Pergamon

*Tetrahedron* Vol. 51, No. 45, pp. 12263-12276, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00783-0

# Highly Chemoselective Acylation of Substituted Aminophenols with 3-(Trimethylacetyl)-1,3-thiazolidine-2-thione

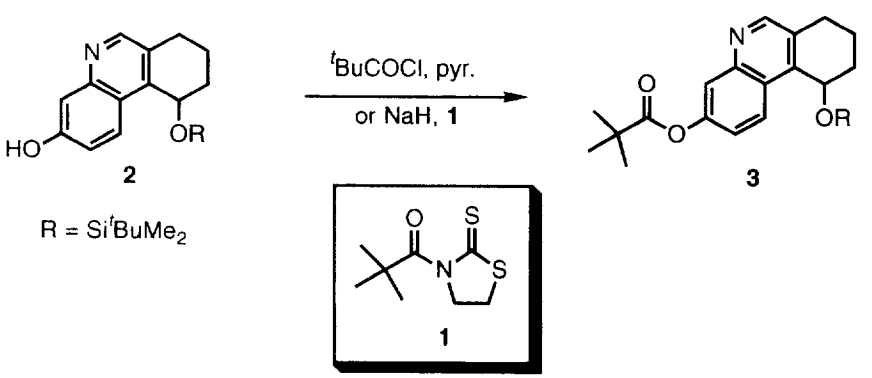
**Wei-Min Dai,* Yuk King Cheung, Kit Wan Tang, Pui Yiu Choi, and Suet Lam Chung**

Department of Chemistry, The Hong Kong University of Science and Technology
Clear Water Bay, Kowloon, Hong Kong

***Abstract***: A general procedure for chemoselective acylation of substituted aminophenols has been developed. The *N*-acylated products **7** and **10a-h** were prepared by treating the aminophenols with 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) in refluxing THF in 70-100% yield. The esters **8** and **13d,b,j** of 3- and 4-amino phenols could be obtained in 70-94% yield by treating with NaH and **1**.

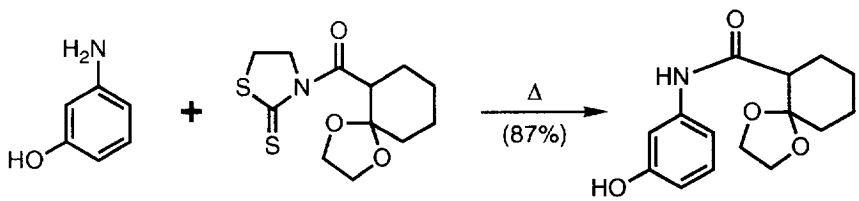
Selective reaction of a particular functional group in polyfunctionalized molecules is a challenging task in multi-step organic synthesis.[1] For protecting alcohols, phenols, and amines, acylation is one of the most widely used methods. There are a number of acylating reagents available for converting alcohols, phenols, and amines into the corresponding esters and amides with acyl chlorides being the most popular reagents of choice.[1] However, under certain circumstance, acyl chlorides may fail to complete the desired transformation in good chemical yield. One such example[2] is illustrated in Scheme 1. The hydroxylated quinoline derivative **2** is an intermediate in the synthesis of enediyne antitumor agents of the Dynemicin A type.[2,3] In the synthetic scheme, protection of the phenolic hydroxyl group in **2** was required before pursuing the subsequent transformations. However, the required pivalate **3** was prepared by the standard method ($^t$BuCOCl/pyridine) only in *ca.* 20% yield, probably due to the interference of the nitrogen atom in the quinoline skeleton with the acyl chloride. In contrast to this, reaction of **2** with 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**)[2,4,5] in the presence of NaH (THF, room temperature, 5 min) gave **3** in 99% yield.[2]

## Scheme 1



Acylating agents other than acyl chloride used in organic synthesis are rich in varieties including mixed anhydrides, activated esters/thioesters, and acyl imidazolides.[1] Among them, some of the reagents are not suitable for isolation and are normally used in the reaction by in situ formation. 3-Acyl-1,3-thiazolidine-2-thiones are stable and mild acylating agents which can be easily prepared and purified by conventional methods such as crystallization and column chromatography. The use of 3-acyl-1,3-thiazolidine-2-thiones has been the subjects of many recent reports[5,6] in which selective formation of esters and amides from aliphatic amino alcohols, diamines, or diols were described. If chiral thiazolidine reagents were used, asymmetric differentiation can be achieved in the bond-forming step.[6h-l] Under neutral conditions, aliphatic amino alcohols reacted with 3-acyl-1,3-thiazolidine-2-thiones to form the *N*-acylated products with extremely high chemoselectivity. This result is consistent with the higher nucleophilicity of an amino group over a hydroxyl group. However, attachment of an amino group to an aromatic ring should diminish its reactivity due to the conjugation of the lone electron pair of the nitrogen atom with the $\pi$ system. This was the case for the reaction of 3-acyl-1,3-thiazolidine-2-thiones with aminophenols which needed heating and longer reaction time.[2,6a] For this reason, 3-acyl-1,3-thiazolidine-2-thiones have not found general application in chemoselective acylation of substituted aminophenols. Only few examples are known in literature.[2,6a] For example, bond formation between 3-aminophenol (**4**) and **5** took placed only in refluxing THF and a prolonged heating (96 h) was necessary to drive the reaction to complete (Scheme 2).[2] Fortunately, the chemoselectivity of the reaction remained very high; the amide **6** was isolated in 87% yield. With 4-aminophenol, the same reaction could be completed within

**Scheme 2**



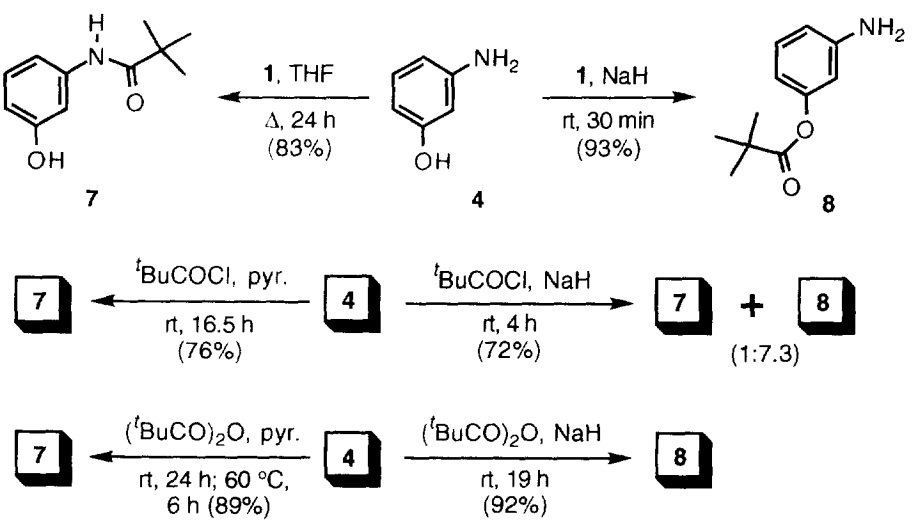

**4** **5** **6**

a much short time period (15 h).[2] This observation may be attributed to the increased nucleophilicity of the amino group in 4-aminophenol. Steric effect on the reactions of 2-aminophenol and other substituted aminophenols with 3-acyl-1,3-thiazolidine-2-thiones has not been investigated yet. In this article we report on a general method for synthesizing highly functionalized *N*-trimethylacetyl 2-, 3- or 4-aminophenols **7** and **10a-h** and the esters **8** and **13a-d** of 3- and 4-aminophenols by treating various aminophenols with 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) in either refluxing THF or in the presence of NaH at room temperature. Synthetic application of the products based on the $^t$BuCONH-directed *ortho* lithiation of aromatic rings[7] has been also demonstrated in Scheme 7 (*vide infra*).

Recently, 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) has been applied in selective formation of monoesters from di- and polyhydroxy compounds including the phenolic hydroxyl group under neutral or basic conditions.[5a,b] The excellent reactivity of **1** comparing with other 3-acyl-1,3-thiazolidine-2-thiones, for example, 3-acetyl-1,3-thiazolidine-2-thione in these reactions was proposed as the consequence of the highly twisted amide structure of **1**.[5c] However, use of **1** for the selective acylation of amino alcohols and aminophenols has not been investigated. Considering the low reactivity of the amino group in substituted

aminophenols, the more reactive acylating agent, 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) might be a suitable choice for our purpose. As a working protocol, the reaction of 3-aminophenol (**4**) with 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) under different conditions was examined (Scheme 3). Thus, treatment of **4** with an equal mole amount of **1** in THF at refluxing temperature for ca. 24 h afforded the amide **7** in 83% yield. Comparing with the reaction between **4** and **5** mentioned in Scheme 2,[2] the reaction of **1** with **4** is much fast (24 h *versus* 96 h). The remarkable difference in the reactivity calls again for the highly twisted amide conformation of **1**. Indeed, the IR absorption of the carbonyl group in **1** is differed with that of **5** by 30 $cm^{-1}$ (1738 $cm^{-1}$ for **1** *versus* 1708 $cm^{-1}$ for **5** in $CHCl_3$).[2] This is attributed to the extensive amide conjugation in **5** than in **1**. For compound **1**, an orthogonal relationship of the carbonyl group in respect to the 1,3-thiazolidine-2-thione ring has been determined by an X-ray crystallographic analysis.[5c] Such orientation should eliminate the amide conjugation and makes the amide carbonyl group in **1** more electrophilic. On the other hand, reaction of **4** with **1** in the presence of one mole equivalent of NaH at room temperature for 30 min provided the ester **8** in 93% isolated yield. The reactivities of the amino and hydroxy groups in **4** toward the acylating agent **1** originate from the difference in their nucleophilicity (basicity) under the particular reaction conditions. The amino group is more nucleophilic (basic) than the hydroxy group under neutral conditions. But, the conjugated base of the phenol becomes more nucleophilic after converting into the negatively charged phenoxide species by deprotonation using NaH. The mono-protected compounds **7** and **8** are considered synthetically useful: (a) the

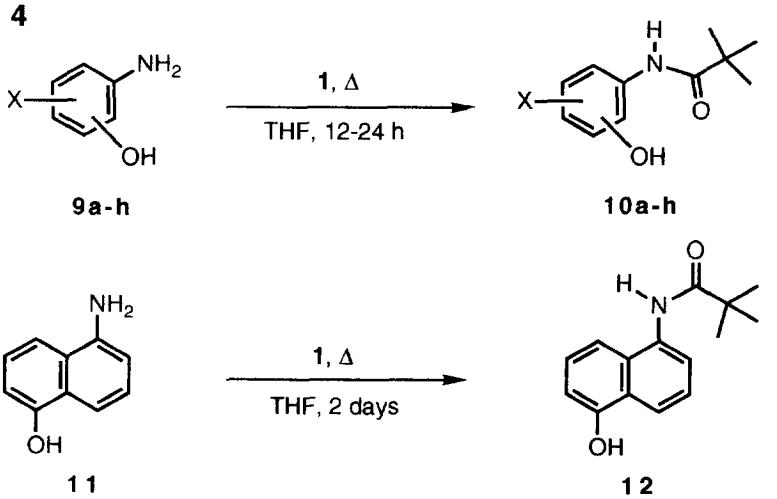
**Scheme 3**




*N*-trimethylacetylamido moiety in **7** can be utilized as a directing group in the *ortho* lithiation of aromatic ring;[7a-c] this allows the synthesis of a variety of highly functionalized aromatic compounds with an electrophile attached at the *ortho* position of the nitrogen substituent; (b) the trimethylacetyloxy group in **8** has reasonable stability toward most of the routine transformations using Grignard reagents, LDA, $BF_3$•$OEt_2$, $^nBu_3SnH$-AIBN, and *m*CPBA;[2] thus, it is possible to perform various reactions on the nitrogen atom without interference with the oxygen substituent.

For comparison, the acylation of aminophenols with trimethylacetyl chloride or trimethylacetic anhydride (1 mole equivalent each) in the presence of pyridine or NaH (1.2 mole equivalent each) has been performed. For example, 3-aminophenol (**4**) was treated with the combination of trimethylacetyl chloride and pyridine in THF at room temperature for 16.5 h to afford the amide **7** as the single product. However, the isolated yield of **7** was slightly low (76%) than the same acylation using 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) (83%, Scheme 3). This may be due to the interference of HCl generated during the acylation reaction with the reactivity of the amino group in **4** by salt formation. A similar problem was noted with the use of trimethylacetic anhydride which produces trimethylacetic acid during the acylation. The reaction of **4** with trimethylacetic anhydride and pyridine in THF did not complete after 24 h at room temperature and required heating at 60 °C for 5 h. The amide **7** was isolated in 89% yield together with the stating material **4** (3%) (Scheme 3). In an attempt to chemoselectively prepare the ester **8** from 3-aminophenol (**4**) using NaH and trimethylacetyl chloride, a very complicated mixture resulted. Treatment of **4** with NaH (1.2 mole equivalent) in THF following by trimethylacetyl chloride (1 mole equivalent) at room temperature for 4 h afforded the amide **7** (9%), the ester **8** (63%), the bisacylation product (16%), and the substrate **4** (10%). In contrast with trimethylacetyl chloride, reaction of **4** with NaH (1.2 mole equivalent) in THF following by trimethylacetic anhydride (1 mole equivalent) at room temperature for 19 h gave the ester **8** in 92% yield without the formation of the amide **7** (Scheme 3). However, under the same conditions, 4-aminophenol (**9b**) gave the amide **10b** (Scheme 4) and the ester **13b** (Scheme 6) in 12% and 81% yield, respectively. Another weak point in using trimethylacetic anhydride is that the sodium trimethylacetate generated from the reaction solidifies in THF. It then requires the use of large quantity of solvent and longer reaction time. Based on the above results, it seems apparent that 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) is a mild and highly chemoselective acylating agent for mono protection of aminophenols.

**Scheme 4**




Next, we examined the scope of the chemoselective acylation of **1** in refluxing THF using a number of commercially available aminophenols (Scheme 4). As shown in Table 1, the reaction completed within 24 h for most of the substrates to provide the amides **10** in good to excellent isolated yield except for 5-amino-1-

naphthol (**11**), which needed longer reaction time (2 days) and gave **12** in low yield.[8] In terms of the substituent effect on the reactivity, a rapid reaction was observed for 4-aminophenol (**9b**) which was converted into **10b** within 12 h in 87% isolated yield. This might be the consequence of two combined factors, the increased nucleophilicity of the amino group in **9b** due to the electron donating nature of the *para* hydroxy group and the accessibility of the amino group toward the acylating agent compared to the *ortho* aminophenols. But, one can note that the steric effect in the *ortho* aminophenols **9a,c,e-h** is not critical as the acylation of these substrates provided the desired products in excellent yield. The weakly electron-withdrawing chlorine atom in **9g** also had no significant effect on the reaction. Based on these results, we conclude that the thermal reaction of substituted aminophenols with 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) generally gives the *N*-acylated products in good chemical yield regardless of the nature and pattern of the substituent(s) on the aromatic ring.

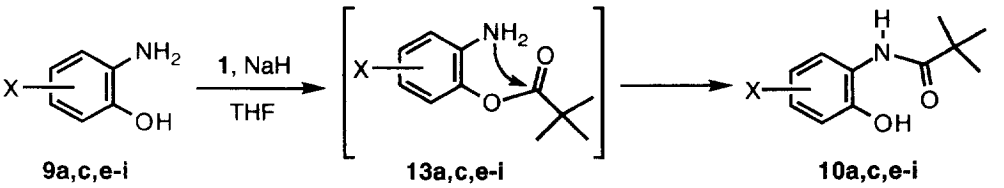
**Table 1.** Selective acylation of **4**,**9a-h** and **11** with **1** in refluxing THF.

| Entry | Substrate | Product | Yield (%) | mp, °C |
|---|---|---|---|---|
| 1 | **4** | **7** | 83 | 140.0-141.0 |
| 2 | **9a**: X = H<br>2-$NH_2$, 1-OH | **10a** | 99 | 133.5-134.0 |
| 3 | **9b**: X = H<br>4-$NH_2$, 1-OH | **10b** | 87 | 170.0-170.5 |
| 4 | **9c**: X = 4-Me<br>2-$NH_2$, 1-OH | **10c** | 100 | 142.4-143.0 |
| 5 | **9d**: X = 3-Me<br>4-$NH_2$, 1-OH | **10d** | 70 | 177.5-178.5 |
| 6 | **9e**: X = 5-Me<br>2-$NH_2$, 1-OH | **10e** | 94 | 139.0-140.5 |
| 7 | **9f**: X = 4-Me, 6-Me<br>2-$NH_2$, 1-OH | **10f** | 93 | 139.0-140.0 |
| 8 | **9g**: X = 4-Cl<br>2-$NH_2$, 1-OH | **10g** | 100 | 173.0-173.5 |
| 9 | **9h**: X = 4,5-$(CH_2)_4$-<br>2-$NH_2$, 1-OH | **10h** | 85 | 165.5-166.0 |
| 10 | **11** | **12** | 48 | 256.0-258.0 |

Substituted 2- and 4-aminophenols provided different products under the NaH conditions. It was found that reaction of substituted 2-aminophenols **9a,c,e-i** with the acylating agent **1** in the presence of NaH in THF at room temperature furnished the amide **10a,c,e-i** rather than the expected esters **13a,c,e-i** (Scheme 5 and Table 2). The products listed in Table 2 posess the characteristic IR absorptions of the secondary amide at *ca.* 3438 (sharp, N-H) and *ca.* 1648 (C=O) $cm^{-1}$. The melting points of **10a,c,e-h** are identical with those listed in

Table 1. An acyl group migration within the initially formed esters **13a,c,e-i** could account for the fromation of the amides **10a,c,e-i** which are thermally more stable.

## Scheme 5



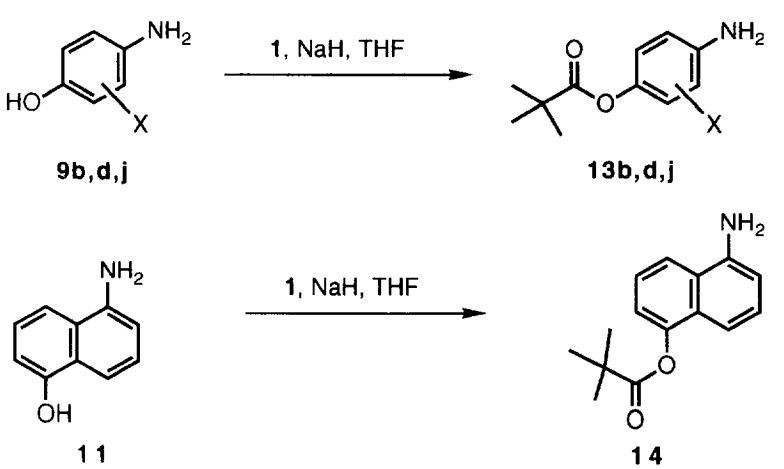

**9a,c,e-i** **13a,c,e-i** **10a,c,e-i**

**Table 2.** Selective acylation of 2-aminophenols **9a,c,e-i** with **1** and NaH in THF.

| Substrate | Product | Yield (%) | Substrate | Product | Yield (%) |
|---|---|---|---|---|---|
| **9a** | **10a** | 74 | **9g** | **10g** | 91 |
| **9c** | **10c** | 90 | **9h** | **10h** | 71 |
| **9e** | **10e** | 86 | **9i**: X = 3-Me, 2-$NH_2$, 1-OH | **10i** | 78 |
| **9f** | **10f** | 92 | | | |

Acylation of the sodium salt of 4-aminophenoxide derived from **9b** with **1** at room temperature gave the corresponding ester **13b** in 70% isolated yield (Scheme 6 and Table 3). 3-Methyl and 2,6-dibromo substituted 4-aminophenols **9d** and **9j** gave the esters **13d** and **13j** in 77% and 88% yield, respectively. The highest yield was obtained with the most stable ester **13j** in which the 2,6-dibromo substituents prevent further reaction of

## Scheme 6




**9b,d,j** **13b,d,j**

**11** **14**

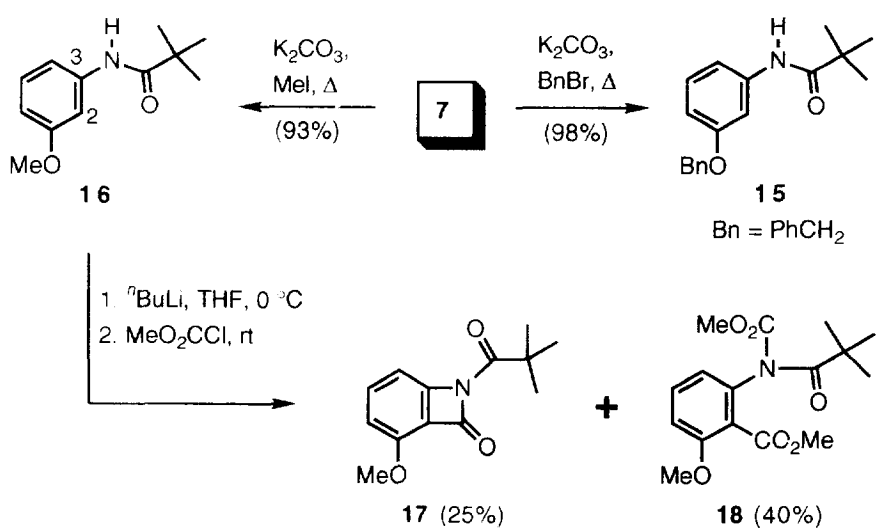
the ester functionality. 5-Amino-1-naphthol (**11**) gave the ester **14** under the same reaction conditions in excellent yield. The IR spectra of the products **13b,d** and **14** show a strong absorption at *ca.* 1740 $cm^{-1}$ which is consistent with the structure of the phenolic ester.

**Table 3.** Selective acylation of **9b,d,j** and **11** with **1** and NaH in THF.

| Entry | Substrate | Product | Yield (%) | mp, °C |
|---|---|---|---|---|
| 1 | **9b**: X = H<br>4-$NH_2$, 1-OH | **13b** | 70 | 53.0-54.0 |
| 2 | **9d**: X = 3-Me<br>4-$NH_2$, 1-OH | **13d** | 77 | 67.0-70.0 |
| 3 | **9j**: X = 2-Br, 6-Br<br>4-$NH_2$, 1-OH | **13j** | 88 | 190.0-194.0 |
| 4 | **11** | **14** | 94 | 117.0-118.0 |

In order to demonstrate the synthetic application of the described acylation reaction, transformations of the amide **7** were carried out to synthesize multiply functionalized aromatic compounds (Scheme 7). The phenolic hydroxy group in **7** can be protected as the benzyl ether **15** or methyl ether **16**[7a] by treating **7** with benzyl bromide or iodomethane in the presence of solid $K_2CO_3$ in refluxing acetone in high yield. Lithiation of **16** using 2.2 mole equivalent of $^nBuLi$ in THF at ice-cooling temperature took place at the C2 position exclusively.[7a] The resultant aryl lithium species reacted with 2.2 mole equivalent of methyl chloroformate to provide the β-lactam **17** and the methyl benzoate **18** in 25% and 40% yield, respectively. The later compound

**Scheme 7**



can be converted into 2-amino-6-methoxybenzoic acid which is an intermediate in the synthesis of some antitumor heterocyclic compounds.[7c]

In summary, we have developed a general method for highly selective acylation of substituted aminophenols using 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) as the mild and chemoselective acylating agent. This reaction tolerates different substituents in the substrate and can be performed simply by heating the reactants in refluxing THF to provide the amides exclusively in excellent chemical yield. Under the basic conditions using NaH in THF at room temperature, esters of 3- and 4-amino phenols could be prepared by using **1** in good to excellent yield. Among the acylating agents examined in these studies, 3-(trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) is superb in chemoselectivity over trimethylacetyl chloride and trimethylactic anhydride. In connection with the established chemistry such as *ortho* lithiation technique, it is possible that a variety of highly functionalized aromatic compounds can be derived from commercially available aminophenols. Useful applications of these compounds in organic synthesis are expected.

*Acknowledgment.* Thanks are given to the Department of Chemistry, HKUST for financial support.

## Experimental Section

*General Techniques.* Melting points were recorded on a MEL-TEMP II capillary melting point apparatus and are uncorrected. NMR spectra were recorded on a Bruker ARX 300 instrument. IR spectra were taken on a Perkin-Elmer FT-IR spectrophotometer. Low-resolution mass spectra (MS) were measured on a Finnigan TSQ 7000 mass spectrometer. Elemental analyses were performed by Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, China. All reactions were carried out under a nitrogen atmosphere and monitored by thin-layer chromatography on 0.25-mm E. Merck silica gel plates (60 F-254) using UV light, or 7% ethanolic phosphomolybdic acid and heating as the visualizing methods. E. Merck silica gel (60, particle size 0.040-0.063 mm) was used for flash column chromatography. Yields refer to chromatographically and spectroscopically ($^1$H NMR) homogeneous materials, unless otherwise stated. 3-(Trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) was prepared according to the reported procedures.[2,4,5] Compounds **4**, **9a-j**, and **11** were obtained commercially and used as received.

**Acylation of Aminophenols with 1 in Refluxing THF. General Procedure:** A mixture of the aminophenols **4, 9a-h**, or **11** (2.46 mmol) with **1** (0.500 g, 2.46 mmol) in THF (10 mL) was heated at *ca.* 80 °C under a nitrogen atmosphere until the TLC showed the disappearance of the starting materials (*ca.* 12 h for **9b**; 24 h for **4**, **9a,c-h**; 48 h for **11**). After cooling the reaction mixture to rt, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography over silica gel to provide the products **7**, **10a-h**, or **12** in the yield given in Table 1. The spectroscopic data for **7**, **10a-h**, and **12** are given below:

**3'-Hydroxy-2,2-dimethylpropionanilide (7).** The solvents for flash column chromatography are 33% ethyl acetate in hexane. Colorless crystalline solid, mp 140.0-141.0 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3452, 3282 (br), 3020, 2968, 1662, 1604, 1534, 1446 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.83 (s, 1 H), 7.37 (br s, 1 H), 7.17 (t, $J$ = 8.06 Hz, 1 H), 6.65 (dd, $J$ = 8.20, 2.31 Hz, 1 H), 6.58 (ddd, $J$ = 8.00,

1.94, 0.78 Hz, 1 H), 1.33 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 177.6, 157.5, 138.8, 129.8, 111.9, 110.9, 107.5, 39.5, 27.7; MS (EI$^+$) *m/z* (relative intensity) 193 ($M^+$, 100), 109 (87), 57 (93). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.42; H, 7.90; N, 7.22.

**2'-Hydroxy-2,2-dimethylpropionanilide (10a).** The solvents for flash column chromatography are 33% ethyl acetate in hexane. Colorless crystalline solid, mp 133.5-134.0 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3438, 3300 (br), 2970, 1648, 1600, 1522, 1498, 1454 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 9.10-8.70 (br s, 1 H), 7.88 (br s, 1 H), 7.29 (d, *J* = 7.91 Hz, 1 H), 7.07 (t, *J* = 7.64 Hz, 1 H), 6.98 (d, *J* = 7.97 Hz, 1 H), 6.85 (t, *J* = 7.54 Hz, 1 H), 1.34 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 178.9, 148.2, 126.6, 125.7, 121.9, 120.4, 118.7, 39.6, 27.6; MS (EI$^+$) *m/z* (relative intensity) 193 ($M^+$, 50), 109 (100), 57 (58). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.29; H, 7.84; N, 7.19.

**4'-Hydroxy-2,2-dimethylpropionanilide (10b).** The solvents for flash column chromatography are 20% ethyl acetate in benzene. Colorless crystalline solid, mp 170.0-170.5 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3598, 3454, 3300 (br), 2966, 1668, 1514 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.33-7.29 and 6.79-6.74 (AA'BB', 4 H), 7.22 (br s, 1 H), 2.00-1.40 (br s, 1 H), 1.31 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 176.5, 152.7, 130.7, 122.5, 115.7, 39.4, 27.6; MS (EI$^+$) *m/z* (relative intensity) 193 ($M^+$, 98), 109 (100), 57 (80). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.40; H, 7.81; N, 7.29.

**2'-Hydroxy-2,2,5'-trimethylpropionanilide (10c).** The solvents for flash column chromatography are 17% ethyl acetate in hexane. Colorless crystalline solid, mp 142.4-143.0 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3438, 3250 (br), 2968, 1648, 1602, 1536, 1506 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.80-8.15 (br s, 1 H), 7.56 (br s, 1 H), 6.91 (s, 2 H), 6.84 (s, 1 H), 2.26 (s, 3 H), 1.35 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 178.8, 146.5, 129.8, 127.7, 125.1, 122.5, 119.7, 39.4, 27.7, 20.3; MS (EI$^+$) *m/z* (relative intensity) 207 ($M^+$, 38), 123 (100), 57 (43). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.61; H, 8.30; N, 6.74.

**4'-Hydroxy-2,2,2'-trimethylpropionanilide (10d).** The solvents for flash column chromatography are 20% ethyl acetate in benzene. Colorless crystalline solid, mp 177.5-178.5 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3598, 3444, 3306 (br), 2966, 1666, 1504 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.13 Hz, 1 H), 7.11 (br s, 1 H), 6.50 (s, 1 H), 6.49 (d, *J* = 7.79 Hz, 1 H), 2.12 (s, 3 H), 2.10-1.40 (br s, 1 H), 1.34 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 178.1, 154.6, 133.8, 127.2, 126.8, 117.5, 113.8, 39.3, 27.7, 17.7; MS (EI$^+$) *m/z* (relative intensity) 207 ($M^+$, 100), 123 (99), 57 (99). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.63; H, 8.40; N, 6.79.

**2'-Hydroxy-2,2,4'-trimethylpropionanilide (10e).** The solvents for flash column chromatography are 10% ethyl acetate in hexane. Colorless crystalline solid, mp 139.0-140.5 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3440, 2968, 1646, 1604, 1522 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 9.30-8.30 (br s, 1 H), 7.63 (br s, 1 H), 6.93 (d, *J* = 8.03 Hz, 1 H), 6.82 (s, 1 H), 6.66 (d, *J* = 7.98 Hz, 1 H), 2.27 (s, 3 H), 1.34 (s, 9 H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 178.8, 148.5, 137.2, 123.0, 121.9, 121.1, 120.1, 39.4,

27.7, 20.8; MS (EI+) *m/z* (relative intensity) 207 ($M^+$, 51), 123 (100), 57 (45). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.51; H, 8.38; N, 6.81.

**2'-Hydroxy-2,2,3',5'-tetramethylpropionanilide (10f).** The solvents for flash column chromatography are 15% ethyl acetate in hexane. Colorless crystalline solid, mp 139.0-140.0 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3440, 2968, 1646, 1532, 1490 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.80-8.10 (br s, 1 H), 7.50 (s, 1 H), 6.84 (s, 1 H), 6.64 (s, 1 H), 2.26 (s, 3 H), 2.22 (s, 3 H), 1.35 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 177.0, 171.3, 129.2, 128.0, 124.2, 120.3, 39.0, 27.7, 20.3, 16.5; MS (EI+) *m/z* (relative intensity) 221 ($M^+$, 40), 137 (100), 57 (47). Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.22; H, 8.69; N, 6.26.

**5'-Chloro-2'-hydroxy-2,2-dimethylpropionanilide (10g).** The solvents for flash column chromatography are 33% ethyl acetate in hexane. Colorless crystalline solid, mp 173.0-173.5 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3436, 3250 (br), 2968, 1652, 1522, 1494, 1420 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.56 (br s, 1 H), 7.59 (br s, 1 H), 7.13 (d, $J$ = 2.18 Hz, 1 H), 7.07 (dd, $J$ = 2.46, 8.66 Hz, 1 H), 6.93 (d, $J$ = 8.64 Hz, 1 H), 1.35 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 179.0, 147.4, 126.7, 126.5, 124.9, 121.9, 120.7, 39.6, 27.6; MS (EI+) *m/z* (relative intensity) 229 ($M^+$+2, 12), 227 ($M^+$, 37), 145 (22), 143 (69), 57 (100). Anal. Calcd for $C_{11}H_{14}ClNO_2$: C, 58.03; H, 6.20; N, 6.15. Found: C, 58.08; H, 6.15; N, 6.16.

**3-((Trimethylacetyl)amido)-5,6,7,8-tetrahydro-2-naphthol (10h).** The solvents for flash column chromatography are 5% ethyl acetate in hexane. Colorless crystalline solid, mp 165.5-166.0 °C (from ethyl ether-hexane); IR ($CHCl_3$) 3440, 2936, 1650, 1512 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.90-8.00 (br s, 1 H), 7.50 (br, s 1 H), 6.72 (s, 1 H), 6.69 (s, 1 H), 2.70-2.60 (m, 4 H), 1.80-1.70 (m, 4 H), 1.34 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 178.7, 146.5, 136.3, 129.0, 123.1, 122.2, 119.6, 39.3, 28.8, 28.5, 27.7, 23.3, 23.1; MS (EI+) *m/z* (relative intensity) 247 ($M^+$, 36), 163 (100), 57 (30). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.73; H, 8.48; N, 5.67.

**5-((Trimethylacetyl)amido)-1-naphthol (12).** The solvents for flash column chromatography are 5% ethyl acetate in benzene. Colorless crystalline solid, mp 256.0-258.0 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3688, 3600, 3446 (br), 2962, 1676, 1602, 1530, 1490 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$+DMSO-$d_6$) δ 9.58 (s, 1 H), 8.51 (br s, 1 H), 8.15 (d, $J$ = 8.37 Hz, 1 H), 7.72 (d, $J$ = 7.31 Hz, 1 H), 7.42 (t, $J$ = 7.92 Hz, 1 H), 7.37-7.30 (m, 2 H), 6.96-6.90 (m, 1 H), 1.44 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$+DMSO-$d_6$) δ 176.9, 153.1, 132.1, 129.3, 125.9, 125.1, 123.4, 122.1, 119.6, 111.7, 107.8, (one signal is overlapped with DMSO-$d_6$), 27.1; MS (EI+) *m/z* (relative intensity) 243 ($M^+$, 89), 159 (100), 57 (93). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.91; H, 6.88; N, 5.81.

**Reaction of Aminophenols with 1 in the Presence of NaH. General Procedure: 3-((Trimethylacetyl)oxy)aniline (8).** To a suspension of NaH (60%, 0.125 g, 3.13 mmol) in dry THF (5 mL) cooled in an ice-water bath (ca. 0 °C) was added a solution of **4** (0.340 g, 3.12 mmol) in dry THF (5 mL) followed by stirring for 10 min at the same temperature. To the resultant solution was added **1** (0.760 g, 3.74

mmol) dissolved in dry THF (10 mL). After stirring for 30 min at rt, the reaction mixture was treated with saturated aqueous $NH_4Cl$, and extracted with ethyl acetate (2 x 20 mL). The combined organic layer was then washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 33% ethyl acetate in hexane) to give **8** (0.608 g, 93%): colorless crystalline solid, mp 47-50 °C (from ethyl ether-hexane); IR ($CHCl_3$) 3500 (br), 3402, 2976, 1742, 1622, 1492, 1276, 1148, 1122 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.14 (t, $J$ = 8.00 Hz, 1 H), 6.53 (ddd, $J$ = 7.94, 2.22, 0.77 Hz, 1 H), 6.44 (ddd, $J$ = 7.94, 2.12, 0.72 Hz, 1 H), 6.39 (t, $J$ = 2.16 Hz, 1 H), 3.30-2.30 (br, 2 H), 1.35 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 177.1, 152.1, 146.9, 130.0, 112.7, 111.8, 108.6, 39.0, 27.1; MS ($EI^+$) *m/z* (relative intensity) 193 ($M^+$, 43), 109 (100), 57 (30). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.22; H, 7.84; N, 7.25.

For the reactions of other substituted aminophenols under the NaH conditions, the results are given in Tables 2 and 3. The spectroscopic data of **10i**, **13b,d,j** and **14** are given follow.

**2'-Hydroxy-2,2,6'-trimethylpropionanilide (10i).** The solvents for flash column chromatography are 15% ethyl acetate in hexane. Colorless crystalline solid, mp 141.0-142.0 °C (from ethyl ether-hexane); IR ($CHCl_3$) 3450, 2968, 1646, 1518, 1400 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 1 H), 7.40 (br, 1 H), 7.07 (t, $J$ = 7.80 Hz, 1 H), 6.92 (d, $J$ = 7.80 Hz, 1 H), 6.76 (d, $J$ = 7.5 Hz, 1 H), 2.28 (s, 3 H), 1.39 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 178.9, 150.1, 130.0, 127.1, 124.2, 122.1, 118.3, 39.6, 27.6, 18.0; MS ($EI^+$) *m/z* (relative intensity) 207 ($M^+$, 40), 123 (100), 57 (46).

**4-((Trimethylacetyl)oxy)aniline (13b).** The solvents for flash column chromatography are 5% ethyl acetate in benzene. Brownish crystalline solid, mp 53.0-54.0 °C (from ethyl ehter-hexane); IR ($CHCl_3$) 3460, 3376, 2978, 1740, 1622, 1510, 1194, 1128 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.83 and 6.66 (AA'BB', 4 H), 3.80-3.20 (br, 2 H), 1.33 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 177.5, 143.8, 143.1, 121.9, 115.5, 38.8, 27.0; MS ($EI^+$) *m/z* (relative intensity) 193 ($M^+$, 22), 109 (100). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.25; H, 7.85; N, 7.24.

**2-Methyl-4-((trimethylacetyl)oxy)aniline (13d).** The solvents for flash column chromatography are 10% ethyl acetate in hexane. Colorless crystalline solid, mp 67.0-70.0 °C (from ethyl ehter-hexane); IR ($CHCl_3$) 3460, 3400, 2978, 1740, 1624, 1504, 1154, 1120 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.75 (d, $J$ = 2.7 Hz, 1 H), 6.72 (dd, $J$ = 8.40, 2.40 Hz, 1 H), 6.63 (d, $J$ = 8.40 Hz, 1 H), 3.80-3.10 (br, 2 H), 2.14 (s, 3 H), 1.33 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 177.6, 142.9, 142.0, 123.1, 122.9, 119.3, 115.1, 38.8, 27.0, 17.3; MS ($EI^+$) *m/z* (relative intensity) 207 ($M^+$, 22), 123 (100). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.67; H, 8.48; N, 6.87.

**3,5-Dibromo-4-((trimethylacetyl)oxy)aniline (13j).** The solvents for flash column chromatography are 20% ethyl acetate in hexane. Colorless crystalline solid, mp 190.0-194.0 °C (from ethyl ehter-hexane); IR (KBr) 3338, 3240, 2974, 1720 (weak), 1630, 1574, 1510, 1480, 1406, 1280, 1220, 1172 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$+DMSO-$d_6$) δ 8.89 (br, 2 H), 7.90 (s, 2 H), 1.28 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$+DMSO-$d_6$) δ 176.3, 145.7, 132.3, 123.4, 110.1, 38.4, 26.4; MS ($EI^+$) *m/z* (relative intensity)

353 ($M^+$+4, 10), 351 ($M^+$+2, 22), 349 ($M^+$, 11), 269 (8), 267 (17), 265 (9), 85 (20), 57 (100). Anal. Calcd for $C_{11}H_{13}Br_2NO_2$: C, 37.64; H, 3.73; N, 3.99. Found: C, 37.62; H, 3.66; N, 3.94.

**1-Amino-5-((trimethylacetyl)oxy)naphthalene (14).** The solvents for flash column chromatography are 20% ethyl acetate in hexane. Grayish crystalline solid, mp 117.0-118.0 °C (from ethyl ehter-hexane); IR ($CHCl_3$) 3470, 3398, 2978, 1748, 1622, 1516, 1410, 1228, 1120 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.61 (d, $J$ = 8.40 Hz, 1 H), 7.40-7.28 (m, 3 H), 7.21 (d, $J$ = 7.20 Hz, 1 H), 6.69 (dd, $J$ = 6.90, 1.80 Hz, 1 H), 4.07 (br, 2 H), 1.55 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 177.1, 147.2, 142.6, 127.9, 126.9, 124.8, 123.9, 118.8, 117.9, 111.2, 110.0, 39.4, 27.3; MS ($EI^+$) *m/z* (relative intensity) 243 ($M^+$, 33), 159 (100), 130 (28), 57 (22). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.26; H, 7.16; N, 5.94.

**Reaction of 4 with Trimethylacetyl Chloride or Trimethylacetic Anhydride in the Presence of Pyridine.** To a solution of **4** (436 mg, 4.0 mmol) in dry THF (20 mL) cooled in an ice-water bath was added pyridine (0.40 mL, 5.0 mmol). Trimethylacetyl chloride (0.50 mL, 4.0 mmol) or trimethylacetic anhydride (0.81 mL, 4.0 mmol) was added through syringe. After stirring for the indicated time period (see Scheme 3 and text for details), water was added to the reaction mixture. The resultant mixture was extracted with ethyl acetate (2 x 20 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 33% ethyl acetate in hexane) to give **7** (0.588 g, 76% or 0.687 g, 89%). Some of **3** (12.3 mg, 3%) was recovered from the reaction with trimethylacetic anhydride.

**Reaction of 4 with Trimethylacetyl Chloride or Trimethylacetic Anhydride in the Presence of NaH.** To a suspension of NaH (60%, 0.200 g, 5.0 mmol) in dry THF (10 mL) cooled in an ice-water bath was added a solution of 3-aminophenol (**4**, 0.436 g, 4.0 mmol) in dry THF (10 mL) followed by stirring for 10 min at the same temperature. To the resultant mixture was added trimethylacetyl chloride (0.50 mL, 4.0 mmol). After stirring for 4 h at rt, the reaction mixture was treated with saturated aqueous $NH_4Cl$, and extracted with ethyl acetate (2 x 20 mL). The combined organic layer was then washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 20% ethyl acetate in hexane) to give **7** (66.7 mg, 9%), **8** (0.486 g, 63%), the bisacylation product (0.177 g, 16%), and the starting material **4** (42.3 mg, 10%).

The same reaction was performed with trimethylacetic anhydride (0.82 mL, 4.0 mmol) in dry THF (50 mL in total) at rt for 19 h. The ester **8** (0.710 g, 92%) was isolated as the sole product.

The spectroscopic data of compounds **7** and **8** obtained here are identical with those given in the previous paragraphs.

**3'-(Benzyloxy)-2,2-dimethylpropionanilide (15).** A mixture of **7** (1.000 g, 5.18 mmol), benzyl bromide (0.74 mL, 6.22 mmol), and solid $K_2CO_3$ (1.430 g, 10.36 mmol) in wet acetone (15 mL) was heated at 40 °C until TLC indicated the complete conversion of **7** (ca. 24 h). The reaction mixture was condensed under reduced pressure to remove acetone. To the residue water was added followed by extraction with ethyl acetate (2 x 30 mL). The combined organic layer was washed with brine, dried over anhydrous

$MgSO_4$, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 25% ethyl acetate in hexane) to afford **15** (1.426 g, 98%): colorless crystalline solid, mp 93.0-94.0 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3454, 2968, 1680, 1606, 1524, 1490, 1434, 1288, 1190 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.51-7.18 (m, 8 H), 6.97 (m, 1 H), 6.75 (m, 1 H), 5.07 (s, 2 H), 1.32 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 176.6, 159.4, 139.3, 136.9, 129.6, 128.5, 127.9, 127.5, 112.9, 111.1, 106.3, 70.0, 39.7, 27.6; MS ($EI^+$) *m/z* (relative intensity) 283 ($M^+$, 23), 226 (22), 91 (100), 57 (19). Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 76.43; H, 7.51; N, 5.01.

**3'-Methoxy-2,2-dimethylpropionanilide (16).** Prepared in 93% yield from **7** and iodomethane in the presence of solid $K_2CO_3$ in the same manner as described for **15**. The solvents for flash column chromatography are 33% ethyl acetate in hexane. **16**: colorless crystalline solid, mp 106.0-109.0 °C (from ethyl acetate-hexane); IR ($CHCl_3$) 3454, 2966, 1678, 1608, 1526, 1492, 1452 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.39 (t, *J* = 2.12 Hz, 1 H), 7.30 (br s, 1 H), 7.20 (t, *J* = 8.14 Hz, 1 H), 6.93 (dd, *J* = 1.09, 7.94 Hz, 1 H), 6.66 (dd, *J* = 2.23, 8.26 Hz, 1 H), 3.81 (s, 3 H), 1.32 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 176.6, 160.2, 139.3, 137.4, 129.5, 111.8, 110.4, 105.3, 55.3, 39.7, 27.6; MS ($EI^+$) *m/z* (relative intensity) 207 ($M^+$, 100), 123 (63), 57 (93).

***Ortho* Lithiation of 16. Preparation of Compounds 17 and 18.** To a solution of **16** (0.834 g, 4.03 mmol) in dry THF (20 mL) cooled in an ice-water bath (*ca.* 0 °C) was added dropwise $^n$BuLi (1.6 M, 5.5 mL, 8.80 mmol) followed by stirring at the same temperature for 3.5 h. To the yellow solution was added methyl chloroformate (0.68 mL, 8.80 mmol). After stirring at rt for overnight, the reaction mixture was quenched with saturated aqueous $NH_4Cl$, and extracted with ethyl acetate (2 x 30 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 10% ethyl acetate in hexane) to furnish **17** (0.224 g, 25%) and **18** (0.489 g, 40%) with the recovery of **16** (48 mg). **17**: colorless crystalline solid, mp 107.5-110.0 °C (from ethyl ether-hexane); IR ($CHCl_3$) 2974, 1756, 1708, 1638, 1604, 1578, 1478, 1260, 1136 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.67 (t, *J* = 8.27 Hz, 1 H), 7.14 (d, *J* = 8.08 Hz, 1 H), 6.92 (d, J = 8.42 Hz, 1 H), 3.99 (s, 3 H), 1.37 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.0, 160.8, 156.7, 149.0, 136.7, 118.8, 109.5, 105.9, 56.4, 37.7, 27.6; MS ($EI^+$) *m/z* (relative intensity) 233 ($M^+$, 22), 218 (16), 176 (100). **18**: colorless crystalline solid, mp 90.0-91.0 °C (from ethyl ether-hexane); IR ($CHCl_3$) 2956, 1736, 1602, 1472, 1438, 1274, 1122, 1056 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.36 (t, *J* = 8.16 Hz, 1 H), 6.95 (d, *J* = 8.41 Hz, 1 H), 6.75 (d, J = 7.97 Hz, 1 H), 3.85 (s, 6 H), 3.71 (s, 3 H), 1.34 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 183.1, 165.9, 157.6, 154.6, 138.0, 131.1, 121.2, 111.3, 56.2, 53.8, 52.4, 43.6, 27.8; MS ($EI^+$) *m/z* (relative intensity) 323 ($M^+$, 15), 239 (90), 207 (76), 176 (100), 57 (37). Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.58; H, 6.60; N, 4.38.

*References and notes:*

1. (a) Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991. (b) Kocienski, P. J. *Protecting Groups*, Thieme: Stuttgart, 1994.
2. Nicolaou, K. C.; Dai, W.-M. *J. Am. Chem. Soc.* **1992**, *114*, 8908.

3. (a) Nicolaou, K. C.; Dai, W.-M.; Wendeborn, S. V.; Smith, A. L.; Torisawa, Y.; Maligres, P.; Hwang, C.-K. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1032. (b) Nicolaou, K. C.; Dai, W.-M.; Tsay, S.-C.; Estevez, V. A. Wrasidlo, W. *Science* **1992**, *256*, 1172.

4. 3-(Trimethylacetyl)-1,3-thiazolidine-2-thione (**1**) was prepared by reacting of trimethylacetyl chloride with the sodium salt of 2-mercaptothiazoline in THF in 91% yield. Alternatively, **1** can be prepared from trimethylacetyl chloride and 2-mercaptothiazoline using Et3N as the base in 78% yield (see ref. 5a). Both methods produce the same crystalline substance having the characteristic pale yellow color. The mp of **1** should be 58-59 °C rather than 99-102 °C reported in ref. 2.

5. (a) Yamada, S. *J. Org. Chem.* **1992**, *57*, 1591. (b) Yamada, S. *Tetrahedron Lett.* **1992**, *33*, 2171. (c) Yamada, S. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1083.

6. (a) Nagao, Y.; Seno, K.; Kawabata, K.; Miyasaka, T.; Takao, S.; Fujita, E. *Chem. Pharm. Bull. Jpn.* **1984**, *32*, 2687. (b) Izawa, T.; Mukaiyama, T. *Chem. Lett.* **1977**, 1443. (c) Nagao, Y.; Kawabata, K.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1978**, 330. (d) Izawa, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1979**, *53*, 555. (e) Fujita, E. *Pure Appl. Chem.* **1981**, *53*, 1141. (f) Chung-shi, L.; Yuen-hwa, Y.; Yao, L.; Yong-jun, L.; Ai-hsueh, L.; Chi-yi, H. *Tetrahedron Lett.* **1981**, *22*, 3467. (g) Kuramoto, T.; Kihara, K.; Matsumoto, N.; Hoshita, T. *Chem. Pharm. Bull.* **1981**, *29*, 1136. (h) Nagao, Y.; Ikeda, T.; Yagi, M.; Fujita, E.; Shiro, M. *J. Am. Chem. Soc.* **1982**, *104*, 2079. (i) Nagao, Y.; Ikeda, T.; Inoue, T.; Yagi, M.; Shiro, M.; Fujita, E. *J. Org. Chem.* **1985**, *50*, 4072. (j) Fujita, E.; Nagao, Y. *Adv. Heterocycl. Chem.* **1989**, *45*, 1. (k) Nagao, Y.; Ochiai, M. *Yuki Goshei Kagaku Kyokaishi* **1990**, *48*, 986-987. (l) Nagao, Y. *Kikan Kagaku Sosetsu* **1993**, *19*, 191-205. (m) Arnaud, N.; Cazaux, L.; Tisnès, P.; Picard, C. *Synlett* **1994**, 553.

7. (a) Fuhrer, W.; Gschwend, H. W. *J. Org. Chem.* **1979**, *44*, 1133. (b) Reed, J. N.; Rotchford, J.; Strickland, D. *Tetrahedron Lett.* **1988**, *29*, 5725. (c) Sugaya, T.; Mimura, Y.; Kato, N.; Ikuta, M.; Mimura, T.; Kasai, M.; Tomioka, S. *Synthesis* **1994**, 73. (d) A review: Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

8. A complicated reaction mixture was obtained by heating the black powder of **11** with **1** in THF under a nitrogen atmosphere as shown by TLC.

(*Received in China* 16 *June* 1995; *accepted* 6 *September* 1995)