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An efficient synthesis of α-aryl β-(*N*-tosyl)ami derivatives from α-diazophosphonat

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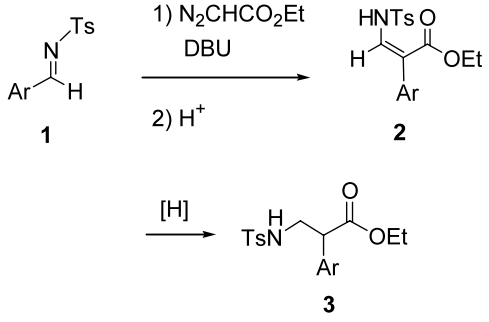
Abstract—The α-diazophosphonate was added to aryl (*N*-tosyl)imine to give β-aryl β-(*N*-tosyl)amino α-diazophosphonates, which were further subjected to TsOH-catalyzed diazo decomposition to yield α-aryl β-(*N*-tosyl)enaminophosphonates through 1,2 aryl migration. The α-aryl β-(*N*-tosyl)enamino phosphonates were hydrogenated to give α-aryl β-(*N*-tosyl)amino phosphonates.

α- Or β-amino phosphonic acid derivatives have attracted considerable attention in recent years because of their involvement in certain biologically important processes.[1] For example, amino phosphonic acid derivatives have been served as the transition state analog in drug design and as haptens in the development of catalytic antibody enzymes.[2] Consequently, it is desirable to develop efficient approach to synthesize racemic or optically active amino phosphonates.[1a,3]

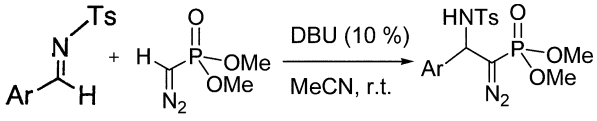
We have recently reported the based-catalyzed addition of ethyl diazoacetate to aryl (*N*-tosyl)imines **1** and the subsequent 1,2 aryl migration reaction of the resulting β-(*N*-tosyl)amino α-diazo carbonyl products under Rh(II) complex- or TsOH-catalysis condition.[4] This two-step reaction sequence transforms ethyl diazoacetate to α-aryl β-(*N*-tosyl)enamino esters **2**, which can be further hydrogenated to give α-aryl β-(*N*-tosyl)amino esters **3** (Scheme 1).[5] We conceived that this highly efficient reaction sequence may be similarly applied to the corresponding α-diazophosphonate to give the corresponding β-amino phosphonate derivatives. The results of our investigation are described herein.



1 **2** **3**

Scheme 1.

The α-diazophosphonate **4** was prepared according to the literature procedure.[6] The DBU-catalyzed addition of α-diazophosphonate **4** to aryl *N*-tosylimine **1a**–**g** was carried out at room temperature and the β-aryl β-(*N*-tosyl)amino α-diazophosphonates **5a**–**g** were obtained in 54–89% isolated yields (Scheme 2).[7]



1 **4** **5a-g**

a Ar = C_6H_5, 75 %
b Ar = *p*-ClC_6H_4, 76 %
c Ar = *p*-FC_6H_4, 52 %
d Ar = *p*-$MeOC_6H_4$, 65 %
e Ar = 4-Ph-C_6H_4, 54 %
f Ar = *m*-$CF_3C_6H_4$, 89 %
g =  , 79 %

Scheme 2.

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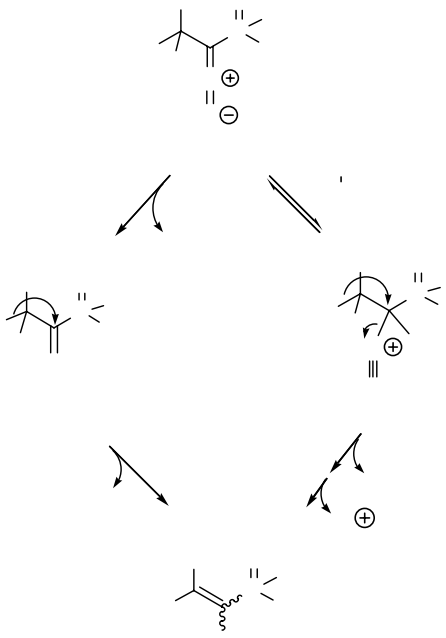

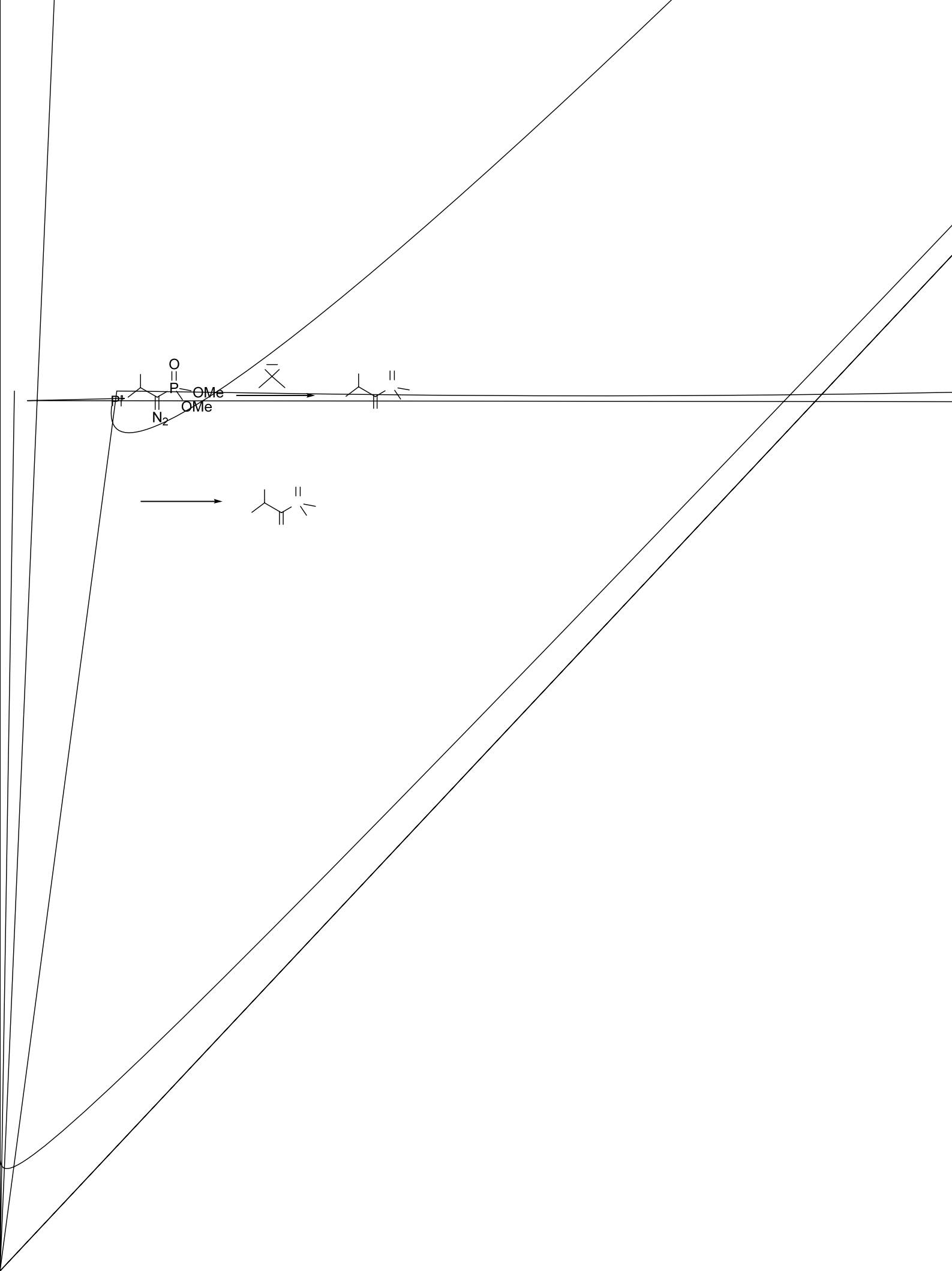
O
P
OMe
OMe
Pt
N2

9. **General procedure for the hydrogenation of α-aryl β-enaminophosphonates 8a–g**. To a solution of α-aryl β-enaminophosphonate (0.1 mmol) in absolute MeOH (15 mL) was added 10% Pd/C catalyst (10 mg). The reaction mixture was stirred for 24 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. Dimethyl[1-(*p*-phenylphenyl)-2-(*N*-tosylamino)ethyl]phosphonate (**12e**): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.43–3.52 (m, 1H), 3.54 (d, $J_{HP}=8.4$ Hz, 3H), 3.67 (d, $J_{HP}=11.4$, 1H), 5.28 (t, $J=9.0$ Hz, 1H), 6.90–7.80 (m, 14H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.4, 42.8 (d, $J_{CP}=45.2$ Hz), 45.1, 52.9 (d, $J_{CP}=7.2$ Hz), 53.6 (d, $J_{CP}=6.8$ Hz), 126.9, 127.5, 127.5, 127.9, 129.4, 129.5, 129.7, 129.9, 136.9, 140.2, 140.7, 143.4; IR (film): ν 2954, 1607 cm^{-1}. Anal. calcd for $C_{23}H_{26}NO_5PS$: C, 60.12; H, 5.70; N, 3.05. Found: C, 60.09; H, 5.62; N, 2.83.