Scandium Trifluoromethanesulfonate-Catalyzed Cleavage of Esters Bearing a Coordinative Group at a Vicinal Position

Hiroshi Kajiro, Shuichi Mitamura,[†,#] Atsunori Mori, and Tamejiro Hiyama[*,##]

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503

[†]Advanced Technology Research Laboratories, Nippon Steel Corporation, 3-35-1 Ida, Nakahara-ku, Kawasaki 211-0035

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Scandium trifluoromethanesulfonate is found to be a Lewis acid catalyst for selective cleavage of esters containing a coordinative group adjacent to an ester moiety. The reaction proceeds under weak acidic conditions at room temperature; the catalyst can be recovered and reused. Even α-acyloxy ketones are deacetylated without racemization. Selective monodeacetylation at C-10 of paclitaxel has been achieved.

Ester functionality is the most frequently used protective group for a hydroxy group. In addition, protection of carboxylic acids with alcohols also plays an important role in organic synthesis. Although a number of protocols have been developed for cleavage of esters, a mild and selective deprotection procedure is still a significant target of experimental organic chemistry.[1] The most commonly adopted method for the cleavage of esters is a basic hydrolysis because of its efficiency and irreversible nature. However, this procedure has a potential drawback of such undesired side reactions as elimination and racemization.[2] An alternative ester cleavage employs acidic conditions. However, an acid-catalyzed hydrolysis is a reversible process in favor of ester formation and is, in general, sluggish. Although ester cleavage with a Lewis acid in a nonaqueous medium has also been documented, these procedures sometimes require the use of a nucleophilic agent at elevated temperatures.[3]

During our study concerning the development of a new route to enantiomerically pure (1*S*, 2*R*)-1-amino-2-indanol, we encountered a problem of deacetylation of (*R*)-2-acetoxyindan-1-one without racemization.[4] Since this optically active acyloxy ketone is unstable to heat, the deacetylation must be performed at room or lower temperatures. In addition, the acetate is extremely sensitive to such alkalines as K_2CO_3 or LiOH to racemize with concomitant degradation. After screening for a catalyst appropriate to the acetate cleavage, we have found that rare earth trifluoromethanesulfonates (rare earth triflate, $RE(OTf)_3$), especially $Sc(OTf)_3$, work as an efficient deacetylation catalyst. For example, $Sc(OTf)_3$-catalyzed deacetylation was found to proceed in an aqueous solvent at room temperature without racemization. In studying details of the reaction, we found that such a coordinative group as carbonyl or methoxy adjacent to an acyloxy moiety played a significant role in the efficient cleavage (Scheme 1). Herein we report $Sc(OTf)_3$-catalyzed mild, efficient and selective cleavage of esters bearing a coordinative group and details of the reaction mechanisms.[5]

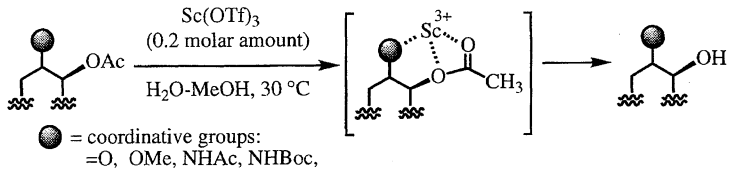
Results and Discussion

First, we studied deacetylation of 2-acetoxyindan-1-one (**1a**) as a model in aqueous MeOH at 30 °C in the presence of acid catalyst, and the catalytic ability of an acid catalyst was compared by the yield of product 2-hydroxyindan-1-one (**1b**) after 24 h. The results are shown in Fig. 1. Scandium triflate catalyzed the reaction smoothly to give **1b** in 96% yield, whereas the reaction catalyzed by HCl was sluggish; the yield was not improved with H_2SO_4 or trifluoromethanesulfonic acid. Although such Lewis acids as $SnCl_4$ and $TiCl_3$ easily decompose in an aqueous solvent to a certain extent, these exhibited better catalytic ability than HCl but far less than $Sc(OTf)_3$.

Next, other rare earth triflates ($RE(OTf)_3$) was compared with $Sc(OTf)_3$ in the catalytic ability. As Fig. 2 shows, most of $RE(OTf)_3$ catalyzed the deacetylation of **1a**; $Sc(OTf)_3$ exhibited still the highest activity. Although Inanaga reported recently that $Yb(OTf)_3$ was an excellent methanolysis catalyst for methoxyacetates,[6] $Sc(OTf)_3$ was found to be more efficient for the deacetylation of **1a**: 96% yield (HPLC) with $Sc(OTf)_3$; 75% yield with $Yb(OTf)_3$ after 24 h.

To explore a possibility of neighboring group participation of a ketone carbonyl group in **1a**, we compared the rate of the deacetylation of 2-acetoxyindan-1-one (**1a**) with that of 2-acetoxyindane (**2a**) using various acids. The results summarized in Fig. 3 clearly show that the rate of H_2SO_4-catalyzed deacetylation of **1a** was comparable to that of **2a** lacking

Present address: Nippon Steel Chemical Co., Ltd., 2nd TOC Building, 7-21-11 Nishigotanda, Shinagawa-ku, Tokyo 141-0031.
Present address: Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Yoshida, Kyoto 606-8501.



Scheme 1.

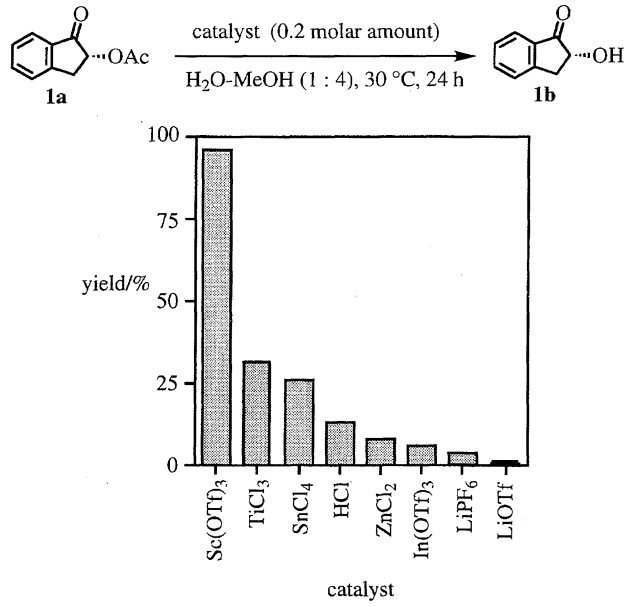


Fig. 1. Deacetylation of **1a** using various Lewis acids.

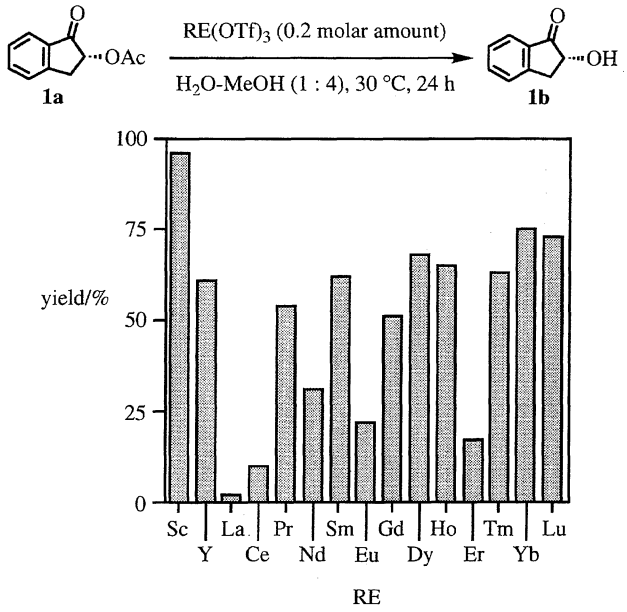


Fig. 2. Deacetylation of **1a** catalyzed by RE(OTf)$_3$.

such a coordinative group. Similar rates were observed also with HCl or trifluoromethanesulfonic acid. Namely, these Brønsted acids cannnot discriminate the structural difference between **1a** and **2a**. When a catalyst was switched to Sc(OTf)$_3$, the reaction rate of **2a** was only 2-fold faster than the H_2SO_4-catalyzed cleavage (after 2 h). With **1a** as a substrate, the rate difference was enhanced to 25-fold after 2 h. These results suggest that the carbonyl group of **1a** participates in the Sc(OTf)$_3$-catalyzed deacetylation through coordination.

The cleavage of various α- or β-acetoxy ketones was examined in an aqueous MeOH (H_2O : MeOH = 1 : 4) in the presence of Sc(OTf)$_3$ (0.2 molar amount) at room temperature (ca. pH 3); the results are summarized in Table 1. Cyclic or acyclic α-acetoxy ketones were smoothly deacetylated to the corresponding α-hydroxy ketones in good yields (Entries 1—6). In contrast, a β-acetoxy ketone required a prolonged reaction time; the yield was disappointedly low due to a

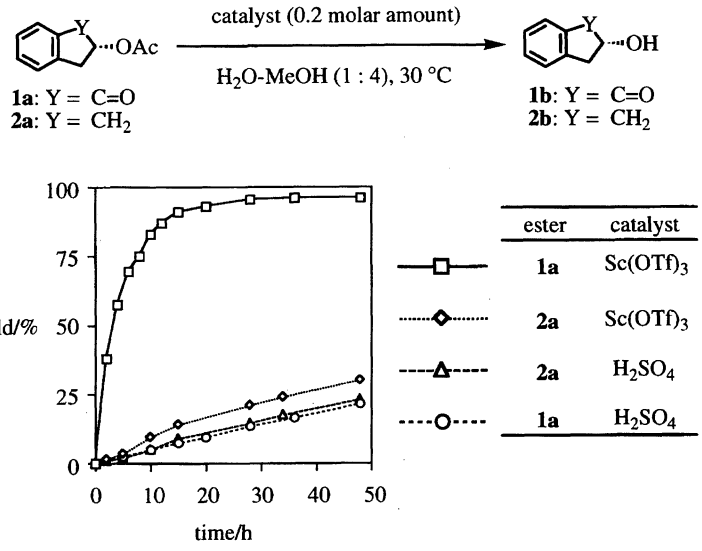
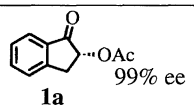
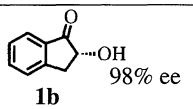
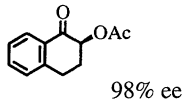
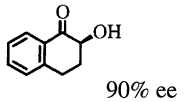
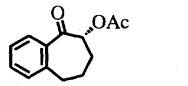
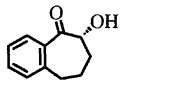
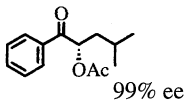
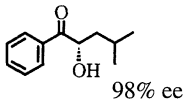
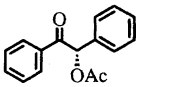
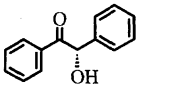
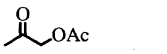
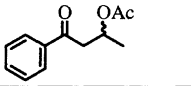
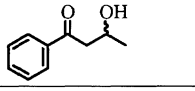


Fig. 3. Time course of deacetylation of **1a** and **2a** catalyzed by Sc(OTf)$_3$ or H_2SO_4.

Table 1. $Sc(OTf)_3$-Catalyzed Cleavage of Acetates Bearing a Carbonyl Group[a)]

Entry	Substrate	Product[b)]	Time/h	Yield[c)]/%
1	 99% ee **1a**	 98% ee **1b** (75% yield, 8% ee)	40	93
2	 98% ee	 90% ee (23% yield, 26% ee)	40	82
3	 94% ee	 94% ee (34% yield, 1% ee)	40	84
4	 99% ee	 98% ee (53% yield, 33% ee)	66	72
5	 99% ee	 91% ee (39% yield, 1% ee)	73	90
6			40	77[b)]
7			112	39

a) A mixture of substrate (1 mol) and $Sc(OTf)_3$ (0.2 mol) dissolved in H_2O and MeOH (1 : 4) was stirred at 30 °C. b) Yield and ee in parentheses are those of the hydrolysis with LiOH (1.5 mol). c) Isolated yield unless otherwise specified. d) HPLC yield.

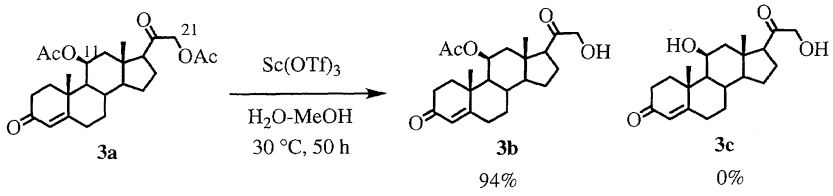
side reaction such as dehydration (Entry 7). The catalyst was recovered and reused. Because of the high solubility of $Sc(OTf)_3$ in H_2O, extraction of a reaction mixture by an appropriate organic solvent followed by concentration of an aqueous phase allows one to recover the catalyst quantitatively. Deacetylation of **1a** was performed using recovered $Sc(OTf)_3$ equally well: use of a fresh catalyst, 93% yield and a 100% catalyst recovery; 2nd use, 91% yield and a 100% catalyst recovery.

A salient feature of this reaction is that the racemization of such stereochemically labile acetates as α-acetoxy ketones is negligible, if any (Entries 1—5). The advantage of the present method is obvious, if one compares with the results of control experiments using an alkaline catalyst. Treatment of **1a** with K_2CO_3 in aqueous MeOH induced decomposition to give none of alcohol **1b**.[4] A LiOH catalyst[7] suppressed the decomposition to a certain extent, but considerable racemization accompanied the reaction.

Another feature of this procedure is selective cleavage of an acetyl moiety closest to a coordinative group. When corticosterone 11,21-diacetate (**3a**) was subjected to the ester cleavage, the acetoxy group at C-21 was selectively cleaved to give monoacetate **3b** in 94% yield; no formation of diol **3c** was observed (Scheme 2). In contrast, the deacetylation of **3a** catalyzed by K_2CO_3 produced in 91% yield **3b** which was contaminated with **3c** (3% yield).

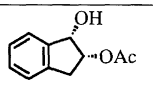
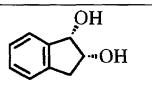
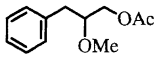
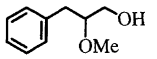
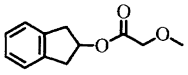
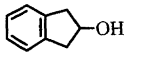
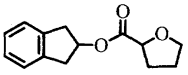
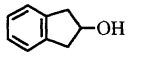
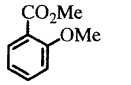
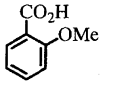
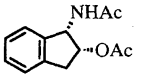
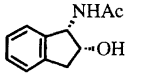
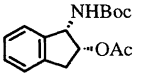
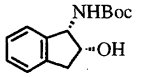
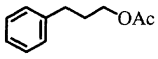
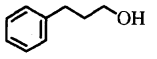
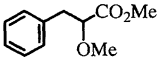
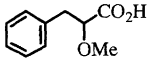
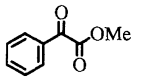
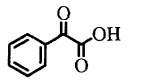
Cleavage of various esters bearing a coordinative group other than a carbonyl group was next examined, and the results are summarized in Table 2. A hydroxy or methoxy group at a vicinal position of an acetoxy group also served as a good coordinative group for $Sc(OTf)_3$ (Entries 1 and 2).

Indan-2-yl methoxyacetate and tetrahydrofuran-2-carboxylate also gave smoothly indan-2-ol in contrast to **2a** (Entries 3 and 4). The methoxy group of methyl 2-methoxybenzoate did not participate well in the $Sc(OTf)_3$ mediated cleavage (Entry 5).



Scheme 2.

Table 2. Sc(OTf)$_3$-Catalyzed Cleavage of Esters Bearing a Various Coordinative Group[a)]

Entry	Substrate	Product	Time/h	Yield[b)]/%
1			48	87
2			18	99
3			48	73[c)]
4			29	96[c)]
5			40	5[c)]
6			26	81
7			76	73
8			46	80
9	 **4a**	 **4b**	72	18[c)]
10	 **5a**	 **5b**	96	47[c)]

a) A mixture of substrate (1 mmol) and Sc(OTf)$_3$ (0.2 mmol) dissolved in H_2O and MeOH (1 : 4) was stirred at 30 °C. b) Isolated yield unless otherwise specified. c) HPLC yield.

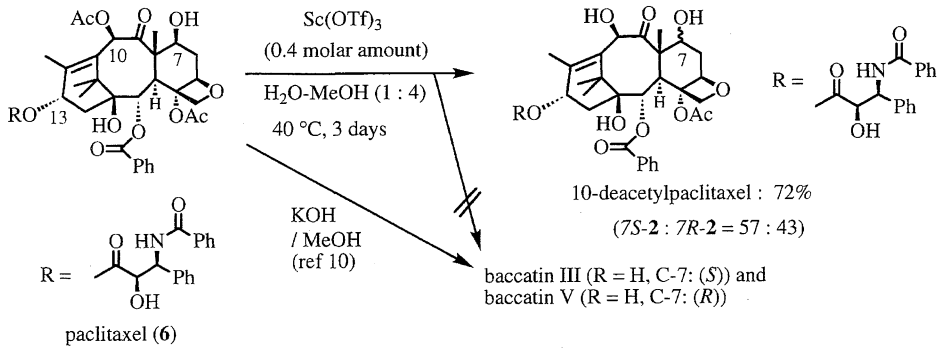
Amide and carbamate moieties are also available as a coordinative group, as seen in Entries 6 and 7. It is noteworthy that an acid-sensitive *N*-Boc group could survive the reaction conditions in spite of the acidic nature of Sc(OTf)$_3$.[8] Although the ester cleavage of an acetate of secondary alcohol such as **2a** was sluggish, an acetate of primary alcohol without a coordinative group was cleaved in a good yield but in a longer time (Entry 8).

Esters of an α-methoxy and an α-keto carboxylic acid were reluctantly cleaved to give the corresponding acids in moderate yields after long periods (Entries 9 and 10). Methyl phenylglyoxalate (**5a**, Entry 10) was also cleaved by RE(OTf)$_3$ other than Sc(OTf)$_3$, but yields of **5b** were not necessarily high. Catalyst and yield of **5b** after 24 h are given in this order: Sc(OTf)$_3$, 40%; Lu(OTf)$_3$, 11%; Yb(OTf)$_3$, 11%; Dy(OTf)$_3$, 9%; Pr(OTf)$_3$, 6%. The activity of the triflate salt is parallel to the one in the deacetylation of **1a**. The slow reaction of **4a** and **5a** may be explained by product inhibition of the catalyst through formation of a strongly chelated complex. An NMR experiment support this assumption. A ^{1}H NMR signal of $OC\underline{H}_3$ of **4b** appeared at 3.31 ppm in CD_3OD at room temperature. When 1.0 mol amount of Sc(OTf)$_3$ was added to the solution, 0.06 ppm downfield shift of the signal was observed even at room temperature. To the contrary, addition of Sc(OTf)$_3$ to ester **4a** in CD_3OD caused no shift of the ^{1}H NMR signals. These results suggest tight coordination by α-methoxy carboxylic acid **4b** through the carboxyl and methoxy groups to Sc(OTf)$_3$ to deactivate the catalyst. Throughout these experiments, neither cleavage nor elimination reaction of the coordinative group was observed.

We applied this procedure to selective deacetylation of paclitaxel (**6**) (Scheme 3).[9] Among four ester and one amido groups of paclitaxel, the acetyl group at C-10 adjacent to the carbonyl group at C-9 was selectively removed to give 10-deacetyl paclitaxel in 72% yield with recovery of **6** in 25% yield. Miller and Kingston reported that basic hydrolysis of **6** caused predominant removal of the C-13 side chain ester group to give baccatin III and V with concomitant epimerization at C-7.[10] In contrast, formation of baccatin III and V was not observed when Sc(OTf)$_3$ was used as a catalyst. These experimental results clearly demonstrate the unique selectivity of the Sc(OTf)$_3$-promoted ester cleavage. Modification of the substituent groups on the paclitaxel ring is a powerful method for improvement of the activity of **6**.[10,11] Modification at C-10 of **6** to polar residue contributes to improvement of activity, while the C-13 ester group is necessary for the full activity of **6**. Therefore, selective deacetylation at C-10 of **6** using Sc(OTf)$_3$ is an effective modification procedure.

It is worth noting that no cleavage of the C-13 ester group took place in spite of neighboring coordinative hydroxy and amido groups. Probably the C-13 ester moiety in paclitaxel is already forming such a firm intramolecular hydrogen bond that the chelation of the hydroxy and amido groups on the side chain is no longer possible for Sc(OTf)$_3$.[10d]

Scandium triflate has found a wide use in organic synthesis owing to such unique properties as high coordination num-



Scheme 3.

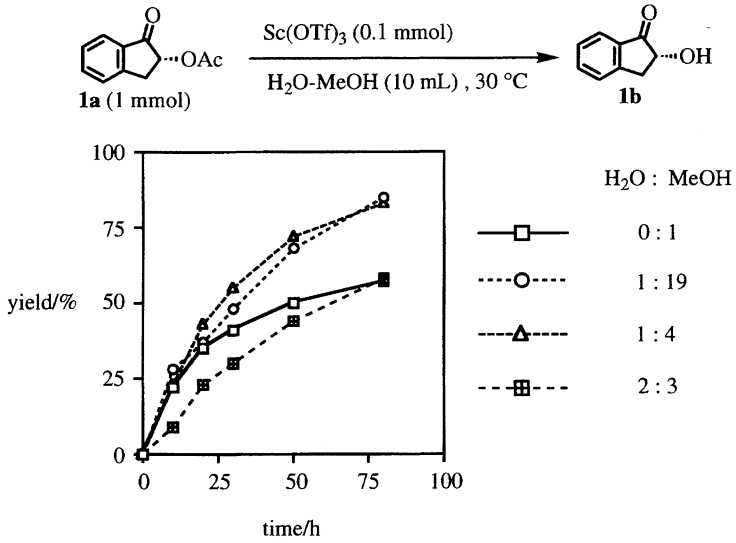


Fig. 4. Effect of water on deacetylation of **1a**.

bers, fast coordination-dissociation ability in equilibrium, and water-tolerant strong and hard Lewis acidity.[12] The effective deacetylation catalysis by $Sc(OTf)_3$ should arise, we consider, from coordination of Sc(III) to an acetyl group to activate the acetyl carbonyl.[6,13] In such a presumed mechanism, a coordinative group that can chelate to $Sc(OTf)_3$ plays a significant role in enhancing of the interaction of the catalyst and a substrate and in raising the reaction rate.

We further examined the effect of water content in MeOH. We monitored the ester cleavage in H_2O–MeOH (0 : 1, 1 : 19, 1 : 4, and 2 : 3) as shown in Fig. 4.

In all the tested solvents, the reaction proceeded in clear homogenous solution. When the reaction was carried out in an appropriate aqueous MeOH (H_2O : MeOH = 1 : 19 and 1 : 4), the reaction proceeded smoothly. To the contrary, progress of the reaction in absolute methanol was slower than that of in aqueous MeOH. The addition of excess amounts of H_2O to MeOH (H_2O : MeOH = 2 : 3) also slowed down the reaction. These results suggest that the deacetylation reaction catalyzed by $Sc(OTf)_3$ in H_2O–MeOH might occur by a nucleophilic attack of H_2O to an acetate carbonyl to give an alcohol and acetic acid. To confirm this presumption, we analyzed the $Sc(OTf)_3$-catalyzed deacetylation of **1a** in H_2O–MeOH (1 : 4) in more detail. The major products turned out to be alcohol **1b**, acetic acid (22% yield), and methyl acetate (72% HPLC yield after 24 h). Thus, the nucleophilic attack to the ester carbonyl was preferentially effected by MeOH rather than H_2O in a H_2O–MeOH (1 : 4) mixed solvent system. Although an exact mechanism is not clear yet, we consider that a water molecule in the solvent system may alter the chelation structure between a substrate and $Sc(OTf)_3$ or alternatively alter an aggregation structure of $Sc(OTf)_3$.

Conclusion

We have demonstrated that $Sc(OTf)_3$ acts as a catalyst for the cleavage of esters bearing an adjacent coordinative group. The reaction proceeds at room temperature; the catalyst is recoverable and reusable. Chemoselectivity of $Sc(OTf)_3$-catalyzed deacetylation differs from that of alkaline hydrolysis. Because of its weak acidic nature, an acetoxy group is selectively cleaved in preference to an acetylamino or *N*-Boc group. Since racemization rarely accompanies the reaction, we consider that this procedure will find wide use in the cleavage of racemizable substrates.

Experimental

All temperatures are uncorrected. Melting points were measured with a Mettler FP 62 auto melting point recorder. ^1H NMR spectra (TMS as an internal standard); ^{13}C NMR spectra ($CDCl_3$ as an internal standard) were measured on a Varian Mercury 300

NMR spectrometer. Chemical shifts are given in ppm; $CDCl_3$ was used as a solvent unless otherwise specified. Infrared (IR) spectra were recorded on a Shimadzu FT IR-8100A spectrometer. Optical rotations were recorded on a JASCO DIP-370 digital polarimeter in a 50 mm cell. Elemental analyses were carried out at Elemental Analysis Center, Tokyo Institute of Technology, using a Yanako MT2 CHN CORDER. Mass spectra were measured with a Finnigan MAT SSQ 7000 mass spectrometer using an ESI technique, MeOH as a mobile phase. High-resolution mass spectra (HRMS) were obtained on a JEOL MStation JMS 700 using EI technique. For thin layer chromatography (TLC) analyses throughout this work, Merck precoated HPTLC plates (silica gel 60 F_{254}) were used. Ee's were determined by HPLC using a Daicel analytical chiral column (0.46 mm×25 cm) at room temperature and a UV detector of 254 nm unless otherwise noted. HPLC analysis for the determination of yield was performed on ODS column (GL Science, inertsil ODS-2 column, 4.6 mm×10 cm, 40 °C) and MeOH in phosphoric acid aqueous solution (0.2 v/v%) as an eluent (1 mL min^{-1}). Silica gel preparative thin layer chromatography was carried out using Merck Silica Gel 60 PF_{254}. Anhydrous MeOH was purchased from Merck Co., Ltd. Scandium triflate was purchased from Aldrich Chemical Inc. Rare earth triflate other than $Sc(OTf)_3$ was prepared according to the reported procedure.[14]

The following esters: (*R*)-2-Acetoxyindan-1-one,[15] 2-acetoxyindane,[16] (*S*)-2-acetoxy-3,4-dihydronaphthalen-1(2*H*)-one,[17] (*S*)-2-acetoxy-1,2-diphenylethan-1-one,[17] 1-acetoxy-propan-2-one,[18] (±)-3-acetoxy-1-phenylbutan-1-on,[19] corticosterone 11,21-diacetate,[13b] (1*S*, 2*R*)-2-acetoxyindan-1-ol,[13b] 1-acetoxy-2-methoxy-3-phenylpropane,[20] 1-acetoxy-3-phenylpropane,[13b] and methyl 2-methoxy-3-phenylpropanoate,[21] were synthesized according to the reported procedures.

(*R*)-6-Acetoxy-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one: This compound was obtained as a colorless oil by optical resolution of (±)-6-acetoxy-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one[22] through HPLC using DAICEL CHIRALPAK AD (10×250 mm) with propan-2-ol in hexane (20 v/v%) as an eluent (2.4 mL min^{-1}). (*R*)-Isomer was eluted at t_R = 9.6 min and (*S*)-isomer at t_R = 8.6 min. $[\alpha]_D^{25}$ = +11.3° (*c* 1.0, EtOH, 94% ee); IR (neat) 2942, 1742, 1701, 1599, 1449, 1238, 1082, 963 cm^{-1}; ^{1}H NMR δ = 1.76—1.88 (m, 1 H), 1.98—2.28 (m, 3 H), 2.15 (s, 3 H), 2.92—3.09 (m, 2 H), 5.43 (dd, *J* = 5.5, 11.0 Hz, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 7.30 (t, *J* = 7.5 Hz, 1 H), 7.39—7.43 (m, 1 H), 7.72 (dd, *J* = 1.0, 8.0 Hz, 1 H); ^{13}C NMR δ = 20.66, 23.50, 29.14, 34.04, 77.50, 126.69, 129.06, 129.93, 131.98, 136.58, 141.53, 170.13, 199.57. Found: C, 71.33; H, 6.14%. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47%.

(*S*)-2-Acetoxy-4-methyl-1-phenylpentan-1-one:[15] Colorless oil. The ee was 93% as determined by HPLC with CHIRALPAK AD (5 v/v% EtOH/hexane, 0.8 mL min^{-1}), t_R = 5.8 min (D-(*R*)-(+)) and 6.2 min (L-(*S*)-(−)). $[\alpha]_D^{24}$ = −3.1° (*c* 1.0, EtOH, 93% ee). IR (neat) 2959, 1744, 1700, 1597, 1449, 1372, 1235, 1071 cm^{-1}; ^{1}H NMR δ = 0.96 (d, *J* = 6.6 Hz, 3 H), 1.02 (d, *J* = 6.6 Hz, 3 H), 1.56—1.65 (m, 1 H), 1.75—1.92 (m, 2 H), 2.15 (s, 3 H), 5.93 (dd, *J* = 3.0, 10.5 Hz, 1 H), 7.44—7.55 (m, 2 H), 7.56—7.59 (m, 1 H), 7.92—7.96 (m, 2 H); ^{13}C NMR δ = 20.57, 21.36, 23.10, 24.94, 39.91, 73.86, 128.26, 128.66, 133.37, 134.51, 170.50, 196.74. HRMS. Found: *m/z* 234.1256. Calcd for $C_{14}H_{18}O_3$: M, 234.1255.

Indan-2-yl Methoxyacetate: IR (neat) 2951, 2828, 1752, 1460, 1277, 1190, 1129, 1010, 745 cm^{-1}; ^{1}H NMR δ = 3.03 (dd, *J* = 3.0, 17.0 Hz, 2 H), 3.34 (dd, *J* = 3.0, 14.0 Hz, 2 H), 3.42 (s, 3 H), 3.98 (s, 3 H), 5.63 (m, 1 H), 7.16—7.28 (m, 4 H); ^{13}C NMR δ = 39.48, 59.25, 69.81, 75.79, 124.54, 126.77, 140.07, 170.12. Found: C, 69.61; H, 6.60%. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84%.

Indan-2-yl Tetrahydrofuran-2-carboxylate: IR (neat) 2979, 2880, 1748, 1483, 1345, 1277, 1179, 1088, 1011, 745 cm^{-1}; ^{1}H NMR δ = 1.81—2.01 (m, 3 H), 2.12—2.24 (m, 1 H), 2.99 (dd, *J* = 3.0, 17.0 Hz, 1 H), 3.02 (dd, *J* = 3.0, 17.0 Hz, 1 H), 3.33 (dd, *J* = 6.0, 17.0 Hz, 2 H), 3.08—3.91 (m, 1 H), 3.93—4.03 (m, 1 H), 4.39 (dd, *J* = 4.5, 8.0 Hz, 1 H), 5.54—5.61 (m, 1 H), 7.14—7.25 (m, 4 H); ^{13}C NMR δ = 25.04, 30.04, 39.38, 39.40, 69.19, 75.52, 76.50, 124.42, 124.46, 126.62, 126.65, 140.00, 140.06, 173.21. HRMS. Found: *m/z* 232.1080. Calcd for $C_{14}H_{16}O_3$: M, 232.1099.

(1*S*, 2*R*)-1-Acetylamino-2-acetoxyindane: Mp 147.4—147.8 °C; IR (KBr) 3305, 1732, 1651, 1551, 1377, 1246, 1043, 729 cm^{-1}; ^{1}H NMR δ = 2.03 (s, 3 H), 2.10 (s, 3 H), 3.01 (dd, *J* = 1.5, 17.5 Hz, 1 H), 3.22 (dd, *J* = 5.0, 17.5 Hz, 1 H), 5.55 (td, *J* = 1.5, 5.0, 5.0 Hz, 1 H), 5.68 (dd, *J* = 5.0, 9.0 Hz, 1 H), 5.92 (br d, *J* = 9.0 Hz, 1 H), 7.21—7.30 (m, 4 H); ^{13}C NMR δ = 21.09, 23.30, 37.56, 55.31, 75.86, 123.68, 125.03, 127.24, 128.28, 139.35, 140.53, 169.95, 170.13. HRMS. Found: *m/z* 233.1051. Calcd for $C_{13}H_{15}NO_3$: M, 233.1051.

(1*S*, 2*R*)-2-Acetoxy-1-(*t*-butoxycarbonylamino)indane: Mp 147.1—147.8 °C; IR (KBr) 3360, 2984, 1736, 1690, 1518, 1391, 1277, 1167 cm^{-1}; ^{1}H NMR δ = 1.51 (s, 9 H), 2.03 (s, 3 H), 2.99 (dd, *J* = 2.0, 17.0 Hz, 1 H), 3.22 (dd, *J* = 5.0, 17.0 Hz, 1 H), 4.93 (br d, *J* = 9.5 Hz, 1 H), 5.35 (dd, *J* = 5.0, 9.5 Hz, 1 H), 5.58 (td, *J* = 2.0, 5.0, 5.0 Hz, 1 H), 7.19—7.35 (m, 4 H); ^{13}C NMR δ = 21.10, 28.36, 37.29, 56.93, 75.73, 79.84, 123.88, 124.97, 127.19, 128.21, 139.25, 140.84, 155.62, 170.27. Anal. Found: C, 65.87; H, 7.48; N, 4.82%. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27, N 4.81%.

A General Procedure for the Sc(OTf)$_3$-Catalyzed Cleavage of Esters: To a solution of an acetate (1.0 mmol) in MeOH (8.0 mL) was added an aqueous solution of $Sc(OTf)_3$ (98 mg, 0.20 mmol) in H_2O (2.0 mL); the resulting mixture was stirred at 30 °C for a period specified in Tables 1 and 2 before concentration in vacuo. The residue was diluted with H_2O (2.0 mL) and extracted with CH_2Cl_2 (5.0 mL×3). The organic layer was washed with brine (5.0 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel preparative thin layer chromatography to give a pure product.

Recovery of $Sc(OTf)_3$: The aqueous layer was washed with CH_2Cl_2 (1.0 mL) and concentrated in vacuo. The residue was dried under reduced pressure (133 Pa) at 60 °C for 16 h to give a brown residual solid which was used for the reaction without further purification.

(*R*)-2-Hydroxyindan-1-one (1b):[15] HPLC analysis, MeOH : aqueous H_3PO_4 (0.2 v/v%) = 50 : 50, t_R = 2.6 min; ^{1}H NMR δ = 3.02 (dd, *J* = 5.0, 16.5 Hz, 1 H), 3.30 (s, 1 H), 3.58 (dd, *J* = 8.0, 16.5 Hz, 1 H), 4.56 (dd, *J* = 5.0, 8.0 Hz, 1 H), 7.37—7.47 (m, 2 H), 7.61—7.67 (m, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H); ^{13}C NMR δ = 35.3, 74.2, 124.4, 126.9, 128.0, 134.0, 135.9, 151.0, 206.7.

Indan-2-ol (2b): HPLC analysis, MeOH : aqueous H_3PO_4 (0.2 v/v%) = 50 : 50, t_R = 4.9 min; ^{1}H NMR δ = 1.83 (br s, 1 H), 2.89 (dd, *J* = 3.5, 16.0 Hz, 1 H), 3.20 (dd, *J* = 5.5, 16.0 Hz, 1 H), 4.64—4.70 (m, 1 H), 7.14—7.25 (m, 4 H); ^{13}C NMR δ = 42.62, 73.13, 124.95, 126.61, 140.75.

(*S*)-3,4-Dihydro-2-hydroxynaphthalen-1(2*H*)-one:[17] ^{1}H NMR δ = 1.99 (td, *J* = 4.0, 12.5, 25.5 Hz, 1 H), 2.44—2.52 (m, 1 H), 2.93—3.15 (m, 2 H), 3.94 (br s, 1 H), 4.33 (d, *J* = 5.5, 14.0 Hz, 1 H), 7.20—7.31 (m, 2 H), 7.47 (dd, *J* = 7.2, 7.2 Hz, 1 H), 7.98 (d, *J* = 8.0 Hz, 1 H); ^{13}C NMR δ = 27.62, 31.76, 73.74, 126.75,

127.41, 128.78, 130.32, 134.02, 144.19, 199.47.

(*R*)-6,7,8,9-Tetrahydro-6-hydroxy-5*H*-benzocyclohepten-5-one: Determination of ee: CHIRALPAK AD (20 v/v% propan-2-ol/hexane, 0.8 mL min^{-1}), t_R = 15.5 min ((*S*)-isomer was eluted at 20.9 min). Colorless oil. $[\alpha]_D^{27}$ = +72.5°, (*c* 1.0, EtOH, ee = 94%); IR (neat) 3468, 2939, 2867, 1676, 1599, 1451, 1280, 1098, 1053, 1009, 997 cm^{-1}; ^{1}H NMR δ = 1.62—1.86 (m, 2 H), 2.07—2.23 (m, 1 H), 2.32—2.43 (m, 1 H), 2.72—3.07 (m, 1 H), 4.02 (d, *J* = 4.5 Hz, 1 H), 4.50—4.57 (m, 1 H), 7.25 (d, *J* = 9.0 Hz, 1 H), 7.32—7.37 (m, 1 H), 7.44—7.49 (m, 1 H), 7.93 (d, *J* = 8.0 Hz, 1 H); ^{13}C NMR δ = 23.50, 32.15, 34.54, 75.86, 126.74, 129.67, 130.47, 132.99, 134.96, 142.93, 204.58. Found: C, 74.65; H, 6.84%. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86%.

(*S*)-2-Hydroxy-4-methyl-1-phenylpentan-1-one: Colorless oil. $[\alpha]_D^{23}$ = −18° (*c* 1.0, EtOH, 98% ee); IR (neat) 3483, 2959, 2361, 1684, 1264, 1142, 1007, 997 cm^{-1}; ^{1}H NMR δ = 0.96 (d, *J* = 6.6 Hz, 3 H), 1.02 (d, *J* = 6.6 Hz, 3 H), 1.56—1.65 (m, 1 H), 1.75—1.92 (m, 2 H), 2.15 (s, 3 H), 5.93 (dd, *J* = 3.0, 10.5 Hz, 1 H), 7.44—7.55 (m, 2 H), 7.56—7.59 (m, 1 H), 7.92—7.96 (m, 2 H); ^{13}C NMR δ = 20.57, 21.36, 23.10, 24.94, 39.91, 73.86, 128.26, 128.66, 133.37, 134.51, 170.50, 196.74. HRMS. Found: *m/z* 192.1152. Calcd for $C_{12}H_{13}O_3$: M, 192.1150.

(*S*)-Benzoin: ^{1}H NMR δ = 4.57 (d, *J* = 6.0 Hz, 1 H), 5.95 (d, *J* = 6.0 Hz, 1 H), 7.24—7.41 (m, 7 H), 7.48—7.53 (m, 1 H), 7.89—7.93 (m, 2 H); ^{13}C NMR δ = 76.15, 127.71, 128.51, 128.62, 129.06, 129.08, 133.40, 133.85, 138.93, 198.87.

1-Hydroxypropan-2-one: HPLC analysis, MeOH : aqueous H_3PO_4 (0.2 v/v%) = 50 : 50, t_R = 2.2 min; ^{1}H NMR ($CDCl_3$) δ = 2.17 (t, *J* = 0.6 Hz, 3 H), 3.37 (br s, 1 H), 4.27 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ = 25.13, 68.49, 207.33.

3-Hydroxy-1-phenylbutan-1-one:[23] ^{1}H NMR δ = 1.30 (d, *J* = 6.0 Hz, 3 H), 3.05 (dd, *J* = 8.5, 17.5 Hz, 1 H), 3.07 (dd, *J* = 3.5, 17.5 Hz, 1 H), 3.441 (br s, 1 H), 4.36—4.46 (m, 1 H), 7.44—7.49 (m, 2 H), 7.55—7.61 (m, 1 H), 7.94—7.96 (m, 2 H); ^{13}C NMR δ = 22.37, 46.44, 63.92, 127.97, 128.58, 133.44, 136.58, 200.70.

Corticosterone 11-Acetate : Colorless solid. Mp 126—131 °C; IR (KBr) 3438, 2498, 1734, 1669, 1377, 1244, 1084, 1028, 949 cm^{-1}; ^{1}H NMR δ = 0.82 (s, 3 H), 1.08—1.56 (m, 5 H), 1.28 (s, 3 H), 1.72—1.90 (m, 3 H), 1.94—2.10 (m, 3 H), 2.04 (s, 3 H), 2.14—2.52 (m, 7 H), 3.28 (t, *J* = 4.8 Hz, 1 H), 4.16 (d, *J* = 4.8 Hz, 2 H), 5.42—5.45 (m, 1 H), 5.69 (s, 1 H); ^{13}C NMR δ = 15.46, 20.60, 21.69, 22.49, 24.25, 31.77, 32.18, 33.50, 35.23, 38.44, 43.25, 43.38, 54.89, 57.05, 58.88, 69.11, 122.66, 169.59, 170.29, 198.70, 209.49. HRMS. Found: *m/z* 388.2246. Calcd for $C_{23}H_{32}O_5$: M, 388.2248.

(1*S*, 2*R*)-Indane-1,2-diol: ^{1}H NMR δ = 2.48 (br s, 1 H), 2.56 (br s, 1 H), 2.95 (dd, *J* = 3.5, 16.5 Hz, 1 H), 3.13 (dd, *J* = 6.0, 16.5 Hz, 1 H), 4.51 (br s, 1 H), 5.00 (br s, 1 H), 7.23—7.31 (m, 3 H), 7.41—7.44 (m, 1 H); ^{13}C NMR δ = 38.68, 73.46, 75.96, 125.03, 125.38, 127.20, 128.86, 140.10, 141.90.

2-Methoxy-3-phenylpropan-1-ol:[24] ^{1}H NMR δ = 2.13 (br s, 1H), 2.73 (dd, *J* = 7.0, 13.5 Hz, 1 H), 2.91 (dd, *J* = 5.5, 13.5 Hz, 1 H), 3.38—3.52 (m, 2 H), 3.40 (s, 3 H), 3.63—3.66 (m, 1 H), 7.19—7.32 (m, 5 H); ^{13}C NMR δ = 36.75, 57.42, 63.23, 82.75, 126.28, 128.38, 129.28, 137.97.

2-Methoxybenzoic Acid: HPLC analysis, MeOH : aqueous H_3PO_4 (0.2 v/v%) = 2 : 3, t_R = 4.6 min.

(1*S*, 2*R*)-1-Acetylaminoindan-2-ol: Mp 76.1—76.7 °C; IR (KBr) 3449, 3301, 2934, 1649, 1619, 1541, 1375, 1051, 737 cm^{-1}; ^{1}H NMR (CD_3OD) δ = 2.08 (s, 3 H), 2.91 (dd, *J* = 2.0, 16.5 Hz, 1 H), 3.12 (dd, *J* = 5.0, 16.5 Hz, 1 H), 4.52 (m, 1 H), 5.29 (d, *J* = 5.0 Hz, 1 H), 7.20—7.25 (m, 4 H); ^{13}C NMR (CD_3OD) δ = 22.67, 40.45, 58.93, 73.97, 125.15, 126.11, 127.78, 128.91, 141.78, 142.16, 173.75. Found: C, 68.86; H, 6.60; N, 7.06%. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32%.

(1*S*, 2*R*)-1-(*t*-Butoxycarbonylamino)indan-2-ol: Mp 76.1—76.8 °C; IR (KBr) 3355, 2982, 1692, 1671, 1526, 1368, 1246, 1171, 737 cm^{-1}; ^{1}H NMR δ = 1.51 (s, 9 H), 2.01 (d, *J* = 5.5 Hz, 1 H), 2.94 (dd, *J* = 2.0, 16.5 Hz, 1 H), 3.15 (dd, *J* = 5.0, 16.5 Hz, 1 H), 4.61 (m, 1 H), 5.10 (br s, 1 H), 7.22—7.26 (m, 3 H), 7.28—7.32 (m, 1 H); ^{13}C NMR δ = 28.37, 39.35, 58.79, 73.54, 79.83, 124.41, 125.25, 127.03, 128.09, 139.78, 140.81, 156.24. Found: C, 67.15; H, 7.68; N, 5.62%. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62%.

3-Phenylpropan-1-ol: ^{1}H NMR δ = 1.86—1.93 (m, 2 H), 2.71 (t, *J* = 7.5 Hz, 2 H), 3.67 (t, *J* = 6.5 Hz, 2 H), 7.16—7.31 (m, 5 H); ^{13}C NMR δ = 32.02, 34.17, 62.18, 125.79, 128.33, 128.36, 141.76.

2-Methoxy-3-phenylpropanoic Acid:[25] HPLC analysis, MeOH : aqueous H_3PO_4 (0.2 v/v%) = 2 : 3, t_R = 8.9 min; ^{1}H NMR δ = 3.02 (dd, *J* = 8.0, 14.5 Hz, 1 H), 3.14 (dd, *J* = 4.5, 14.5 Hz, 1 H), 3.39 (s, 3H), 4.02 (dd, *J* = 4.5, 8.0 Hz, 1 H), 7.21—7.33 (m, 5 H); ^{13}C NMR δ = 38.58, 58.67, 81.21, 126.86, 128.41, 129.35, 136.48, 176.12.

2-Oxophenylacetic Acid: HPLC analysis, MeOH : aqueous H_3PO_4 (0.2 v/v%) = 1 : 1, t_R = 3.8 min; ^{1}H NMR δ = 7.51—7.57 (m, 2 H), 7.68—7.74 (m, 1 H), 8.29—8.32 (m, 2 H), 9.43 (br s, 1 H); ^{13}C NMR δ = 128.97, 131.15, 131.63, 135.65, 162.48, 184.40.

10-Deacetylpaclitaxel:[10d] Isolated by HPLC using Merck LiChrospher 100 RP 18(e) column (10×250 mm) and 60 v/v% MeOH in 0.2% phosphoric acid aqueous solution (10 mL min^{-1}), t_R = 12.2 min; ^{1}H NMR δ = 1.12 (s, 3 H, C17), 1.21 (s, 3 H, C16), 1.76 (s, 3 H, C19), 1.77 (s, 3 H, C18), 1.80—1.90 (m, 1 H, C14), 2.30 (dd, *J* = 4.0, 9.0 Hz, 1 H, C14), 2.39 (s, 3 H, OAc), 2.52—2.64 (m, 2 H, C6), 3.53 (br s, 1 H, OH), 3.91 (d, *J* = 7.0 Hz, 1 H, C3), 4.20—4.23 (m, 3 H, C7+C20+OH), 4.32 (d, *J* = 8.0 Hz, 1 H, C20), 4.79 (br s, 1 H, C2′), 4.94 (d, *J* = 7.0 Hz, 1 H, C5), 5.18 (s, 1 H, C10), 5.68 (d, *J* = 7.0 Hz, 1 H, C2), 5.78 (dd, *J* = 3.0, 9.0 Hz, 1 H, C3′), 6.17—6.23 (m, 1 H, C13), 7.07 (d, *J* = 9.0 Hz, 1 H, NH), 7.34—7.43 (m, 5 H, Ar–H), 7.47—7.53 (m, 5 H, Ar–H), 7.59—7.64 (m, 1 H, 2-OBz), 7.74—7.77 (m, 2 H, 3′-NBz), 8.13 (dd, *J* = 2.0, 8.5 Hz, 2 H, 2-OBz). MS *m/z* 810.5 $(M-1)^-$, 846.3 $(M+Cl)^-$, 900.3 $(M+NaCl+MeOH-1)^-$.

10-Deacetyl-7-epipaclitaxel:[10d] Isolated by HPLC using Merck LiChrospher 100 RP 18(e) column (10×250 mm) and 60 v/v% MeOH in 0.2% phosphoric acid aqueous solution (10 mL min^{-1}), t_R = 18.9 min. ^{1}H NMR ($CDCl_3$) δ = 1.09 (s, 3 H, C17), 1.21 (s, 3 H, C16), 1.73 (s, 3 H, C19), 1.75 (d, *J* = 1.5 Hz, 3H, C18), 2.20—2.40 (m, 4 H, C6+C14), 2.52 (s, 3 H, OAc), 3.44 (br s, 1 H, OH), 3.63—3.70 (m, 1 H, C7), 3.93 (d, *J* = 7.0 Hz, 1 H, C3), 4.11 (br s, 1 H, OH), 4.41 (s, 2 H, C20), 4.72 (d, *J* = 12.0 Hz, 1 H, C2′), 4.80 (br s, 1 H, OH), 4.91 (dd, *J* = 5.0, 8.5 Hz, 1 H, C5), 5.40 (s, 1 H, C10), 5.74 (d, *J* = 7.5 Hz, 1 H, C2), 5.81 (dd, *J* = 3.0, 9.0 Hz, 1 H, C3′), 6.13—6.28 (m, 1 H, C13), 7.01 (d, *J* = 9.5 Hz, 1 H, NH), 7.33—7.55 (m, 10 H, Ar–H), 7.59—7.64 (m, 1 H, Ar–H), 7.72—7.75 (m, 2 H, NBz), 8.16—8.20 (m, 2 H, 2-OBz). MS *m/z* 810.5 $(M-1)^-$, 846.3 $(M+Cl)^-$, 900.3 $(M+NaCl+MeOH-1)^-$.

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