An Effective Method for Acylation of Weakly Nucleophilic Anilines with Silyl Carboxylates via Mixed Anhydrides

Mitsutomo MIYASHITA, Isamu SHIINA,* and Teruaki MUKAIYAMA*
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162
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In the presence of a catalytic amount of active titanium(IV) salt generated in situ from 1 mol of $TiCl_4$ and 2 mol of AgOTf, *weakly nucleophilic anilines* react under mild conditions with nearly equimolar amounts of silyl carboxylates to afford the corresponding anilides in excellent yields using 4-(trifluoromethyl)benzoic anhydride. The mixed anhydride formed in situ from trimethylsily acetate and 4-(trifluoxomethyl)benzoic anhydride, a key intermediate of this reaction, was detected by ^{1}H NMR experiment. Further, it was shown that the reaction of the mixed anhydrides and 2-nitroaniline was faster than that of the corresponding homo anhydrides and 2-nitroaniline.

The preparation of amides is one of the most important and fundamental processes in organic synthesis and many methods have been already reported. Most of the acylation reactions of amines were carried out using acyl halides or carboxylic anhydrides under basic conditons. Further, many coupling reagents of free carboxylic acids and amines have been developed in order to achieve the effective synthesis of amides.[1] However, in the acylation of *weakly nucleophilic amines* such as nitroanilines or trihaloanilines, rather drastic reaction conditions have been required for the completion of the reaction; for example, the acylation of 2-nitroaniline was carried out using protic acids such as acetic or sulfuric acid in acetic anhydride at reflux temperature, or with excess amount of acetyl chloride and pyridine at high temperature. On the other hand, milder reaction condition, treatment of 2-nitroaniline with 3-phenylpropionyl chloride in the presence of triethylamine at room temperature for 90 h in dichloromethane, afforded the desired anilide in 14% yield.

Recently, two efficient methods for the preparation of anilides from *weakly nucleophilic anilines* were reported; that is, a) transamination of *S*-*t*-butyl carbothioates with 2-nitroaniline by the use of more than stoichiometric amounts of silver(I) trifluoroacetate,[2] and b) acylation of 2-nitroaniline with acyl trimethylsilyl polyphosphates, prepared from trimethylsilyl carbonxylates and phosphorus pentoxide, by heating at 80 °C for several hours.[3] However, it is still desired to develop a more efficient and convenient method for the synthesis of anilides from simple carboxylic acid derivatives and *weakly nucleophilic anilines* under mild reaction conditions. In this paper, we would like to describe fully the results of our investigation on the development of an effective method for the preparation of anilides starting from nearly equimolar amounts of silyl carboxylates and *weakly nucleophilic anilines* under mild conditions using an equimolar amount of 4-(trifluoromethyl)benzoic anhydride and the active titanium(IV) salt catalyst.[4]

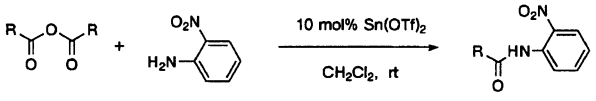
Results and Discussion

Reaction of Carboxylic Anhydrides with *Weakly Nucleophilic Anilines*. During our studies on the development of new catalytic synthetic reactions using active Lewis acid such as $SnCl_4 + AgClO_4$,[5] $GaCl_3 + AgClO_4$,[6] $Sn(OTf)_2$ (Tf = trifluoromethanesulfonyl),[7,8] $MeSiCl_3 + AgClO_4$,[9] $SbCl_5 + AgSbF_6$,[6,10] $TiCl_4 + 2AgOTf$,[7,11] $SiCl_4 + 3AgClO_4$,[12] $SiCl_4 + 2AgOTf$,[13] $Ph_2Sn{=}S + AgClO_4$,[14] $TiCl_4 + 2AgClO_4$,[15] it was demonstrated that alcoholysis of a carboxylic anhydride with an alkyl silyl ether proceeded smoothly to form the corresponding ester by using the above active Lewis acid catalysts.[7] These results suggested us to investigate the use of the above catalyst for the preparation of an anilide from a carboxylic anhydride and a *weakly nucleophilic aniline*.

Firstly, the acylation of 2-nitroaniline with 2-methylpropanoic anhydride was examined by our using a catalytic amount of $Sn(OTf)_2$. The reaction proceeded at room temperature in dichloromethane to give the corresponding anilide in 73% yield. The results with other typical anhydrides are shown in Table 1. It is noteworthy that 2,2-dimethyl-2′-nitropropananilide was also obtained in moderate yield from pivalic anhydride.

An Effective Method for the Acylation of *Weakly Nucleophilic Anilines* with Silyl Carboxylates via Mixed Anhydrides. In the preparation of carboxylic esters from silyl carboxylates and alkyl silyl ethers, it was suggested that the mixed anhydrides were smoothly produced from silyl carboxyl-

Table 1. Acylation of 2-Nitroaniline with Carboxylic Anhydrides



Entry	R	Reaction Time /h	Products	Yield/%[a]
1	Me	20	**1**	72
2	*i*-Pr	20	**2**	73
3	*t*-Bu	40	**3**	71
4	2-Me–C_6H_4	4	**4**	80

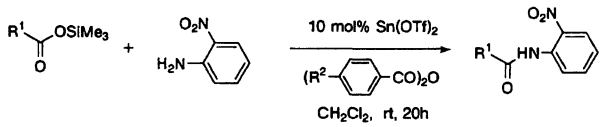
a) Isolated yield.

ates and 4-(trifluoromethyl)benzoic anhydride in the presence of the active Lewis acid catalyst such as Sn(OTf)$_2$ or a titanium(IV) salt, generated in situ from $TiCl_4$ and AgOTf or $AgClO_4$, and the mixed anhydrides were in turn efficiently converted into the corresponding carboxylic esters on treatment with trimethylsily alkyl ethers.[7]

Since the desired anilides are formed from equimolar amounts of carboxylic anhydride and 2-nitroaniline as mentioned above, it was anticipated that the reaction between silyl carboxylates and *weakly nucleophilic anilines* would proceed smoothly according to the mixed anhydride method. Thus, acylation of 2-nitroaniline with trimethylsilyl 2,2-dimethylpropionate was examined by our using a catalytic amount of Sn(OTf)$_2$ in the presence of 4-fluorobenzoic anhydride, a co-reagent. The reaction proceeded at room temperature in dichloromethane to give the corresponding anilide in 72% yield along with a small amount of 4-fluoro-2′-nitrobenzanilide. On the other hand, the yield of the desired anilide was improved up to 88% when 4-(trifluoromethyl)benzoic anhydride was used instead of 4-fluorobenzoic anhydride, and undesirable 4-trifluoromethyl-2′-nitrobenzanilide was not obtained (Table 2, Entry 8). These results are listed in Table 2. It was shown that 4-(trifluoromethyl)benzoic anhydride was the superior co-reagent to 4-florobenzoic anhydride not only the yield but also the chemoselectivity.

In order to optimize the reaction conditions, several catalysts and solvents were examined in the reaction of trimethylsilyl 2-methylpropionate and 2-nitroaniline with 4-(trifluoromethyl)benzoic anhydride (See Table 3). It was found that the reaction completed at room temperature by the use of a catalytic amount of titanium(IV) salt generated in situ from 1 mol of $TiCl_4$ and 2 mol of AgOTf without accompanying undesirable by-product formed from 4-(trifluoromethyl)benzoic anhydride. Concerning the solvent, the best result was obtained when the reaction was carried out in dichloromethane in the presence of the active titanium(IV) salt. It should be noted that neither $TiCl_4$ nor AgOTf alone is effecitve in the present reaction, and that trifluoromethanesulfonic acid is not efficient catalyst in the present reaction (See Entries 12—14). Furthermore, when the reaction was carried out in the absence of 4-(trifluoromethyl)benzoic anhydride, desired anilide was not obtained. Some examples of the present acylation of *weakly nucleophilic anilines* are listed in Table 4. In every case, the reactions proceeded smoothly at room temperature in dichloromethane to give the corresponding anilides in excellent yields starting from nearly equimolar amounts of silyl carboxylates and *weakly nucleophilic anilines* such as 2,4-dinitroaniline and 2,4,6-trichloroaniline. It is noteworthy that the use of only 1 mol% of active titanium(IV) catalyst gave the desired anilides in high yields (See Table 4).

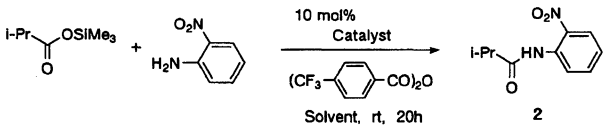
Table 2. Effect of Substituted Benzoic Anhydrides



Entry	R^1	R^2	Products	Yield/%[a]
1	Me	F	**1**	82
2	Me	CF_3	**1**	92
3	*i*-Pr	F	**2**	93
4	*i*-Pr	CF_3	**2**	96
5	*i*-Bu	F	**5**	95
6	*i*-Bu	CF_3	**5**	95
7	*t*-Bu	F	**3**	72[b] (2)[c]
8	*t*-Bu	CF_3	**3**	88
9	$Ph(CH_2)_2$	F	**6**	78 (3)[c]
10	$Ph(CH_2)_2$	CF_3	**6**	89

a) Isolated yield. b) The reaction time was 40 h. c) Yield of 4-fluoro-2′-nitrobenzanilide.

Table 3. Effect of Catalysts and Solvents

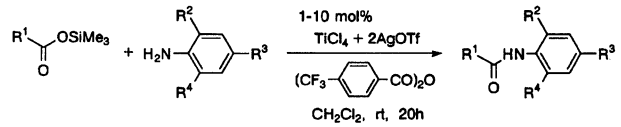


Entry	Catalyst	Solvent	Yield/%[a]
1	$Sn(OTf)_2$	CH_2Cl_2	96
2	$AlCl_3$+2AgOTf	CH_2Cl_2	70
3	$FeCl_3$+2AgOTf	CH_2Cl_2	81
4	$SiCl_4$+2AgOTf	CH_2Cl_2	33
5	$SnCl_4$+2AgOTf	CH_2Cl_2	77
6	$TiCl_2(OTf)_2$	CH_2Cl_2	93
7	$TiCl_4$+2AgOTf	CH_2Cl_2	97
8	$TiCl_4$+2AgOTf	Et_2O	91
9	$TiCl_4$+2AgOTf	THF	7
10	$TiCl_4$+2AgOTf	CH_3CN	84
11	$TiCl_4$+2AgOTf	Toluene	85
12	$TiCl_4$	CH_2Cl_2	19 (1)[b]
13	AgOTf	CH_2Cl_2	0
14	TfOH	CH_2Cl_2	31 (1)[b]

a) Isolated yield. b) Yield of 4-trifluoromethyl-2′-nitrobenzanilide.

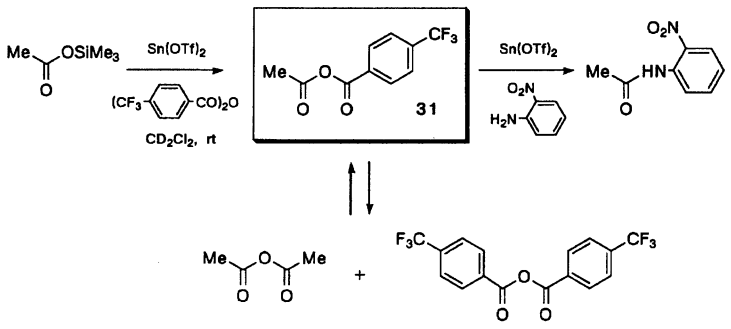
Reaction Pathway. In order to confirm the existence of the mixed anhydride, the reaction of trimethylsilyl acetate and 4-(trifluoromethyl)benzoic anhydride was monitored by ^{1}H NMR spectroscopy in the presence of a catalytic amount of Sn(OTf)$_2$. It was indicated that the mixed anhydride was generated smoothly in situ accompanied with the partial disproportionation of the mixed anhydride to form two kinds of homo anhydrieds (Scheme 1). The same partial disproportionation occurred in the case of our using 4-(trifluoromethyl)benzoyl chloride and acetic acid in the presence of triethylamine in dichloromethane-d_2. While 2′-nitroacetanilide was produced in high yield in the present acylation of 2-nitroaniline via mixed anhydride (Table 2, Entry 2, 92%

Table 4. Synthesis of Substituted Anilides Derived from *Weakly Nucleophilic Anilines*



Entry	R^1	R^2	R^3	R^4	Products	Yield/%[a]
1	Me	NO_2	H	H	**1**	96 (95)[b]
2	*i*-Pr	NO_2	H	H	**2**	97
3	*i*-Bu	NO_2	H	H	**5**	99
4	*t*-Bu	NO_2	H	H	**3**	97
5	$Ph(CH_2)_2$	NO_2	H	H	**6**	92
6	2-Me–C_6H_4	NO_2	H	H	**4**	95[c]
7	Me	NO_2	NO_2	H	**7**	93
8	*i*-Pr	NO_2	NO_2	H	**8**	97 (91)[b]
9	*i*-Bu	NO_2	NO_2	H	**9**	95
10	*t*-Bu	NO_2	NO_2	H	**10**	97
11	$Ph(CH_2)_2$	NO_2	NO_2	H	**11**	99
12	2-Me-C_6H_4	NO_2	NO_2	H	**12**	97
13	Me	NO_2	Cl	H	**13**	99
14	*i*-Pr	NO_2	Cl	H	**14**	99
15	*i*-Bu	NO_2	Cl	H	**15**	99 (97)[b]
16	*t*-Bu	NO_2	Cl	H	**16**	99
17	$Ph(CH_2)_2$	NO_2	Cl	H	**17**	97
18	2-Me-C_6H_4	NO_2	Cl	H	**18**	98
19	Me	Cl	NO_2	H	**19**	95
20	*i*-Pr	Cl	NO_2	H	**20**	98
21	*i*-Bu	Cl	NO_2	H	**21**	98
22	*t*-Bu	Cl	NO_2	H	**22**	97 (97)[b]
23	$Ph(CH_2)_2$	Cl	NO_2	H	**23**	99
24	2-Me-C_6H_4	Cl	NO_2	H	**24**	95
25	Me	Cl	Cl	Cl	**25**	89
26	*i*-Pr	Cl	Cl	Cl	**26**	96
27	*i*-Bu	Cl	Cl	Cl	**27**	96
28	*t*-Bu	Cl	Cl	Cl	**28**	98
29	$Ph(CH_2)_2$	Cl	Cl	Cl	**29**	95
30	2-Me-C_6H_4	Cl	Cl	Cl	**30**	99 (91)[b]

a) Isolated yield. 10 mol% of catalyst was used. b) One mol% of catalyst was used. The reaction time was 50 h. c) 10 mol% of $TiCl_4$ and 30 mol% of AgOTf were used as a catalyst.



Scheme 1.

yield), the yield was moderate when acetic anhydride was used under the same reaction conditions (Table 1, Entry 1, 72% yield). This result indicates that the acylation by the mixed anhydrides is faster than that of the corresponding homo anhydrides (See Tables 1 and 2). Unsymmetrical nature of charge density of acyloxy groups of the mixed anhydrides may play some role in facile acylation. Consequently, 4-(trifluoromethyl)-benzoyloxy group of the mixed anhydride would be an excellent leaving group in the presence of active Lewis acid catalyst. On the other hand, leaving ability of the acyloxy group of homo anhydrides is lower than that

of the mixed anhydrides, because the electric charge of acyloxy group of the homo anhydrides is equal.

Thus, various anilides are produced in excellent yields from nearly equimolar amounts of silyl carboxylates and corresponding *weakly nucleophilic anilines* at room temperature in the coexistence of 4-(trifluoromethyl)-benzoic anhydride and a catalytic amount of active titanium(IV) salt.

Experimental

All melting points were uncorrected. IR spectra were recorded on a Horiba FT-300 infrared spectrophtometer. ^{1}H NMR spectra were recorded on a Hitachi R-1200 or JEOL JNR-EX270L spectrometer, and tetramethylsilane (TMS) served as internal standard. Preparative TLC was performed on Wakogel B5F. All reactions were carried out under argon atmosphere.

Dichloromethane was distilled from P_2O_5, then CaH_2, and stored over MS4Å.

Trimethylsilyl acetate was purchased from Aldrich. Other trimethylsilyl carboxylates were prepared from the corresponding carboxylic acids by the treatment with trimethylsilyl chloride and pyridine in dichloromethane, and were purified by distillation. 4-(Trifluoromethyl)benzoic anhydride was prepared by the literature method.[7]

Typical Experimental Procedure for the Acylation of *Weakly Nucleophilic Anilines* with Silyl Carboxylates. A typical experimental procedure is described for the reaction of trimethylsilyl 2,2-dimethylpropionate and 2-nitroaniline in the presence of a catalytic amount of active titanium(IV) salt generated from $TiCl_4$ and AgOTf; to a suspension of AgOTf (0.05 mmol) and $TiCl_4$ (0.025 mmol) in dichloromethane (2.0 ml), were added successively a mixture of 4-(trifluoromethyl)benzoic anhydride (0.275 mmol) and trimethylsilyl 2,2-dimethylpropionate (0.275 mmol) in dichloromethane (1.0 ml) and a solution of 2-nitroaniline (0.25 mmol) in dichloromethane (1.0 ml). The reaction mixture was kept stirring for an additional 20 h at room temperature, and then quenched with aq sat. $NaHCO_3$. After the usual work up, the crude product was purified by preparative TLC on silica gel to afford 2,2-dimethyl-2′-nitropropananilide (97% yield) with excellent chemoselectivity (>200/1).

The following spectroscopic data were observed for the substituted anilides (see Table 4).

2′-Nitroacetanilide (1). Mp 91—92 °C (Lit,[16] 92—93 °C); IR (KBr) 3371, 1699, 1514, 1342 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.30 (3H, s), 7.18 (1H, td, J=8.6, 1.3 Hz), 7.65 (1H, td, J=8.6, 1.3 Hz), 8.21 (1H, dd, J=8.6, 1.3 Hz), 8.77 (1H, dd, J=8.6, 1.3 Hz), 10.34 (1H, brs).

2-Methyl-2′-nitropropananilide (2). Mp 75—75.5 °C; IR (KBr) 3332, 1678, 1506, 1340 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.32 (6H, d, J=6.9 Hz), 2.66 (1H, m), 7.17 (1H, td, J=8.6, 1.3 Hz), 7.65 (1H, td, J=8.6, 1.6 Hz), 8.23 (1H, dd, J=8.6, 1.6 Hz), 8.83 (1H, dd, J=8.6, 1.3 Hz), 10.48 (1H, brs). Found: C, 57.43; H, 5.78; N, 13.39%. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.45%.

2,2-Dimethyl-2′-nitropropananilide (3). Mp 42 °C; IR (KBr) 3371, 1707, 1500, 1336 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.37 (9H, s), 7.17 (1H, td, J=8.6, 1.3 Hz), 7.65 (1H, td, J=8.6, 1.6 Hz), 8.24 (1H, dd, J=8.6, 1.6 Hz), 8.84 (1H, dd, J=8.6, 1.3 Hz), 10.75 (1H, brs). Found: C, 59.16; H, 6.17; N, 12.57%. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.61%.

2-Methyl-2′-nitrobenzanilide (4). Mp 114.5—115 °C; IR (KBr) 3369, 1689, 1502, 1338 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.57 (3H, s), 7.20—7.45 (4H, m), 7.61 (1H, d, J=6.6 Hz), 7.72 (1H, td, J=8.6, 1.6 Hz), 8.27 (1H, dd, J=8.6, 1.6 Hz), 8.97 (1H, dd, J=8.6, 1.3 Hz), 10.76 (1H, brs). Found: C, 65.67; H, 4.70; N, 10.89%. Calcd for $C_{14}H_{12}N_2O_3$: C, 65.62; H, 4.72; N, 10.93%.

3-Methyl-2′-nitrobutananilide (5). Mp 70.5—71 °C; IR (KBr) 3357, 1676, 1514, 1348 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.05 (6H, d, J=6.6 Hz), 2.25 (1H, m), 2.36 (2H, d, J=6.6 Hz), 7.18 (1H, td, J=8.6, 1.3 Hz), 7.65 (1H, td, J=8.6, 1.6 Hz), 8.23 (1H, dd, J=8.6, 1.6 Hz), 8.82 (1H, dd, J=8.6, 1.3 Hz), 10.35 (1H, brs). Found: C, 59.16; H, 6.23; N, 12.49%. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.61%.

2′-Nitro-3-phenylpropananilide (6). Mp 75 °C; IR (KBr) 3290, 1660, 1515, 1361 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.80 (2H, t, J=7.6 Hz), 3.08 (2H, t, J=7.6 Hz), 7.13—7.33 (6H, m), 7.63 (1H, td, J=8.6, 1.6 Hz), 8.18 (1H, dd, J=8.6, 1.6 Hz), 8.77 (1H, dd, J=8.6, 1.3 Hz), 10.28 (1H, brs). Found: C, 66.49; H, 5.19; N, 10.40%. Calcd for $C_{15}H_{14}N_2O_3$: C, 66.66; H, 5.22; N, 10.36%.

2′,4′-Dinitroacetanilide (7). Mp 121—122 °C (Lit,[17] 118.5—119 °C); IR (KBr) 3330, 1711, 1502, 1348 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.40 (3H, s), 8.48 (1H, dd, J=9, 2 Hz), 9.00—9.24 (2H, m), 10.75 (1H, brs).

2′,4′-Dinitro-2-methylpropananilide (8). Mp 97—97.5 °C; IR (KBr) 3350, 1701, 1498, 1351 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.32 (6H, d, J=7 Hz), 2.75 (1H, m), 8.48 (1H, dd, J=9, 2 Hz), 9.00—9.25 (2H, m), 10.80 (1H, brs). Found: C, 47.27; H, 4.34; N, 16.59%. Calcd for $C_{10}H_{11}N_3O_5$: C, 47.43; H, 4.38; N, 16.59%.

2′,4′-Dinitro-3-methylbutananilide (9). Mp 73 °C; IR (KBr) 3354, 1718, 1506, 1340 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.06 (6H, d, J=6 Hz), 1.93—2.60 (3H, m), 8.48 (1H, dd, J=9, 2 Hz), 9.00—9.24 (2H, m), 10.75 (1H, brs). Found: C, 49.36; H, 4.69; N, 15.70%. Calcd for $C_{11}H_{13}N_3O_5$: C, 49.44; H, 4.90; N, 15.72%.

2,2-Dimethyl-2′,4′-dinitropropananilide (10). Mp 106 °C; IR (KBr) 3369, 1709, 1508, 1340 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.40 (9H, s), 8.52 (1H, dd, J=9, 2Hz), 9.20—9.45 (2H, m), 11.20 (1H, brs). Found: C, 49.35; H, 4.82; N, 15.71%. Calcd for $C_{11}H_{13}N_3O_5$: C, 49.44; H, 4.90; N, 15.72%.

2′,4′-Dinitro-3-phenylpropananilide (11). Mp 147—148 °C; IR (KBr) 3338, 1709, 1500, 1352 cm^{-1}; ^{1}H NMR (CD_3OD–$CDCl_3$) δ=2.80—3.23 (4H, m), 7.30 (6H, brs), 8.50 (1H, dd, J=9, 2 Hz), 8.95—9.23 (2H, m). Found: C, 56.93; H, 4.22; N, 13.29%. Calcd for $C_{15}H_{13}N_3O_5$: C, 57.14; H, 4.16; N, 13.33%.

2′,4′-Dinitro-2-methylbenzanilide (12). Mp 165—166 °C; IR (KBr) 3377, 1695, 1504, 1342 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.58 (3H, s), 7.34—7.66 (4H, m), 8.54 (1H, dd, J=9.6, 2.6 Hz), 9.18 (1H, d, J=2.6 Hz), 9.29 (1H, d, J=9.6 Hz), 11.13 (1H, brs). Found: C, 55.76; H, 3.61; N, 13.89%. Calcd for $C_{14}H_{11}N_3O_5$: C, 55.82; H, 3.68; N, 13.95%.

4′-Chloro-2′-nitroacetanilide (13). Mp 99—100 °C(Lit,[18] 100—102 °C); IR (KBr) 3369, 1718, 1498, 1340 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.33 (3H, s), 7.62 (1H, dd, J=9, 2 Hz), 8.20 (1H, d, J=2 Hz), 8.82 (1H, d, J=9 Hz), 10.35

(1H, brs).

4′- Chloro- 2- methyl- 2′- nitropropananilide (14). Mp 90—90.5 °C; IR (KBr) 3369, 1689, 1504, 1336 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.30 (6H, d, J=7 Hz), 2.68 (1H, m), 7.26 (1H, dd, J=9, 2 Hz), 8.25 (1H, d, J=2 Hz), 8.90 (1H, d, J=9 Hz), 10.40 (1H, brs). Found: C, 49.35; H, 4.50; N, 11.53%. Calcd for $C_{10}H_{11}ClN_2O_3$: C, 49.50; H, 4.57; N, 11.54%.

4′-Chloro-3-methyl-2′-nitrobutananilide (15). Mp 83—83.5 °C; IR (KBr) 3379, 1703, 1500, 1344 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.03 (6H, d, J=6 Hz), 2.00—2.50 (3H, m), 7.60 (1H, dd, J=9, 2 Hz), 8.20 (1H, d, J=2 Hz), 8.83 (1H, d, J=9 Hz), 10.30 (1H, brs). Found: C, 51.32; H, 4.96; N, 10.89%. Calcd for $C_{11}H_{13}ClN_2O_3$: C, 51.47; H, 5.10; N, 10.91%.

4′-Chloro-2,2-dimethyl-2′-nitropropananilide (16). Mp 65—66 °C; IR (KBr) 3417, 1699, 1491, 1348 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.42 (9H, s), 7.70 (1H, dd, J=9, 2 Hz), 8.30 (1H, d, J=2 Hz), 8.98 (1H, d, J=9 Hz), 10.70 (1H, brs). Found: C, 51.45; H, 5.17; N, 10.83%. Calcd for $C_{11}H_{13}ClN_2O_3$: C, 51.47; H, 5.10; N, 10.91%.

4′- Chloro- 2′- nitro- 3- phenylpropananilide (17). Mp 145—146 °C; IR (KBr) 3379, 1707, 1506, 1342 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.60—3.30 (4H, m), 7.25 (5H, brs), 7.55 (1H, dd, J=9, 2 Hz), 8.20 (1H, d, J=2 Hz), 8.80 (1H, d, J=9 Hz), 10.20 (1H, brs). Found: C, 58.94; H, 4.30; N, 9.16%. Calcd for $C_{15}H_{13}ClN_2O_3$: C, 59.12; H, 4.30; N, 9.19%.

4′-Chloro-2-methyl-2′-nitrobenzanilide (18). Mp 152.5—153 °C; IR (KBr) 3371, 1689, 1500, 1338 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.56 (3H, s), 7.30—7.69 (5H, m), 8.25 (1H, d, J=2.6 Hz), 8.98 (1H, d, J=8.9 Hz), 10.69 (1H, brs). Found: C, 57.93; H, 3.77; N, 9.70%. Calcd for $C_{14}H_{11}ClN_2O_3$: C, 57.84; H, 3.81; N, 9.64%.

2′-Chloro-4′-nitroacetanilide (19). Mp 139—139.5 °C (Lit,[19] 139 °C); IR (KBr) 3300, 1685, 1504, 1352 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.32 (3H, s), 7.90—8.34 (3H, m), 8.70 (1H, d, J=9 Hz).

2′- Chloro- 2- methyl- 4′- nitropropananilide (20). Mp 107—107.5 °C; IR (KBr) 3315, 1674, 1506, 1344 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.32 (6H, d, J=7 Hz), 2.72 (1H, m), 7.90—8.34 (3H, m), 8.72(1H, d, J=9 Hz). Found: C, 49.30; H, 4.46; N, 11.52%. Calcd for $C_{10}H_{11}ClN_2O_3$: C, 49.50; H, 4.57; N, 11.54%.

2′-Chloro-3-methyl-4′-nitrobutananilide (21). Mp 86.5—87 °C; IR (KBr) 3292, 1682, 1508, 1348 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.08 (6H, d, J=6 Hz), 2.00—2.50 (3H, m), 7.90 (1H, brs), 8.04—8.40 (2H, m), 8.75 (1H, d, J=9 Hz). Found: C, 51.34; H, 4.97; N, 10.89%. Calcd for $C_{11}H_{13}ClN_2O_3$: C, 51.47; H, 5.10; N, 10.91%.

2′-Chloro-2,2-dimethyl-4′-nitropropananilide (22). Mp 97.5—98 °C; IR (KBr) 3425, 1699, 1506, 1346 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.38 (9H, s), 8.00—8.40 (3H, m), 8.73 (1H, d, J=9 Hz). Found: C, 51.31; H, 5.05; N, 10.90%. Calcd for $C_{11}H_{13}ClN_2O_3$: C, 51.47; H, 5.10; N, 10.91%.

2′- Chloro- 4′- nitro- 3- phenylpropananilide (23). Mp 105—106 °C; IR (KBr) 3408, 1720, 1498, 1346 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.60—3.30 (4H, m), 7.30 (5H, brs), 7.84 (1H, brs), 8.04—8.40 (2H, m), 8.74 (1H, d, J=9 Hz). Found: C, 59.33; H, 4.29; N, 9.18%. Calcd for $C_{15}H_{13}ClN_2O_3$: C, 59.12; H, 4.30; N, 9.19%.

2'-Chloro-2-methyl-4′-nitrobenzanilide (24). Mp 126—126.5 °C; IR (KBr) 3413, 1705, 1508, 1348 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.57 (3H, s), 7.31—7.60 (4H, m), 8.23 (1H, dd, J=8.9, 2.6 Hz), 8.31 (1H, brs), 8.34 (1H, d, J=2.6 Hz), 8.87 (1H, d, J=8.9 Hz). Found: C, 57.87; H, 3.72; N, 9.60%. Calcd for $C_{14}H_{11}ClN_2O_3$: C, 57.84; H, 3.81; N, 9.64%.

2′,4′,6′-Trichloroacetanilide (25). Mp 210 °C (Lit,[20] 207 °C); IR (KBr) 3224, 1654 cm^{-1}; ^1H NMR ($CDCl_3$) δ= 2.24 (3H, s), 6.98 (1H, s), 7.39 (2H, s).

2-Methyl-2′,4′,6′-trichloropropananilide (26). Mp 152—152.5 °C; IR (KBr) 3240, 1674 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.30 (6H, d, J=6.9 Hz), 2.65 (1H, m), 6.90 (1H, s), 7.38 (2H, s). Found: C, 44.85; H, 3.70; N, 5.28%. Calcd for $C_{10}H_{10}Cl_3NO$: C, 45.06; H, 3.78; N, 5.25%.

3-Methyl-2′,4′,6′-trichlorobutananilide (27). Mp 146—146.5 °C; IR (KBr) 3242, 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.06 (6H, d, J=6.3 Hz), 2.16—2.32 (3H, m), 6.90 (1H, s), 7.38 (2H, s). Found: C, 46.91; H, 4.26; N, 4.93%. Calcd for $C_{11}H_{12}Cl_3NO$: C, 47.09; H, 4.31; N, 4.99%.

2,2-Dimethyl-2′,4′,6′-trichloropropananilide (28). Mp 166—166.5 °C; IR (KBr) 3240, 1664 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.36 (9H, s), 7.08 (1H, s), 7.38 (2H, s). Found: C, 47.12; H, 4.35; N, 5.01%. Calcd for $C_{11}H_{12}Cl_3NO$: C, 47.09; H, 4.31; N, 4.99%.

3-Phenyl-2′,4′,6′-trichloropropananilide (29). Mp 170—170.5 °C; IR (KBr) 3230, 1672 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.77 (2H, t, J=7.6 Hz), 3.09 (2H, t, J=7.6 Hz), 6.78 (1H, s), 7.19—7.34 (5H, m), 7.37 (2H, s). Found: C, 54.92; H, 3.57; N, 4.24%. Calcd for $C_{15}H_{12}Cl_3NO$: C, 54.82; H, 3.68; N, 4.26%.

2-Methyl-2′,4′,6′-trichlorobenzanilide (30). Mp 164.5—165 °C; IR (KBr) 3242, 1657 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.54 (3H, s), 7.26—7.39 (4H, m), 7.43 (2H, s), 7.61 (1H, d, J=7.3 Hz). Found: C, 53.55; H, 3.29; N, 4.47%. Calcd for $C_{14}H_{10}Cl_3NO$: C, 53.45; H, 3.20; N, 4.45%.

^1H NMR Experiment Procedure for Reaction Pathway. To a suspension of $Sn(OTf)_2$ (0.01 mmol) in dichloromethane-d_2 (1.0 ml), was added a mixture of 4-(trifluoromethyl)benzoic anhydride (0.10 mmol) and trimethylsilyl acetate (0.10 mmol) in dichloromethane-d_2 (1.0 ml). The singlet at δ=2.36 corresponding to the acyloxy group of the mixed anhydride (**31**) and the singlet at δ=2.17 corresponding to acyloxy group of acetic anhydride were observed (the mole ratio of **31**/acetic anhydride=1/1).

Acetic 4-(Trifluoromethyl)benzoic Anhydride (31). ^1H NMR (CD_2Cl_2) δ=2.36 (3H, s), 7.75 (2H, d, J=8.3 Hz), 8.20 (2H, d, J=8.3 Hz).

References

1) B. M. Trost and I. Fleming, "Comprehensive Organic Synthesis," ed by G. Benz, Pergamon Press, Oxford (1991), Vol. 6, p. 381.

2) S. V. Ley and P. R. Woodward, *Tetrahedron Lett.*, **28**, 3019 (1987).

3) C. S. Rao, M. Rambabu, and P. S. Srinivasan, *Indian J. Chem., Sect. B*, **26B**, 407 (1987).

4) Preliminary communication: M. Miyashita, I. Shiina, and T. Mukaiyama, *Chem. Lett.*, **1993**, 1053.

5) T. Mukaiyama, M. Katsurada, and T. Takashima, *Chem. Lett.*, **1991**, 985; K. Matsubara and T. Mukaiyama, *Chem. Lett.*, **1993**, 581.

6) T. Harada, T. Ohno, S. Kobayashi, and T. Mukaiyama, *Synthesis*, **1991**, 1216.
7) T. Mukaiyama, I. Shiina, and M. Miyashita, *Chem. Lett.*, **1992**, 625; M. Miyashita, I. Shiina, S. Miyoshi, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **66**, 1516 (1993).
8) T. Mukaiyama and K. Matsubara, *Chem. Lett.*, **1992**, 1755.
9) T. Mukaiyama, M. Katsurada, and Y. Iida, *Chem. Lett.*, **1992**, 2105.
10) T. Harada and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **66**, 882 (1993); T. Mukaiyama and K. Suzuki, *Chem. Lett.*, **1993**, 1.
11) T. Mukaiyama, M. Miyashita, and I. Shiina, *Chem. Lett.*, **1992**, 1747.
12) T. Mukaiyama and K. Suzuki, *Chem. Lett.*, **1992**, 1751.
13) I. Shiina and T. Mukaiyama, *Chem. Lett.*, **1992**, 2319.
14) T. Mukaiyama and N. Shimomura, *Chem. Lett.*, **1993**, 781.
15) T. Mukaiyama, J. Izumi, M. Miyashita, and I. Shiina, *Chem. Lett.*, **1993**, 907.
16) L. F. Fieser and E. L. Martin, *J. Am. Chem. Soc.*, **57**, 1835 (1935).
17) A. Kijima and S. Sekiguchi, *J. Chem. Soc., Perkin Trans. 2*, **1987**, 1203.
18) T. Shepherd and D. M. Smith, *J. Chem. Soc., Perkin Trans. 1*, **1987**, 501.
19) F. Beilstein and A. Kurbatow, *Justus Liebigs Ann. Chem.*, **182**, 94 (1876).
20) N. R. Ayyangar and K. V. Srinivasan, *Can. J. Chem.*, **62**, 1292 (1984).