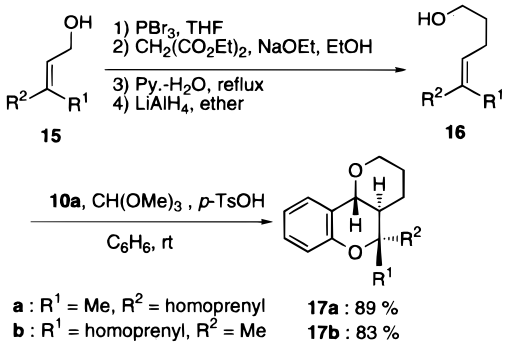


Figure 3.

Scheme 4



Secondary alcohol **13b** and, even, tertiary alcohol **13c** afforded pyranobenzopyrans **14b** and **14c**, respectively, in excellent to good yields. The reaction of salicylaldehyde with **13b** and **13d** afforded the tricyclic products **14b** and **14d**, respectively, as a single stereoisomer. The equatorial orientation of the methyl group was confirmed by NOE experiments as shown in Figure 2.

Reaction of Salicylaldehyde with (*E*)- or (*Z*)-Trisubstituted Olefinic Alcohols. It seemed worthwhile to thoroughly examine the stereospecificity of this reaction from synthetic and mechanistic points of view. For this purpose, we synthesized alcohols **16a** and **16b** from geraniol (**15a**) and nerol (**15b**), respectively. These alcohols were reacted with salicylaldehyde under similar conditions as described above to give the tricyclic products **17** as the single stereoisomer for the respective alcohol (Scheme 4).

The ^{1}H and ^{13}C NMR spectra of these products are quite similar, but chemical shifts of methyl at C-5 (**17a**, 1.17 ppm; **17b**, 1.38 ppm) and olefinic hydrogen (**17a**, 5.13 ppm; **17b**, 5.02 ppm) are different for the two. The configurations of the methyl and homoprenyl substituents at C-5 were again confirmed by NOE experiments (Figure 3). It is worthwhile to note that the homoprenyl group of **17b** is situated at the axial position, despite the energetically unfavored transition state with axial substituent. These results indicate that the present [4 + 2] cyclization reaction proceeds completely in a stereospecific manner.

In summary, we have shown that one-pot reaction of salicylaldehydes with unsaturated alcohols in the presence of trimethyl orthoformate and a catalytic amount of *p*-TsOH provides a new, efficient, and stereoselective

method to *trans*-tetrahydropyrano[3,2-*c*]benzopyrans, which can be of interest for synthesis of natural products with these tricyclic skeletons.

Experimental Section

General Methods. Melting points are uncorrected. ^{1}H NMR (270 MHz) and ^{13}C NMR (68 MHz) spectra were recorded with tetramethylsilane as internal standard in $CDCl_3$. Column chromatography was carried out with Fuji Silysia silica gel BW-127ZH (Fuji Silysia Chemical Industries) or Cica-Merck silica gel 60 (Kanto Chemical Industries). Thin-layer chromatography (TLC) was carried out with Merck TLC plates with silica gel 60 F_{254}.

Materials. *p*-Toluenesulfonic acid monohydrate was recrystallized from ethanol and water. Benzene was distilled from sodium. 5-Methyl-4-hexen-1-ol (**8**),[7] 4,6-dimethyl-2-hydroxybenzaldehyde (**10d**),[8] 3,6-dimethyl-2-hydroxybenzaldehyde (**10e**),[9] 2-hydroxy-6-methoxybenzaldehyde (**10g**),[10] 2,6-dihydroxybenzaldehyde (**10k**),[11] 4-methyl-3-penten-1-ol (**11**),[12] 2,6-dimethyl-5-hepten-2-ol (**13c**),[13] 2,5-dimethyl-4-hexen-1-ol (**13d**),[14] (4*E*,8*E*)-5,9-dimethyl-4,8-decadien-1-ol (**16a**),[15] and (4*E*,8*Z*)-5,9-dimethyl-4,8-decadien-1-ol (**16b**)[15] were prepared as described in the literature. All other reagents were obtained from commercial sources and used as received.

General Procedure for Reaction of Unsaturated Alcohols and 2-Hydroxybenzaldehyde Derivatives. A flask was charged in succession with alcohol **8**, **11**, **13**, or **16** (1 mmol), salicylaldehyde or benzaldehydes **10** (1.2 mmol), trimethyl orthoformate (127 mg, 1.2 mmol), and *p*-toluenesulfonic acid (38.0 mg, 0.2 mmol) in benzene (5 mL). The mixture was then stirred at room temperature and monitored by TLC. The reaction mixture was treated under stirring with 10% NaOH solution (2 mL) or saturated $NaHCO_3$ solution (2 mL), and the organic layer was separated. The aqueous layer was extracted with ether (10 mL × 3), and the combined organic layers were washed with brine. The organic layer was dried over anhydrous $MgSO_4$ and filtered. The filtrate was evaporated in vacuo to give a crude product, which was purified by silica gel chromatography to give a cycloadduct **5**, **12**, **14**, or **17**.

***trans*-5,5-Dimethyl-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5a):** yield 86% as white crystals; mp 66−67 °C; IR (KBr) 1615, 1580, 1100, 1080 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.33 (m, 1H), 1.39 (s,3H), 1.67−1.83 (m, 3H), 1.93 (m, 1H), 3.65 (m, 1H), 4.16 (m, 1H), 4.19 (d, J = 10.6 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 6.89 (t, J = 7.6 Hz, 1H), 7.15 (dd, J = 7.6, 8.2 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.4, 25.1, 26.2, 27.6, 45.1, 68.2, 73.6, 78.3, 116.7, 119.9, 122.5, 126.0, 128.8, 152.7; HRMS (EI, *m*/*e*) calcd for $C_{14}H_{18}O_2$ (M^+) 218.1307, found 218.1320. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.10; H, 8.33.

***trans*-9-Bromo-5,5-dimethyl-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5b):** yield 81% as a colorless high viscosity oil; IR (neat) 1590, 1140, 1070 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.18 (s, 3H), 1.35 (m, 1H), 1.38 (s, 3H), 1.63−1.80 (m, 3H), 1.90 (m, 1H), 3.63 (m, 1H), 4.12 (m, 1H), 4.15 (d, J = 10.9 Hz, 1H), 6.64 (d, J = 8.6 Hz, 1H), 7.24 (d, J = 8.6 Hz, 1H), 7.53 (s, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.3, 24.8, 26.0, 27.4, 44.6, 68.2, 72.9, 78.7, 112.0, 118.4, 124.4, 128.8, 131.5, 151.8; HRMS (EI, *m*/*e*) calcd for $C_{14}H_{17}BrO_2$ (M^+) 296.0411, found 296.0413.

***trans*-5,5-Dimethyl-9-nitro-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5c):** yield 60% as white crystals; mp 112−114 °C; IR (KBr) 1585, 1507, 1133, 1091 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.44 (s, 3H), 1.30−2.01 (m, 5H), 3.66 (m, 1H), 4.19 (m, 1H), 4.20 (d, J = 10.9 Hz, 1H), 6.82 (d, J = 8.9 Hz, 1H), 8.05 (ddd, J = 0.7, 3.0, 8.9 Hz, 1H), 8.37 (dd, J = 0.7, 3.0 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.8, 24.8, 25.9, 27.3, 44.5, 68.2, 72.2, 80.7, 117.3, 123.0, 124.8, 140.9, 158.3 (one carbon peak is overlapping); HRMS (EI, *m*/*e*) calcd for $C_{14}H_{17}NO_4$ (M^+) 263.1157, found 263.1153. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.94; H, 6.54; N, 5.34.

***trans*-5,5,8,10-Tetramethyl-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5d):** yield 96% as white crystals; mp 56−57 °C; IR (KBr) 1618, 1577, 1137, 1082 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.28 (m, 1H), 1.35 (s, 3H), 1.68−1.95 (m, 4H), 2.20 (s, 3H), 2.32 (s, 3H), 3.60 (dt, J = 3.6, 11.5 Hz, 1H), 4.06 (m, 1H), 4.15 (d, J = 9.6 Hz, 1H), 6.44 (s, 1H), 6.52 (s, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.6, 21.1, 21.4, 26.0, 26.8, 27.7, 46.9, 68.3, 75.3, 77.9, 115.5, 117.9, 124.1, 138.9, 153.9 (one carbon peak is overlapping); HRMS (EI, *m*/*e*) calcd for $C_{16}H_{22}O_2$ (M^+) 246.1620, found 246.1608.

***trans*-5,5,7,10-Tetramethyl-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5e):** white crystals; mp 48−49 °C.

***trans*-5,5-Dimethyl-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano-[3,2-*c*]benzo[*f*][1]benzopyran (5f):** yield 79% as white crystals; mp 112−114 °C; IR (KBr) 1619, 1595, 1135, 1068 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.45 (s, 3H), 1.52 (m, 1H), 1.80−2.09 (m, 4H), 3.85 (dt, J = 3.6, 11.6 Hz, 1H), 4.22 (m, 1H), 4.59 (d, J = 9.6 Hz, 1H), 6.98 (d, J = 8.9 Hz, 1H), 7.30 (t, J = 7.9 Hz, 1H), 7.44 (m, 1H), 7.66 (d, J = 8.9 Hz, 1H), 7.71 (d, J = 7.9 Hz, 1H), 8.21 (d, J = 8.9 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.0, 25.4, 26.5, 27.2, 46.8, 68.2, 74.5, 78.1, 113.3, 119.2, 123.0, 125.1, 125.9, 128.1, 129.2, 130.0, 132.4, 151.5; HRMS (EI, *m*/*e*) calcd for $C_{18}H_{20}O_2$ (M^+) 268.1463, found 268.1459.

***trans*-5,5-Dimethyl-10-methoxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5g):** yield 8% as a colorless oil; IR (CCl_4) 1590, 1467, 1086 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.11 (s, 3H), 1.34 (m, 1H), 1.37 (s, 3H), 1.61−1.97 (m, 4H), 3.67 (dt, J = 3.7, 11.6 Hz, 1H), 3.82 (s, 3H), 4.12 (dd, J = 5.0, 11.6 Hz, 1H), 4.27 (d, J = 9.9 Hz, 1H), 6.42 (dd, J = 2.7, 8.3 Hz, 2H), 7.10 (t, J = 8.3 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.1, 25.7, 26.6, 27.2, 29.7, 46.7, 56.1, 68.4, 73.7, 78.1, 103.3, 110.2, 129.3, 154.9, 159.5; HRMS (EI, *m*/*e*) calcd for $C_{15}H_{20}O_3$ (M^+) 248.1412, found 248.1398.

***trans*-5,5-Dimethyl-9-methoxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5h):** white crystals; mp 52−53 °C.

***trans*-5,5-Dimethyl-8-methoxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5i):** white crystals; mp 76−77 °C.

***trans*-5,5-Dimethyl-7-methoxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5j):** white crystals; mp 96−97 °C.

***trans*- and *cis*-5,5-Dimethyl-10-hydroxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5k).** Mixture of diastereomers (trans/cis = 62:38): total yield 31% as colorless oil. The mixture was chromatographed on silica gel to give pure *trans*-**5k** as white crystals: mp 94−95 °C (*n*-hexane); IR (KBr) 3312, 1625, 1584, 1070, 1028 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.18 (s, 3H), 1.30 (m, 1H), 1.39 (s, 3H), 1.43−1.97 (m, 4H), 3.72 (dt, J = 4.3, 11.2 Hz, 1H), 4.18 (m, 1H), 4.53 (d, J = 10.6 Hz, 1H), 6.33 (d, J = 8.3 Hz, 1H), 6.42 (d, J = 8.3 Hz, 1H), 7.04 (t, J = 8.3 Hz, 1H), 8.24 (s, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.2, 24.5, 25.9, 27.4, 44.7, 68.3, 75.4, 78.2, 107.3, 108.0, 108.6, 129.9, 153.7, 156.8; HRMS (EI, *m*/*e*) calcd for $C_{14}H_{18}O_3$ (M^+) 234.1256, found 234.1295.

***trans*-5,5-Dimethyl-9-hydroxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5l).** Products were ob-

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tained as a mixture of diastereomers (trans/cis = 99:1 by GC): white crystals; mp 113−114 °C (*n*-hexane).

***trans*- and *cis*-5,5-Dimethyl-8-hydroxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5m)**. Mixture of diastereomers (trans/cis = 73:27): white crystals; mp 93−95 °C.

***trans*-5,5-Dimethyl-7-hydroxy-3,4,4a,10b-tetrahydro-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (5n):** yield 90% as white crystals; mp 135−136 °C; IR (KBr) 3396, 1597, 1138, 1093, 1034 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.34 (m, 1H), 1.44 (s, 3H), 1.57−1.96 (m, 4H), 3.64 (m, 1H), 4.18 (m, 1H), 4.21 (d, J = 10.6 Hz, 1H), 5.48 (s, 1H), 6.81 (m, 2H), 6.94 (m, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.5, 25.0, 26.1, 27.5, 45.2, 68.2, 73.4, 79.7, 113.4, 116.9, 120.0, 122.6, 139.7, 144.5; HRMS (EI, *m*/*e*) calcd for $C_{14}H_{18}O_3$ (M^+) 234.1256, found 234.1280. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.88; H, 7.72.

***trans*- and *cis*-4,4-Dimethyl-2,3,3a,9b-tetrahydro-4*H*-furo[3,2-*c*][1]benzopyran (12).** Mixture of diastereomers (trans/cis = 85:15): yield 66% as white crystals; mp 86−87 °C; IR (KBr) as a mixture of diastereomers; 1612, 1579, 1124, 1078, 1028 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) trans isomer: δ 1.32 (s, 3H), 1.49 (s, 3H), 1.81−2.12 (m, 3H), 4.13−4.29 (m, 2H), 4.43 (d, J = 10.9 Hz, 1H), 6.82 (dd, J = 1.0, 8.3 Hz, 1H), 6.89 (ddd, J = 1.0, 7.3, 7.6 Hz, 1H), 7.16 (ddd, J = 1.0, 7.3, 8.3 Hz, 1H), 7.26 (dd, J = 1.0, 7.6 Hz, 1H); cis isomer: δ 1.32(s, 3H), 1.38 (s, 3H), 1.82−2.27 (m, 2H), 2.44 (dd, J = 7.3, 8.6 Hz, 1H), 3.75−3.91 (m, 2H), 4.99 (d, J = 7.2 Hz, 1H), 6.75 (dd, J = 1.0, 8.3 Hz, 1H), 6.93 (ddd, J = 1.0, 7.3, 7.6 Hz, 1H), 7.16 (ddd, J = 1.0, 7.3, 8.3 Hz, 1H), 7.37 (dd, J = 1.0, 7.6 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) as mixture of diastereomers: δ 21.5, 26.0, 26.4, 26.7, 29.5, 46.3, 50.8, 66.6, 68.9, 73.0, 74.4, 75.7, 79.4, 116.3, 116.9, 119.6, 120.8, 124.3, 124.4, 128.4, 128.9, 129.4, 152.6, 152.8 (two carbon peaks are overlapping); HRMS (EI, *m*/*e*) calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1183.

***trans*-3,4,4a,10b-Tetrahydro-2,5,5-trimethyl-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (14b):** yield 96% as white crystals; mp 81−82 °C; IR (KBr) 1620, 1590, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.30 (d, J = 6.3 Hz, 3H), 1.38 (m, 1H), 1.39 (s, 3H), 1.53−1.93 (m, 4H), 3.71 (m, 1H), 4.25 (d, J = 10.6 Hz, 1H), 6.75 (dd, J = 1.0, 8.3 Hz, 1H), 6.89 (ddd, J = 1.3, 7.3, 7.6 Hz, 1H), 7.14 (ddd, J = 1.0, 7.3, 8.3 Hz, 1H), 7.46 (dd, J = 1.3, 7.6 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.4, 22.0, 25.4, 27.7, 33.4, 44.6, 73.1, 73.8, 78.4, 116.6, 119.9, 122.6, 126.1, 128.7, 152.7; HRMS (EI, *m*/*e*) calcd for $C_{15}H_{20}O_2$ (M^+) 232.1463, found 232.1432. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.82; H, 8.71.

***trans*-3,4,4a,10b-Tetrahydro-2,2,5,5-tetramethyl-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (14c):** white crystals; mp 69−70 °C.

***trans*-3,4,4a,10b-Tetrahydro-3,5,5-trimethyl-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (14d):** white crystals; mp 61−62 °C.

(4a*R,5*R**,10b*R**)-3,4,4a,10b-Tetrahydro-5-methyl-5-(4-methyl-3-pentenyl)-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (17a):** yield 89% as a colorless oil; IR (neat) 1620, 1590, 1190, 1090 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.21−2.23 (m, 7H), 1.63 (s, 3H), 1.70 (s, 3H), 3.66 (dt, J = 3.6, 11.2 Hz, 1H), 4.15 (m, 1H), 4.26 (d, J = 10.2 Hz, 1H), 5.13 (m, 1H), 6.78 (dd, J = 1.0, 8.2 Hz, 1H), 6.88 (ddd, J = 1.0, 7.3, 7.6 Hz, 1H), 7.15 (ddd, J = 1.0, 7.3, 8.2 Hz, 1H), 7.40 (dd, J = 1.0, 7.6 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 17.6, 19.9, 21.1, 24.8, 25.7, 26.2, 39.5, 42.0, 68.2, 73.5, 79.5, 116.7, 119.7, 122.4, 124.1, 125.9, 128.7, 131.8, 153.0; HRMS (EI, *m*/*e*) calcd for $C_{19}H_{26}O_2$ (M^+) 286.1933, found 286.1962.

(4a*R,5*S**,10b*R**)-3,4,4a,10b-Tetrahydro-5-methyl-5-(4-methyl-3-pentenyl)-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran (17b).** The mixture of **16b** and **16a** was used as starting material, and the stereoisomeric ratio of *Z*/*E* was 96:4. This reaction gave a mixture of diastereomers (**17b**/**17a** = 96:4) as colorless oil, and the **17b** was isolated by silica gel chromatography.

Acknowledgment. The authors would like to thank Assoc. Prof. Hiroko Suezawa, Instrumental Analysis Center, Yokohama National University, for ^1H NMR measurements (NOE experiment and NOESY spectra) and Dr. Takeo Kaneko for HRMS measurement on JEOL JMS-AX-500 apparatus. This work was supported in part by a Grant-in-Aid for Scientific Research No. 09450339 from the Ministry of Education, Science, Sport, and Culture, Japan.

Supporting Information Available: Photo copies of ^1H NMR and ^{13}C NMR spectra for **5a**−**n**, **12**, **14b**−**d**, and **17a**,**b** and detailed ^1H NMR, ^{13}C NMR, IR, and MS data for compounds **5e**,**h**−**j**, **l**,**m**, **14c**,**d**, and **17b**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO991132H