

Decarbonylative Diarylation Reaction of *N*-Substituted α -Amino Acids

Mi Ra Seong, Tae Yi Kim, Hong Jung Lee, and Jae Nyoung Kim*

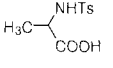
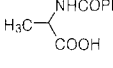
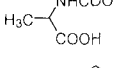
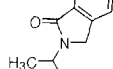
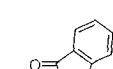
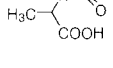
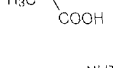
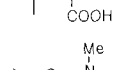
Department of Chemistry, Chonnam National University, Kwangju 500-757, Korea

Received February 22, 1999

Recently, we have reported on the Friedel-Crafts type reaction of arenes with various kinds of nitrogen containing compounds such as 1,3-dicyclohexylcarbodiimide and sulfonamides.¹ Application of the above reaction to *N*-tosylated α -amino acids results in decarbonylative diarylation reaction to give the corresponding diarylated derivatives in moderate to good yields.² In the reactions we did neither alter the *N*-substituent nor optimize the conditions. Thus, we intended to examine the effects of *N*-substituent on the reaction and report herein the results.

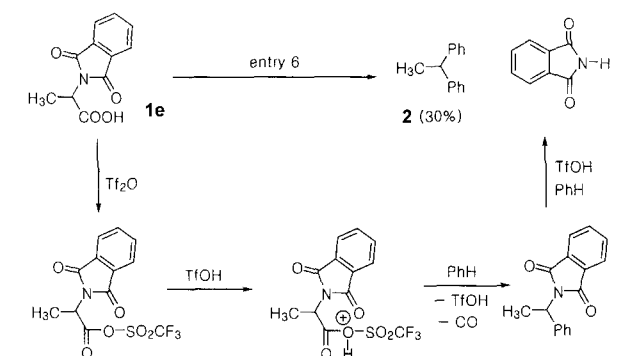
As shown in Table 1, we examined the reaction of *N*-substituted alanine derivatives **1a-f** and three leucine derivatives **1g-i** in the presence of sulfuric acid with benzene as a representative arene nucleophile.

Table 1. Effects of *N*-substituent in the decarbonylative diarylation reaction

Entry	Substrate (1)	Conditions	Product (yield)
1	 (1a)	H ₂ SO ₄ (3 equiv) 60–70 °C, 7 h	 (2, 74%) ^{2a}
2	 (1b)	H ₂ SO ₄ (5 equiv) 60–70 °C, 20 h	no reaction
3	 (1c)	H ₂ SO ₄ (3 equiv) 60–70 °C, 7 h	2 (41%)
4	 (1d)	H ₂ SO ₄ (5 equiv) 60–70 °C, 12 h	no reaction
5	 (1e)	H ₂ SO ₄ (3 equiv) 60–70 °C, 7 h	no reaction
6	1e	Ti ₂ O (1.5 equiv) 60–70 °C, 15 h	2 (30%)
7	 (1f)	H ₂ SO ₄ (3 equiv) 60–70 °C, 4 h	 (3, 82%)
8	 (1g)	H ₂ SO ₄ (3 equiv) 60–70 °C, 7 h	 (4, 68%) ^{2a}
9	 (1h)	H ₂ SO ₄ (3 equiv) 60–70 °C, 7 h	4 (32%)
10	 (1i)	H ₂ SO ₄ (3 equiv) 60–70 °C, 7 h	4 (39%)

By using the *N*-tosyl derivative **1a**, 1,1-diphenylethane (**2**) was obtained in 74% yield as reported.^{2a} However, we could not isolate or detect any arylated compounds in the cases of **1b**, **1d**,^{3a} and **1e**.^{3b} In the case of ethoxycarbonyl derivative **1c**, **2** was obtained in 41%. Urea derivative **1f** gave *N*-phenyl-4-methylimidazolidine-2,5-dione (**3**) in 82% yield instead of **2** via the intramolecular amide bond formation. As mentioned above, **2** was not obtained from **1e** by using sulfuric acid, however, we could obtain **2** in 30% yield by trifluoromethanesulfonic anhydride via the mixed carboxylic sulfonic anhydride as shown in Scheme 1.^{2,4}

The differences in reactivity between the sulfonyl derivative **1a** and the carbonyl derivatives **1b-e** might be explained as follows. As shown in Figure 1, the non-bonding electrons on nitrogen atom of **A** (protonated sulfonyl derivative **1a**)



Scheme 1

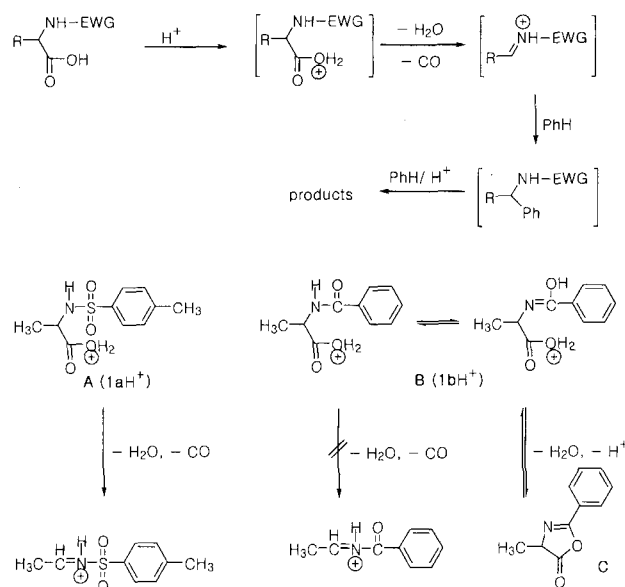


Figure 1

are less delocalized than those of **B** (protonated **1b** as an example of carbonyl derivatives) due to insufficient overlap between *N* and *S* atom,⁵ and consequently are more available to trigger the elimination of water and carbon monoxide from **A**. Thus, the corresponding reactive intermediate, viz *N*-tosylimminium salt, could be generated much more efficiently in the case of *N*-tosyl α -amino acids, and subsequently the decarbonylative diarylation could be conducted via the imminium salt. In the case of benzoyl derivative **1b**, formation of oxazolinone derivative **C** might be the more preferable pathway than the formation of *N*-acylimminium salt.⁶

As shown in entries 9-10, *N*-methyl-*N*-tosyl leucine (**1h**) or ethyl ester derivative **1i** gave the corresponding product **4** with diminished yields as compared with **1g** (entry 8).

In this report we could conclude that in the decarbonylative diarylation reaction of *N*-substituted α -amino acids, tosyl group is the best *N*-substituent of choice.

Experimental Section

The starting materials **1a-c**, and **1f** were prepared from L-alanine by using *p*-toluenesulfonyl chloride, benzoyl chloride, ethyl chloroformate, phenyl isocyanate respectively according to the normal experimental procedures. **1d-e** were synthesized by phthalic dicarboxaldehyde and *N*-carboxyphthalimide respectively by using the literature methods.³ **1g** was synthesized from L-leucine as in the case of **1a**. **1h** was prepared from **1g** by *N,N*-dimethylformamide dimethylacetal in good yield. **1i** was prepared from **1g** by bromoethane and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile.

General procedure. To a stirred suspension of **1** (1 mmol) in dry benzene (5 mL) was added sulfuric acid (0.3-0.5 g, 3-5 mmol) and stirred vigorously at 60-70 °C for the time indicated in Table 1. The reaction mixture was poured into cold water and extracted with ethyl acetate. The organic layers were washed with water, dried with MgSO₄, evaporated to dryness to obtain crude products. After flash column chromatography we could obtain analytically pure products. Physicochemical data of **2-4** was as follows.

2: yellow oil; ¹H NMR (CDCl₃) δ 1.55 (d, *J* = 7.2 Hz, 3H), 4.06 (q, *J* = 7.2 Hz, 1H), 7.06-7.21 (m, 10H); ¹³C NMR

(CDCl₃) δ 21.83, 44.76, 125.99, 127.60, 128.33, 146.35; MS (70 eV) *m/z* (rel intensity) 77 (23), 149 (22), 152 (21), 164 (52), 167 (100), 182 (M⁺, 37).

3: white solid; mp 169-171 °C; ¹H NMR (DMSO-d₆) δ 1.35 (d, *J* = 7.0 Hz, 3H), 4.25 (q, *J* = 7.0 Hz, 1H), 7.31-7.49 (m, 5H), 8.45 (s, 1H); ¹³C NMR (DMSO-d₆) δ 17.20, 52.03, 126.68, 127.65, 128.65, 132.22, 155.34, 174.05; MS (70 eV) *m/z* (rel intensity) 41 (32), 64 (75), 77 (24), 91 (100), 119 (71), 190 (M⁺, 5).

4: yellow oil; ¹H NMR (CDCl₃) δ 0.91 (d, *J* = 6.6 Hz, 6H), 1.37-1.51 (m, 1H), 1.92 (app t, *J* = 7.5 Hz, 2H), 4.01 (t, *J* = 8.0 Hz, 1H), 7.11-7.31 (m, 10H); ¹³C NMR (CDCl₃) δ 22.64, 25.53, 45.05, 48.90, 125.98, 127.88, 128.37, 145.30; MS (70 eV) *m/z* (rel intensity) 91 (7), 152 (10), 165 (21), 167 (100), 168 (15), 224 (M⁺, 20).

Acknowledgment. We wish to thank the Chonnam National University Research Foundation for financial support of this work.

References

- (a) Kim, J. N.; Chung, K. H.; Ryu, E. K. *Tetrahedron Lett.* **1994**, 35, 903. (b) Chung, K. H.; Kim, J. N.; Ryu, E. K. *Tetrahedron Lett.* **1994**, 35, 2913. (c) Lee, H. J.; Seong, M. R.; Kim, J. N. *Tetrahedron Lett.* **1998**, 39, 6223.
- (a) Seong, M. R.; Lee, H. J.; Kim, J. N. *Tetrahedron Lett.* **1998**, 39, 6219. (b) Seong, M. R.; Song, H. N.; Kim, J. N. *Tetrahedron Lett.* **1998**, 39, 7101.
- (a) Adriaens, P.; Meesschaert, B.; Dumon, J. L.; Eyssen, H. *Reac. Trav.* **1978**, 97, 260. (b) Allin, S. M.; Hodgkinson, C. C.; Taj, N. *Synlett* **1996**, 781.
- (a) Yamato, T.; Hideshima, C.; Prakash, G. K. S.; Olah, G. A. *J. Org. Chem.* **1991**, 56, 3955. (b) Hulin, B.; Koreeda, M. *J. Org. Chem.* **1984**, 49, 207. (c) Keumi, T.; Yoshimura, K.; Shimada, M.; Kitajima, H. *Bull. Chem. Soc. Jpn.* **1988**, 61, 455. (d) Effenberger, F.; Sohn, E.; Epple, G. *Chem. Ber.* **1983**, 116, 1195.
- March, J. *Advanced Organic Chemistry*; John Wiley & Sons: 1992; pp 38-40.
- (a) McClure, D. E.; Arison, B. H.; Jones, J. H.; Baldwin, J. J. *J. Org. Chem.* **1981**, 46, 2431. (b) Buckley, T. F.; Rapoport, H. *J. Am. Chem. Soc.* **1981**, 103, 6157. (c) Allinger, N. L.; Wang, G. L.; Dewhurst, B. B. *J. Org. Chem.* **1974**, 39, 1730. (d) Itoh, O.; Honnami, T.; Amano, A.; Murata, K.; Koichi, Y.; Sugita, T. *J. Org. Chem.* **1992**, 57, 7334.