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Phosphine-Catalyzed [3+2] Cycloaddition Reaction of Methyl 2,3-Butadienoate and *N*-Tosylimines. A Novel Approach to Nitrogen Heterocycles

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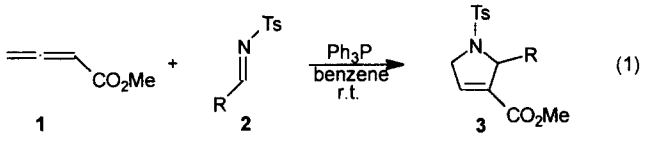
Abstract: In the presence of a catalytic amount of triphenylphosphine, methyl 2,3-butadienoate smoothly reacted with aromatic or heteroaromatic *N*-tosylimines at room temperature to afford the [3+2] cycloaddition product in excellent yield. © 1997 Elsevier Science Ltd.

Cycloaddition reaction has been one of the important methods in synthetic organic chemistry. Among them, the [3+2] cycloaddition including the thermal and transition metal mediated cycloadditions is an efficient strategy for the construction of the five-membered ring systems directly from simple building blocks, because two carbon-carbon bonds are formed in a single operation.[1,2] Recently, our discovery of a new three carbon synthon, generated *in situ* from the reaction of 2,3-butadienoates or 2-butynoates with an appropriate phosphine as the catalyst[3] stimulates us to explore its reaction to other dipolarophiles. Among them, *N*-tosylimines which are readily synthesized from the corresponding aldehydes[4] and exhibit a highly reactive carbon-nitrogen double bond, have been successfully applied in cycloaddition reactions.[5] Herein, we report the preliminary results of triphenylphosphine-catalyzed reaction of methyl 2,3-butadienoate with *N*-tosylimines.

Treatment of methyl 2,3-butadienoate (**1**, 1.1 mmol) with *N*-toluenesulfonyl benzaldimine (**2a**, 1.0 mmol) in the presence of triphenylphosphine (0.1 mmol) in dry benzene at room temperature gave **3a** as the sole product in nearly quantitative yield (eq 1).



1 2 3 (1)

Unlike the reaction of 2,3-butadienoates with electron-deficient olefins,[3] the reaction of **1** with aromatic *N*-tosylimines (**2b-2h**) in the presence of a catalytic amount of triphenylphosphine all afforded the single cycloaddition product (**3b-3h**), respectively, in excellent yield and high chemoselectivity (Table 1).[6] Indeed, aryl imines with both electron-releasing and electron-withdrawing groups all gave satisfactory results. The reaction of **1** with a α,β-unsaturated *N*-tosylimine, *N*-toluenesulfonyl cinnamaldimine (**2i**), also gave the normal [3+2] cycloaddition product **3i** in 53% yield (34% of **2i** was recovered). However, under the same conditions, treatment of **1** with *N*-toluenesulfonyl 2-furaldimine (**2j**) furnished two cycloaddition

Table 1. Triphenylphosphine-Catalyzed Cycloaddition of Methyl 2,3-Butadienoate with *N*-Tosylimines[a]

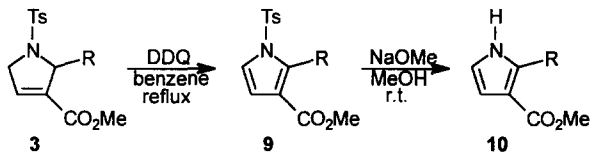
	imine		product	
entry	**2**	R	**3**	yield[b] (%)
1	**2a**	phenyl	**3a**	98
2	**2b**	o-methoxyphenyl	**3b**	96
3	**2c**	p-methoxyphenyl	**3c**	98
4	**2d**	p-methylphenyl	**3d**	98
5	**2e**	p-chlorophenyl	**3e**	97
6	**2f**	p-nitrophenyl	**3f**	88
7	**2g**	piperonyl	**3g**	98
8	**2h**	1-naphthyl	**3h**	98
9	**2i**	cinnamyl	**3i**	53[c]
10	**2j**	2-furyl	**3j**	83[d]
11	**2k**	2-methyl-4-pentenyl	**3k**	trace

[a] Reaction conditions: A mixture of **1** (1.1 mmol), **2** (1.0 mmol), and Ph_3P (0.1 mmol) in dry benzene at rt. [b] Isolated yield. [c] 34% of **2i** was recovered. [d] Another adduct **4j**, methyl 4,5-dihydro-5-furyl-1-tosyl-1*H*-pyrrole-2-carboxylate, was isolated in 15% yield.

products, **3j** and **4j** (85:15), in excellent overall yield. When aliphatic *N*-tosylimine (**2k**) was used, a mere trace of **3k** was detected due to the low reactivity of **2k** and self cycloaddition of **1**.[7] The nitrogen nucleophiles such as DABCO and DMAP could not catalyze this reaction.

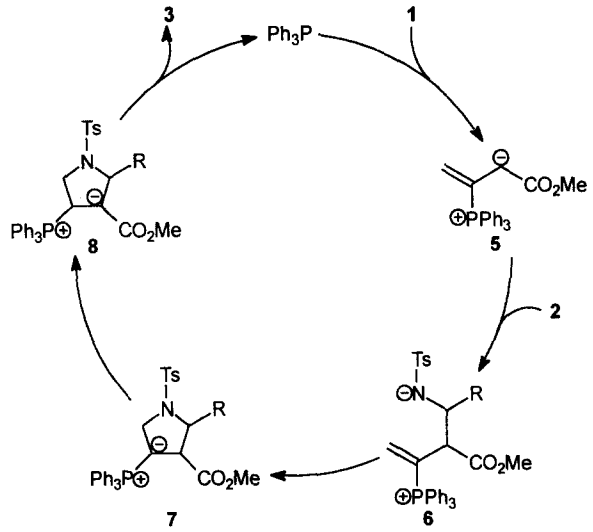
A proposed mechanism of the reaction is outlined in Scheme 1. First, triphenylphosphine as the nucleophilic trigger attacks the β-carbon atom of the allene **1** to generate the reactive dipolar intermediate **5**, which is trapped by the dipolarophilic imine **2** to form an open chain intermediate **6**. Subsequent intramolecular nucleophilic addition gives the intermediate **7**. Finally, the intermediate **8** formed by the hydrogen transfer of **7** affords the cycloadduct **3** along with the regeneration of triphenylphosphine as the catalytic species. Compound **4j** might be formed due to the lower reactivity of **2j** which could not react with **5** quickly enough to prohibit the transformation of **5** to the delocalized structure **5'** (Scheme 2).[8]

To further confirm the structure of the cycloaddition product and to develop a new route to 2-aryl-1*H*-pyrrole-3-carboxylates, we carried out the aromatization of the cycloadduct using DDQ as the oxidant followed by treatment with sodium methoxide in methanol to eliminate p-toluenesulfonyl group (eq 2).

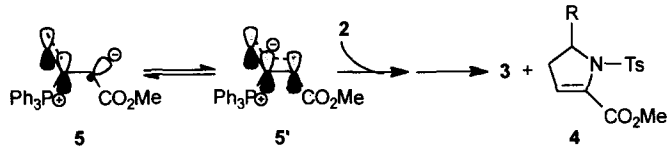


3 **9** **10** (2)

Heating the mixture of the cycloadduct, **3a-b**, **3e**, or **3g-h**, and DDQ (1.5-2.0 equivs) in dry benzene at *ca.* 130 °C for about 2 to 3 days until the starting material completely disappeared as monitored by TLC, gave the dehydrogenation product, **9a-b**, **9e**, or **9g-h**, respectively, in moderate to good yields (Table 2).[9,10] Subsequent detosylation of **9** by using sodium methoxide produced the N-H pyrrole **10** in excellent yield. This provides a new synthetic method of 2-aryl-1*H*-pyrrole-3-carboxylates. Surprisingly, aromatization of **3j** gave the defurylated product (**9**, R = H) in 14% yield.[11]



Scheme 1



Scheme 2

Table 2. Preparation of 2-aryl-1*H*-pyrrole-3-carboxylates

		equiv of	reaction	product			
entry	**3**	DDQ	time, d	**9**	%yield[a]	**10**	%yield[a]
1	**3a**	2.0	1.5	**9a**	92	**10a**	86
2	**3b**	1.5	2.5	**9b**	81	**10b**	92
3	**3e**	1.5	2	**9e**	95	**10e**	88
4	**3g**	2.0	3	**9g**	38	**10g**	87
5	**3h**	1.5	2	**9h**	97	**10h**	95

[a] Isolated Yield.

In conclusion, we present a novel [3+2] cycloaddition approach to nitrogen heterocycles *via* triphenylphosphine-catalyzed reaction of methyl 2,3-butadienoate with *N*-tosylimines. This method is particularly successful to aromatic and heteroaromatic *N*-tosylimines due to their suitable reactivities. In addition, we have developed a convenient systhesis of 2-aryl-1*H*-pyrrole-3-carboxylates on the basis of this [3+2] cycloaddition, dehydrogenation and subsequent removal of tosyl group. The investigation of the appropriate dipolarophiles and the synthetic utilization on the three carbon synthon is in progress.

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6. All new compounds are fully characterized by spectral and elemental analyses or HRMS. Data for **3a**: mp 109-110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.42 (d, J = 8.2 Hz, 2H), 7.23 (s, 5H), 7.14 (d, J = 8.2 Hz, 2H), 6.77 (q, J = 1.9 Hz, 1H), 5.75 (dt, J = 5.7, 1.9 Hz, 1H), 4.53 (dt, J = 17.1, 2.4 Hz, 1H), 4.37 (ddd, J = 17.1, 5.7, 1.9 Hz, 1H), 3.58 (s, 3H) and 2.36 (s, 3H); IR (KBr) cm^{-1} 1726, 1648, 1341, 1275, 1159, 1107 and 673; MS *m/z*(%): 357 (M^+, 3.89), 326 (M^+-OMe, 2.27), 298 (M^+-CO_2Me, 13.56), 280 (M^+-Ph, 42.20), 202 (M^+-Ts, 68.89), 170 (M^+-Ts-OMe-H, 50.52), 155 (Ts, 46.45), 143 (M^+-Ts-CO_2Me, 24.96), 91 ($CH_3C_6H_4$, 100.00), 65 (C_4H_3N, 20.62) and 115 (31.42); Anal. Calcd for $C_{19}H_{19}NO_4S$ (357.44): C, 63.85; H, 5.36; N, 3.92. Found: C, 63.59; H, 5.18; N, 3.65.
7. If a trapping reagent is less active than **1**, the self cycloaddition product of **1** is formed. See ref 3.
8. The π orbitals of the two carbon-carbon double bonds in allenes are perpendicular to each other. In the initially generated intermediate **5**, the orbital of the unshared electron pair is also perpendicular to the π orbital of the α,β-carbon-carbon double bond. After a 90° rotation around the C_α-C_β bond, the delocalized structure **5'** was formed, which results in the formation of **4**. For a similar result, see: Zhang, C.; Lu, X. *Synlett* **1995**, 645-646.
9. All new compounds are fully characterized by spectral and elemental analyses. Data for **9a**: mp 113-114 °C (benzene/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 3.4 Hz, 1H), 7.40 (tt, J = 7.5, 1.5 Hz, 1H), 7.28 (t, J = 7.6 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H), 7.04 (dd, J = 7.5, 1.5 Hz, 2H), 6.73 (d, J = 3.4 Hz, 1H), 3.58 (s, 3H) and 2.38 (s, 3H); IR (KBr) cm^{-1} 1719, 1445, 1358, 1198, 1173, 1157, 1130 and 723; MS m/z 355 (M^+, 52.35), 324 (M^+-OMe, 3.75), 201 (17.76), 200 (M^+-Ts, 100.00), 186 (13.52), 185 (M^+-Ts-Me, 89.37), 169 (M^+-Ts-OMe, 14.16), 91 (MeC_6H_4, 38.10) and 65 (14.14); Anal. Calcd for $C_{19}H_{17}NO_4S$ (355.42): C, 64.21; H, 4.82; N, 3.94. Found: C, 64.21; H, 4.65; N, 3.81. Data for **10a**: mp 99.5-100.5 °C (benzene/hexane), lit.,[10] 96.5-97.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (br s, 1H), 7.59 (dd, J = 7.9, 1.4 Hz, 2H), 7.45-7.37 (m, 3H), 6.76 (t, J = 2.7 Hz, 1H), 6.74 (t, J = 2.9 Hz, 1H) and 3.74 (s, 3H); IR (KBr) cm^{-1} 3314, 3298, 1701, 1682, 1482, 1454, 1292, 1146 and 768; MS m/z 202 (15.96), 201 (M^+, 84.47), 185 (M^+-Me-H, 5.23), 171 (19.73), 170 (M^+-OMe, 100.00), 142 (M^+-CO_2Me, 10.65), 115 (32.85), 114 (8.08) and 89 (5.97).
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