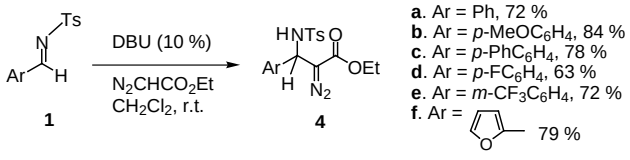
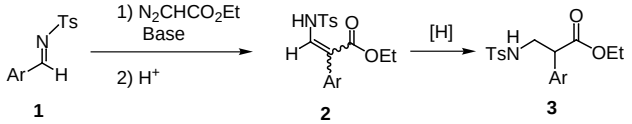


Scheme 2

In our previous investigation, the α-diazo carbonyl compounds are decomposed with Rh(II) or copper catalysts to give α-aryl-β-enamino esters (Scheme 3).[8]

Scheme 3

-Aryl β-amino acids have been found in a number of biologically important natural products. For example, (*S*)-3-Amino-2-phenylpropionic acid is the side chain of taxol, and its ethyl ester is the side chain of docetaxel derivative.[6] The synthesis of α-aryl β-amino acids and their derivatives are particularly challenging and there are only few methods now available.[7] In this communication, we report an efficient approach to the synthesis of this type of β-amino acid derivatives through *p*-toluenesulfonic acid (TsOH) catalyzed 1,2-aryl migration of α-diazo carbonyl compounds, as shown in Scheme 1.



Scheme 1

We have recently reported that the α-diazo carbonyl compounds **4a–f** can be prepared by nucleophilic addition of diazo ethylacetate (EDA) anion to the *N*-tosyl protected imine **1**.[8] The EDA anion was generated through deprotonation by lithium diisopropylamide (LDA) or NaH. In the later investigation, we find that this nucleophilic addition can be promoted by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) under catalytic condition. The reaction condition is milder and the yields are moderate to good (Scheme 2).

We now find that the α-diazo carbonyl compounds, which are in general quite stable at room temperature, can be efficiently decomposed at 0 °C with catalytic TsOH (~ 1 mol%).[9] As in the reaction with Rh(II) or copper catalysts, the 1,2-aryl products are predominate in all cases (Table). However, in Rh(II) or Cu(I) catalyzed reaction, *trans* α-aryl-β-enamino esters are predominant, while the TsOH promoted reaction gave predominately *cis* products. The *cis* isomer is more stable than the *trans* isomer because of the intramolecular hydrogen bonding. We have observed

somerize to their *cis* isomer in
e it is likely that the predomi-
roducts under TsOH catalysis
d-catalyzed isomerization dur-
is point, the diazo decomposi-
ut with 10% TsOH at room
the ratio of the *cis* to *trans* in-
.

ted to be easily reduced to the
ers with $NaBH(OAc)_3$.[10] How-
esters obtained in our investi-
$NaBH(OAc)_3$ under identical
d, the *cis* and *trans* mixture of
–**f** and **6a**–**f** can be easily con-
sters by hydrogenation with 1
e catalyst (Scheme 4).[11,12]

ryl migration, we can propose
sm. The diazo compound was
gatively polarized carbon to
ached, following the extrusion
ctive α-carbonyl cation. The
migrates through a bridged

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o esters. Efforts toward the
ly pure α-aryl-β-amino esters
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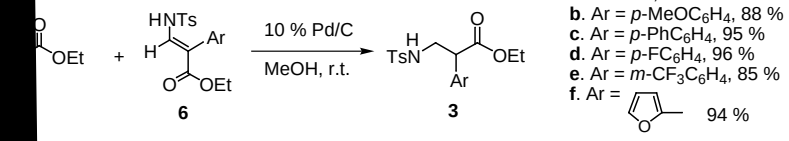
ted by Natural Science Foundation



e 5

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(9) **General procedure for the TsOH catalyzed diazo decomposition:** To a solution of TsOH (1 mg) in anhydrous CH_2Cl_2 (20 mL) at 0 °C under N_2, was added dropwise a solution of diazo compound in anhydrous CH_2Cl_2 (5 mL). The reaction was complete within 30 min as indicated by TLC check. Solvent was removed by evaporation, and the residue was purified by flash column chromatography to give *cis* and *trans* α-aryl-β-enamino esters as a mixture.

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(11) **General procedure for the hydrogenation of α-aryl-β-enamino esters:** To a solution of α-aryl-β-enamino esters (50 mg, *cis* and *trans* mixture) in absolute MeOH (25 mL) was added 10% Pd/C catalyst (10 mg). The reaction mixture was stirred for 10 h under 1 atm hydrogen atmosphere. Then catalyst was removed by filtration and solvent was evaporated to give a residue, which was purified by flash column chromatography.
3a: ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.13 (t, 3 H), 2.36 (s, 3 H), 3.19–352 (m, 2 H), 3.79–3.86 (q, 1 H), 4.04–4.17 (m, 2 H), 5.13 (t, 1 H), 7.13 (m, 7 H), 7.72 (d, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 13.88, 21.42, 45.62, 51.72, 61.27, 126.91,

127.82, 127.84, 128.88, 129.68, 135.63, 136.86, 143.40, 172.34; MS *m/z* (relative intensity): 347 (M^+, 17%), 118 (100%).

3b: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18 (t, 3H), 2.42 (s, 3 H), 3.16–3.50 (m, 2H), 3.77–3.81 (m, 1 H), 3.79 (s, 3H), 4.04–4.17 (m, 2 H), 5.07 (t, 1 H), 6.83 (d, 2 H), 7.06 (d, 2 H), 7.29 (d, 2 H), 7.72 (d, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 13.90, 21.41, 45.67, 50.82, 55.14, 61.18, 114.25, 126.91, 127.60, 128.90, 129.65, 136.90, 143.36, 159.14, 172.56; MS *m/z* (relative intensity): 377 (M^+, 10%), 194 (100%).

3c: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.19 (t, 3 H), 2.39 (s, 3 H), 3.21–3.55 (m, 2 H), 3.84–3.91(q, 1 H), 4.04–4.20 (m, 2 H), 5.07 (t, 1 H), 7.20–7.57 (m, 1 1H), 7.71 (d, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 13.96, 21.45, 45.65, 51.40, 61.39, 126.95, 127.45, 127.60, 128.30, 129.71, 134.60, 136.89, 140.26, 140.82, 143.45, 172.36. *m/z* (relative intensity): 423 (M^+, 11%), 240 (100%).

3d: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.17 (t, 3 H), 2.42 (s, 3 H), 5. (t, 1 m0 6.92–7.30 (m, 6 m0 7.70 (d0 2 m; ^{13}C NMR (50 MHz, $CDCl_3$): δ 13.87, 21.41, 45.57, 50.92, 61.37, 115.55, 115.98, 126.89, 129.44, 129.60, 129.69, 136.79, 143.47, 172.19. *m/z*