General Procedure for Acylation of 3° Alcohols: Scandium Triflate/DMAP Reagent

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Acylation of alcohols and the esterification of carboxylic acids are among the most frequently used processes in organic synthesis. This situation has led to the development of a host of methodologies with which to accomplish this conversion. By comparison with the ease of acylation of primary and secondary alcohols, tertiary alcohol acylation still remains a challenging problem. Typically, acylation of alcohols is performed with activated carboxylic acid derivatives such as (mixed) acid anhydrides,[1a−c] acid chlorides,[1d] acyl imidazoles,[1e] or acyl ureas derived from carbodiimide reagents[1f] in the presence of basic catalysts such as 4-(dimethylamino)pyridine or 4-pyrrolidinopyridine.[1g,h] More recently tributylphosphine[2a,b] and $MgBr_2$[2c] in the presence of a tertiary amine have been shown to be effective reagents for acylations. Acylation of alcohols can also be brought about by the action of Lewis acid reagents[3] such as $CoCl_2$, $ZnCl_2$, and $TiCl_4/AgClO_4$ in conjunction with carboxylic acids, but these reagents preclude the presence of acid-sensitive groups. Yamamoto and co-workers[4a,b] have demonstrated that commercially available scandium triflate ($Sc(OTf)_3$) or $Sc(OAc)_3/3NHTf_2$[5a] are remarkably active Lewis acid catalysts useful for the acylation of alcohols with (mixed) acid anhydrides. The catalytic activity of $Sc(OTf)_3$ is higher than that of other acylation catalysts such as (dimethylamino)pyridine or tributylphosphine. However, due to its acidic properties,[4c] in the case of allylic and certain tertiary alcohols migration or elimination products have been observed. Lanthanide triflates/acetic acid have also been effectively used in the same fashion.[5b] Another important development in acylation chemistry has been disclosed by Procopiou,[5c,d] who employed trimethylsilyl trifluoromethanesulfonate (TMSOTf) with acid anhydrides. Other methods specifically reported for tertiary alcohol esterification include the reaction of carboxylic acids with *tert*-butyl isourea in the presence of cuprous chloride,[6] the reaction of carboxylic acid (*S*)-2-pyridinyl esters with *tert*-butyl alcohol,[7] acetylation using isopropenyl acetate with an oxime and $Cp^*_2Sm(thf)_2$,[8] and a one-pot preparation of *tert*-butyl esters of carboxylic acids using anhydrous magnesium sulfate and concentrated sulfuric acid.[9a] The use of *tert*-butyl fluorocarbonate, [9c] *tert*-butyl bromide in the presence of potassium carbonate,[9b] and *tert*-butyl trichloroacetamidates[9d] to prepare *tert*-butyl esters of protected amino acids has also been detailed. Nevertheless, there are sufficient drawbacks to most of these procedures to justify the need for a general and practical method of generating esters of 3° alcohols under mild conditions, especially a procedure that allows the use of acids of greater complexity than acetic or propionic.

We recently reported[10] on a facile stereoselective esterification of 20-(*S*)-camptothecin (a pentacyclic alkaloid displaying a highly hindered 3° alcohol) with amino acid derivatives effected by the carbodiimide method at low temperature using DIPC/DMAP (DIPC = diisopropylcarbodiimide; DMAP = 4-(dimethylamino)pyridine) in the presence of $Sc(OTf)_3$. The use of this unique combination of catalysts resulted in >97% pure diastereomer of the desired 20-camptothecin ester in 95% yield. Further demonstration of the versatility of the $Sc(OTf)_3$/DMAP combination was provided by eliminating carbodiimide reagents and employing readily available *N*-hydroxysuccinimide (NHS) esters[11] of amino acids in place of the free acids. Using virtually the same reaction conditions, a high-yield esterification with >98% isomeric purity was also achieved.

To explore the generality and scope of the $Sc(OTf)_3$/DMAP-catalyzed acylation reaction, the procedure has been extended to a variety of tertiary alcohols and carboxylic acids. Some of the examples were chosen not only to demonstrate the advantage of this method but also to allow comparisons with literature results for the preparation of the corresponding hindered esters. The results are summarized in Table 1. The main advantages of using the $Sc(OTf)_3$/DMAP reagent combination in place of existing methods lie in the fact that acylation of 3° alcohols can be achieved using complex acids (or NHS esters) without the need for generating acid anhydrides or mixed anhydrides, rearrangements do not occur, the reaction is rapid, and high yields of product result. Previously reported methods for 3° alcohol acylation

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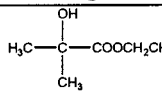
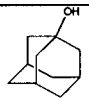
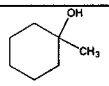
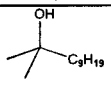
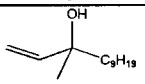
Table 1. Summary of 3° Alcohol Acylations

Entry	Tertiary Alcohol	Acid or Derivative	Ester	Method	Yield(%)[a]
1	*t*-Butanol **1**	$ClCH_2COOH$ **8**	**15**	A	99(95)
2	**1**	*t*-Boc-(*S*)-(-)-Glu(OBz*)* **9**	**16**	B	95(80)[b]
3	**1**	Mesitoic acid **10**	**17**	B	95(86)[b]
4	 **2**	4-Nitrobenzoic acid **11**	**18**	B	99(92)
5	**2**	*t*-Boc-(*S*)-(-)-Phe-OSu **12**	**19**	C	98(90)
6	 **3**	**9**	**20**	A	95(90)
7	**3**	**12**	**21**	D	99(90)
8	 **4**	**12**	**22**	C	98(92)
9	 **5**	**12**	**23**	C	98(88)
10	 **6**	**12**	**24**	C	98(85)[b]
11	20-(*S*)-Camptothecin **7**	*t*-Boc-(*S*)-(-)-Ala-OSu **13**	**25**	D	>99(94)
12	**7**	(*S*)-(+)-2-Methyl butyric acid NHS ester **14**	**26**	D	>98(90)

[a] Yields were determined by HPLC. Isolated yields are indicated in parentheses. [b] No attempts were made to optimize isolated yields of these very volatile products.

using $Sc(OTf)_3$[4a] and TMSOTf [5c] employed mostly simple anhydrides such as acetic and propionic anhydrides to illustrate the generality of the method. However, attempts by Yamamoto et al.[4a] to extend the procedure to more complex acids by generating mixed anhydrides failed in the case of 3° alcohols. As can be seen from Table 1, acylations using $Sc(OTf)_3$/DMAP reagent take place in high yield for all the tertiary alcohol and carboxylic acid combinations.

We initiated our studies with the simplest tertiary alcohol, *tert*-butyl alcohol, and investigated acylation with aliphatic, aromatic, and then amino acids or derivatives. Acylation of *tert*-butyl alcohol (entry 1) with chloroacetic acid, using DIPC and $Sc(OTf)_3$/DMAP reagent, was achieved in 95% isolated yield. Under similar conditions (*tert*-butoxycarbonyl)-L-glutamic acid γ-benzyl ester (**9**) reacted with *tert*-butyl alcohol to afford the corresponding α-*tert*-butyl ester (**16**) in 95% yield and 90% chiral purity as indicated by HPLC employing a Phenomenex chiral column. This ester is an important intermediate used during the synthesis of the anti-cancer drug methotrexate, and its γ-hydrazide derivatives. The previously reported method[1f] used for the synthesis of **9** employed 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide (EDC) with DMAP and gave an 82% yield accompanied by 40−50% racemization. *tert*-Butyl alcohol was also easily acylated with the hindered aromatic acid mesitoic acid (entry 3), to give the corresponding product in 95% yield. Again, reported methods for esterification of this sterically hindered acid involve the use of strongly acidic conditions (trifluoroacetic anhydride as condensing agent, yield 72%)[12] or necessitate specialized reagents such as (*S*)-2-pyridyl esters in the presence of $CuBr_2$ (95% yield).[7] The current methodology using $Sc(OTf)_3$/DMAP reagent appears to offer a great deal of advantage as far as the synthesis of esters of aromatic acids. For example, in the acylation of menthol, a less hindered secondary alcohol,[13] with benzoic anhydride, both Yamamoto et al.[4a] and Procopiou et al.[5c,d] reported that the reaction proceeded to completion in 1−2 h but did not provide any examples of 3° alcohol benzoylation. The advantage of employing the current methodology for aromatic acid ester synthesis was further demonstrated by using a hindered 3° alcohol, ethyl 2-hydroxyisobutyrate (**2**). This model compound was acylated in less than 2 h with 4-nitrobenzoic acid (**11**) in 92% isolated yield with the

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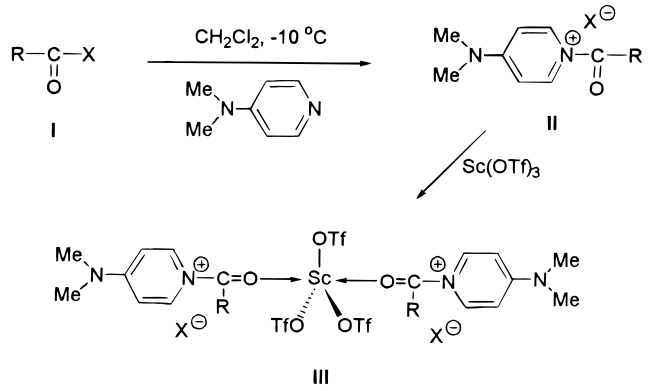
(13) The esterification of hindered 2° alcohols using the $Sc(OTf)_3$/DMAP reagent also proceeded rapidly in high yield (unpublished results).

$Sc(OTf)_3$/DMAP reagent. Alcohol **2** was also successfully reacted with a readily available activated amino acid NHS ester, *t*-Boc-(*S*)-(−)-Phe-OSu (**12**), in greater than 90% isolated yield (entry 5). Similar results were obtained for the acylation of 1-adamantanol (**3**) with amino acid **9** and NHS ester **12** (>90% yield, entries 6 and 7), further underscoring the generality of this method. Simple $Sc(OTf)_3$-catalyzed acylation reactions of certain 3° alcohols in the presence of acid anhydrides were reported to proceed but resulted in partial elimination or rearrangement.[4a,b] For example, in the case of 1-methylcyclohexanol (**4**), $Sc(OTf)_3$ acylation using acetic anhydride produced 91% of the desired acetate along with 9% of the elimination product, while acylation of 2-methyl-2-undecanol (**5**) using mixed anhydrides was believed to initially produce the ester, but only elimination products could be isolated under the reaction conditions. We have now found that tertiary alcohols such as **4** and **5** (entries 8 and 9) undergo facile acylation using $Sc(OTf)_3$/DMAP reagent with NHS ester **12** in high yield (98% by HPLC analysis) without formation of any elimination products. Acylation of 2-allyl-2-undecanol (**6**) using $Sc(OTf)_3$ and Ac_2O was reported to give only 76% of the acetylated product along with substantial amounts of primary acetates due to a competing 1,3-migration.[4a,b] However using $Sc(OTf)_3$/DMAP reagent with **6** and NHS ester **12** (entry 10), the acylated alcohol was produced in 98% yield (HPLC) and the volatile product isolated in 90% yield: no rearranged products were detected in the reaction mixture by HPLC. The hindered 3° alcohol 20-(*S*)-camptothecin can be easily acylated using chiral amino acid derivatives such as *t*-Boc-(*S*)-alanine NHS ester (**13**).[10] Another example utilizing a non-amino-containing chiral acid derivative, (*S*)-2-methylbutyric acid NHS ester (**14**), was carried out with camptothecin and the product **26** was isolated in 90% yield with a 99% isomeric purity (entry 12). In all the examples of esterifications tried to date, we have observed that when chiral centers are present, in either the alcohol or acid, the enantiomeric excess of the product generally exceeds 90%.

To obtain information on the acylation mechanism, reactions utilizing **7** and **13** in combination with $Sc(OTf)_3$ and other bases such as DBU and triethylamine were attempted but these reactions failed: no ester product was formed when DMAP was excluded from the reaction.[10] It is well-established that DMAP is 10^4 times more active as an acylation catalyst than pyridine or other 3° amines.[1c,d] In a simple case, using *tert*-butyl alcohol and **12**, only partial esterification was achieved in the presence of DMAP alone, and attempts to drive the reaction to completion at higher temperatures (refluxing chloroform) led to decomposition of the NHS ester. From these studies, it appears that the greater reactivity of the $Sc(OTf)_3$/DMAP reagent over $Sc(OTf)_3$ per se suggests the intermediacy of acylium ion II (Scheme 1), which must form prior to any involvement of $Sc(OTf)_3$. Since formation of II from DMAP and any activated acid derivative I is a convergent process, it should not be dependent on any particular leaving group, "X". This hypothesis is in agreement with the results obtained from the carbodiimide-mediated reaction of camptothecin (**7**) with *t*-Boc-alanine,[10] where yields and chiral purity of the ester nearly identical with those obtained in the case of NHS ester resulted (entry 11) when the $Sc(OTf)_3$/DMAP reagent was used. Dative bonding of carbonyl oxygen to $Sc(OTf)_3$ during lactonization has been previously postulated.[4a,b] Similarly, in these acylations the role of $Sc(OTf)_3$ may be to coordinate with the initially formed carbonyl oxygen of the acyl pyridinium intermediate II, which would lead to the highly reactive species III.[14] Subsequently, acylation of alcohols by III becomes a kinetically controlled process which allows rapid esterification to proceed under mild conditions.

Scheme 1



Thus, $Sc(OTf)_3$ in combination with DMAP appears to be a novel bipartate reagent that can bring about high-yield acylations of 3° alcohols under very mild conditions (−8 °C, 3 h). The simplicity and convenience of this effective reagent provides a highly practical method for esterification of hindered alcohols. Acids of all types or their NHS esters can be employed directly in this facile reaction, which offers a great deal of flexibility in optimizing acylation yields. Molar ratios of the $Sc(OTf)_3$/DMAP reagent can be easily adjusted to minimize the amounts of alcohol or acid employed without changing the mild reaction conditions. Barrett[5b] has shown that $Sc(OTf)_3$ is a recyclable catalyst which can be recovered quantitatively via a simple aqueous workup and reused with no loss of activity. Therefore, for large-scale processes $Sc(OTf)_3$/DMAP reagent can be considered as a pragmatic procedure.

Experimental Section

$Sc(OTf)_3$ was purchased from Aldrich Chemical Co. (Milwaukee, WI) and was stored in the freezer when not in use. Unless stated otherwise, all reagents and solvents were used without further purification. Organic solutions were dried over $MgSO_4$. Solvents were removed by rotary evaporation at or below 40 °C. TLC was conducted on EM 0.25 mm silica gel 60 F_{254} plates. Products were visualized under UV light and/or by staining with iodine vapor. Analytical HPLC was carried out with a ZORBAX 300 SB C-8 column (150 × 4.6 mm) and a multiwavelength UV detector, using a gradient of 30−90% acetonitrile/0.1 M triethylammonium acetate (TEAA) at a flow rate of 1 mL/min. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-GSX270 FT NMR system using $CDCl_3$ containing 0.1% TMS as the solvent. ESMS analyses were done at the Mass Spectrometry Facility of Yale Medical School, New Haven, CT. Elemental analysis was performed by Galbraith Laboratories, Inc., Knoxville, TN.

Syntheses. Four different methods are illustrated with specific examples as follows. Method A. Carbodiimide Procedure (Acid in Excess), Compound 15. A suspension of **1** (0.094 mL, 1 mmol), scandium triflate (0.30 g, 0.6 mmol), **8** (0.28 g, 3 mmol), and DMAP (0.37 g, 3 mmol) in anhydrous methylene chloride (10 mL) was cooled to −8 °C in an ice-salt bath for 30 min. Diisopropylcarbodiimide (DIPC) (0.49 mL, 3.1 mmol) was added and the reaction mixture stirred at −8 °C for 30 min and then warmed to room temperature over 2 h. The

(14) The coordination number of 2 has been designated arbitrarily.

reaction mixture was filtered to remove any insoluble material and the filtrate washed with 2 × 20 mL of 0.1 N HCl, 2 × 20 mL of 0.1 N sodium bicarbonate, and 20 mL of distilled water. The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure. Trace amounts of DIPU were precipitated with ether and removed by filtration. Evaporation of the ether gave pure **15** (0.14 g, 95%): ^{1}H NMR δ 1.49 (s, 9H), 3.97 (s, 2H); ^{13}C NMR δ 27.84, 41.89, 82.95, 166.23.

Method B. Carbodiimide Procedure (Alcohol in Excess), Compound 16. A suspension of **1** (1.9 mL, 20 mmol), scandium triflate (0.3 g, 0.6 mmol), **9** (0.34 g, 1 mmol), and DMAP (0.61 g, 5 mmol) in anhydrous methylene chloride (10 mL) was cooled to −8 °C in an ice-salt bath for 30 min. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC; 0.38 g, 2 mmol) was added and the reaction mixture stirred at −8 °C for 30 min and then warmed to room temperature over 2 h. The reaction mixture was filtered to remove any insoluble material, and the filtrate was washed with 2 × 20 mL of 0.1 N HCl, 20 mL of 0.1 N sodium bicarbonate, and 20 mL of distilled water. The organic layer was dried ($MgSO_4$), and the solvent was removed under reduced pressure. The product was further purified by chromatography on a silica gel column using 0−5% methanol in methylene chloride as the eluent to give pure **16** (0.32 g, 80%): ^{1}H NMR δ 1.25 (t, J = 5.4 Hz, 2H), 1.43 (s, 9H), 1.46 (s, 9H), 1.95 (m, 1H), 2.10 (m, 1H), 2.46 (m, 2H), 5.12 (s, 2H), 7.35 (m, 5H); ^{13}C NMR δ 21.71, 27.96, 28.27, 30.29, 66.44, 69.25, 77.47, 82.17, 128.23, 128.54, 135.79, 155.35, 171.63, 172.55; ESMS m/z 394 $(M + H)^+$.

Method C. NHS Ester Procedure (Alcohol in Excess), Compound 19. A suspension of **2** (0.68 mL, 5 mmol), scandium triflate (0.49 g, 1 mmol), and DMAP (0.73 g, 6 mmol) in anhydrous methylene chloride (10 mL) was cooled to −8 °C in an ice-salt bath for 30 min. Compound **12** (1.45 g, 4 mmol) was added and the reaction mixture stirred at −8 °C for 30 min and then warmed to room temperature over 2 h. The reaction mixture was filtered to remove any insoluble material, the filtrate was washed with 3 × 20 mL of 0.1 N HCl and 20 mL of distilled water and dried ($MgSO_4$), and the solvent evaporated. The product was further purified by chromatography on a silica gel column using 0−6% ethyl acetate in hexane as eluent to give pure **19** (1.4 g, 90%): ^{1}H NMR δ 1.25 (t, J = 6.8 Hz, 3H), 1.42 (s, 9H), 1.51 (s, 3H), 1.55 (s, 3H), 3.02−3.20 (m, 2H), 4.14−4.27 (m, 2H), 4.55 (m, 1H), 4.92 (m, 1H), 7.21−7.30 (m, 5H); ^{13}C NMR δ 13.98, 24.50, 28.22, 38.17, 54.29, 61.35, 79.38, 79.77, 126.87, 128.38, 129.33, 129.48, 136.16, 155.02, 170.93, 172.04; ESMS m/z 380 $(M + H)^+$.

Method D. NHS Ester Procedure (Acid NHS Ester in Excess), Compound 25. A suspension of **7** (0.2 g, 0.58 mmol), scandium triflate (0.17 g, 0.35 mmol), and DMAP (0.21 g, 1.7 mmol) in anhydrous methylene chloride (5 mL) was cooled to −8 °C using an ice-salt bath for 30 min. Compound **13** (0.50 g, 1.7 mmol) was added and the reaction mixture stirred at −8 °C for 30 min and then warmed to room temperature over 2 h. The reaction mixture was filtered to remove any insoluble material, the filtrate was washed with 3 × 20 mL of 0.1 N HCl and 20 mL of distilled water and dried ($MgSO_4$), and the solvent removed under reduced pressure. The product was further purified by crystallization from 2 mL of methanol (0.28 g, 94%): ^{1}H NMR δ 1.00 (t, J = 8.1 Hz, 3H), 1.28 (s, 9H), 1.51 (d, J = 8.1 Hz, 3H), 2.11−2.16 (m, 2H), 4.47 (m, 1H), 4.51 (m, 1H), 4.98 (m, 1H), 5.23 (s, 2H), 5.32−5.70 (dd, J = 16.2 and 86.4 Hz, 2H), 7.36 (m, 1H), 7.62 (t, J = 8.1 Hz, 1H), 7.78 (t, J = 8.1 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 8.22 (d, J = 8.1 Hz, 1H), 8.34 (s, 1H); ^{13}C NMR δ 7.52, 18.16, 28.49, 31.93, 49.75, 49.98, 67.12, 76.72, 80.23, 96.09, 120.45, 127.19, 128.09, 128.33, 128.57, 130.01, 130.40, 130.81, 145.78, 146.54, 149.27, 152.57, 155.07, 157.46, 166.88, 171.82. Anal. Calcd for $C_{28}H_{29}N_3O_7$: C, 64.73; H, 5.63; N, 8.08. Found: C, 64.64; H, 5.71; N, 7.98.

Compound 17: ^{1}H NMR δ 2.14 (s, 6H), 2.37 (s, 3H), 3.47 (s, 9H), 7.00 (s, 1H); ^{13}C NMR δ 19.18, 21.29, 41.63, 108.79, 129.33, 135.50, 142.50, 158.67, 168.14.

Compound 18: ^{1}H NMR δ 1.26 (t, J = 6.8 Hz, 3H), 1.73 (s, 6H), 4.23 (q, J = 5.4 Hz, 2H), 8.25 (dd, J = 8.1 and 24.3 Hz, 4H); ^{13}C NMR δ 13.99, 24.60, 61.54, 79.93, 123.46, 130.79, 135.53, 150.60, 163.49, 171.91; ESMS m/z 282 $(M + H)^+$.

Compound 20: ^{1}H NMR δ 1.43 (s, 9H), 1.65 (s, 6H), 1.95 (m, 2H), 2.10 (s, 6H), 2.17 (s, 3H), 2.44 (m, 2H), 4.20 (m, 1H), 5.05 (m, 1H), 5.12 (s, 2H), 7.35 (s, 5H); ^{13}C NMR δ 28.17, 28.30, 30.29, 30.83, 36.03, 41.22, 53.37, 66.39, 79.72, 82.24, 128.18, 128.52, 135.84, 155.32, 170.93, 172.63; ESMS m/z 472 $(M + H)^+$.

Compound 21: ^{1}H NMR δ 1.42 (s, 9H), 1.64 (s, 6H), 2.05 (s, 6H), 2.17 (s, 3H), 3.05 (d, J = 8.1 Hz, 2H), 4.45 (m, 1H), 5.00 (m, 1H), 7.16−7.29 (m, 5H); ^{13}C NMR δ 28.30, 30.18, 30.29, 36.07, 38.53, 41.19, 54.80, 66.39, 79.56, 82.04, 126.76, 128.28, 129.56, 130.40, 155.05, 170.56; ESMS m/z 400 $(M + H)^+$.

Compound 22: ^{1}H NMR δ 1.41−1.47 (m, 22H), 3.08 (m, 2H), 4.52 (m, 1H), 4.96 (m, 1H), 7.18−7.29 (m, 5H); ^{13}C NMR δ 21.94, 25.20, 28.25, 36.24, 36.75, 38.56, 54.86, 79.58, 83.65, 126.76, 128.33, 129.45, 136.45, 155.05, 170.92; ESMS m/z 362 $(M + H)^+$.

Compound 23: ^{1}H NMR δ 0.89 (t, J = 8.1 Hz, 3H), 1.26 (m, 16H), 1.37 (s, 3H), 1.39 (s, 3H), 1.41 (s, 9H), 3.04 (m, 2H), 4.46 (m, 1H), 4.97 (m, 1H), 7.16−7.29 (m, 5H); ^{13}C NMR δ 14.09, 22.66, 23.74, 25.66, 25.72, 28.28, 29.30, 29.55, 29.89, 31.87, 38.56, 41.11, 54.86, 79.58, 84.36, 126.77, 128.31, 129.48, 136.42, 155.05, 170.95; ESMS m/z 434 $(M + H)^+$.

Compound 24: ^{1}H NMR δ 0.88 (t, J = 5.4 Hz, 3H), 1.26 (m, 16H), 1.37 (s, 3H), 1.41 (s, 9H), 2.51−2.53 (m, 2H), 2.99−3.06 (m, 2H), 4.47 (m, 1H), 4.96 (m, 1H), 5.04 (s, 1H), 5.08 (s, 1H), 5.61−5.71 (m, 1H), 7.17−7.31 (m, 5H); ^{13}C NMR δ 14.08, 22.66, 23.42, 28.27, 29.29, 29.48, 29.55, 29.87, 31.87, 38.21, 38.29, 38.56, 42.67, 54.93, 79.61, 85.95, 118.39, 126.79, 128.36, 129.43, 133.08, 136.44, 155.05, 170.96; ESMS m/z 460 $(M + H)^+$.

Compound 26: ^{1}H NMR δ 0.92−1.02 (m, 6H), 1.26 (d, J = 5.4 Hz, 3H), 1.53 (m, 2H), 1.78 (m, 2H), 2.18−2.40 (m, 2H), 2.56 (m, 1H), 5.27 (s, 2H), 5.38−5.71 (dd, J = 16.2, 72.9 Hz, 2H), 7.22 (m, 1H), 7.69 (t, J = 8.1 Hz, 1H), 7.83 (t, J = 8.1 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 8.22 (d, J = 8.1 Hz, 1H), 8.38 (s, 1H); ^{13}C NMR δ 7.51, 11.35, 16.18, 26.40, 31.96, 40.79, 49.88, 67.07, 75.62, 95.94, 120.56, 127.87, 128.10, 128.31, 128.60, 129.92, 130.42, 130.86, 146.25, 149.18, 152.62, 157.47, 167.24, 175.25; ESMS m/z 433 $(M + H)^+$.

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