JOC Article

Cycloaddition of Alkynyl Ketones with *N*-Tosylimines Catalyzed by Bu_3P and DMAP: Synthesis of Highly Functionalized Pyrrolidines and Azetidines

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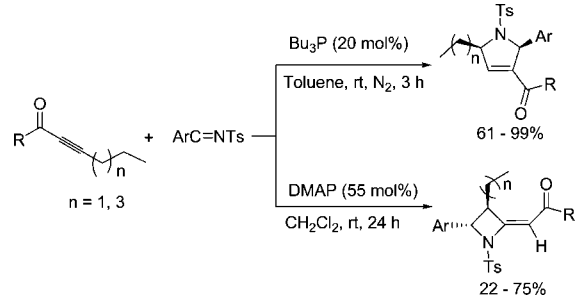

Cycloadditions of alkynyl ketones with *N*-tosylimines catalyzed by Lewis bases to synthesize azetidines and pyrrolidines were systematically described. In the reaction of alkynyl ketones with *N*-tosylimines catalyzed by Bu_3P at room temperature in toluene, highly functionalized pyrrolidines were formed in good to excellent yields. When DMAP was used in place of Bu_3P as catalyst to facilitate the cycloaddition, completely substituted azetidines were produced in moderate to good yields in CH_2Cl_2. Both cyclization reactions proceeded smoothly with complete stereoselectivity. The scope and limitations of these cycloadditon reactions were also investigated.

Introduction

Nitrogen-containing molecules have attracted much attention from organic chemists due to their potential biological activity and pharmaceutical significance. Specifically, azetidines and pyrrolidines are important nitrogen heterocyclic compounds which exhibit interesting biological and pharmacological properties.[1−3] Many useful and new methodologies were developed for the synthesis of such types of compounds as targets for important ligands and intermediates in organic synthesis.[4−8] Recently, reaction based on nucleophilic catalysis via conjugate addition of N- and P- nucleophiles has proven to be useful in the development of cycloaddition providing various carbo-[9] and heterocycles.[10,11] Shi and Kwon et al. reported the cyclization of activated allenes with *N*-tosylimines catalyzed by phosphine to produce pyrrolidine derivatives, respectively

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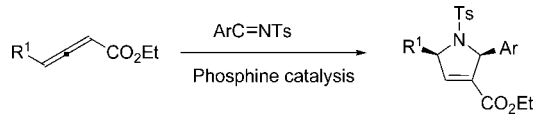
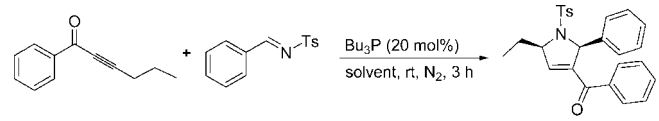
SCHEME 1



(Scheme 1).[12] The pyrrolidines were afforded in high yields, but in some cases, mixtures of *syn* and *anti* isomers were found. Therefore, further studies are still necessary to find methods to synthesize nitrogen heterocyclic compounds with high efficiency and stereoselectivity.

Very recently, we have described DMAP-catalyzed benzannulation reactions of terminal acetylenic ketones or esters in the presence of β-dicarbonyl compounds to provide highly substituted benzenes.[13] Our effort to expand the scope of annulations catalyzed by Lewis bases let us investigate a new series of cycloaddition reactions. Here, we wish to report full details on the Lewis base-catalyzed reactions of alkynyl ketones with *N*-tosylimines for the synthesis of pyrrolidines and azetidines. Compared with the previous reports,[12] the obvious advantage of this work is it is more diverse and it is easier to synthesize the starting materials, and it involved stereoselectivity.

TABLE 1. Reactions of 1-Phenylhex-2-yn-1-one with *N*-Tosyl Benzaldimine Catalyzed by Bu_3P (20 mol %)



1 2a 3a

entry	**1** (equiv)	**2a** (equiv)	solvent	yield (%)
1	1.0	1.0	CH_2Cl_2	48
2	1.0	1.5	CH_2Cl_2	68
3	1.5	1.0	CH_2Cl_2	84
4	2.0	1.0	CH_2Cl_2	82
5	1.5	1.0	CH_2Cl_2	72[a]
6	1.5	1.0	CH_2Cl_2	83[b]
7	1.5	1.0	Et_2O	80
8	1.5	1.0	THF	49
9	1.5	1.0	CH_3CN	58
10	1.5	1.0	DMF	trace
11	1.5	1.0	acetone	53
12	1.5	1.0	benzene	87
13	1.5	1.0	toluene	90

[a] At 0 °C. [b] At reflux.

Results and Discussion

Bu_3P-Catalyzed [3+2] Annulation Reaction of Alkynyl Ketones with *N*-Tosylimines. Our studies were initiated by addition of 20 mol % of Bu_3P to a solution of 1-phenylhex-2-yn-1-one **1** and *N*-tosyl benzaldimine **2a** under various reaction conditions, and the results are shown in Table 1. The reaction of 1-phenylhex-2-yn-1-one with *N*-tosyl benzaldimine in the presence of Bu_3P (20 mol %) in CH_2Cl_2 at room temperature for 3 h afforded a white solid in 48% yield, which was characterized as compound **3a** by NMR and HRMS spectra. The ratio of alkynyl ketone and *N*-tosylimine had an effect on this reaction. The desired product **3a** was obtained in 84% yield when 1.5 equiv of alkynyl ketone was used, but the yield of product was unsuccessfully improved with further increasing the amount of alkynyl ketone. The yield could not be improved when the reaction was stirred at 0 °C or at reflux. Bu_3P as a catalyst was crucial for the course of this reaction. The use of other organic bases, such as PPh_3, 1,4-diazabicyclo[2,2,2]-octane (DABCO), triethylamine (Et_3N), and pyridine, could not give the desired products. In addtion, the employed solvent played an important role in this reaction. With use of Et_2O, tetrahydrofuran (THF), CH_3CN, or acetone as a solvent, the product **3a** was produced in a relatively lower yield. When *N*,*N*-dimethylformamide (DMF) was used as the solvent, only a trace amount of **3a** was formed. With benzene or toluene as a solvent, reactions proceeded smoothly to produce **3a** in higher yields of 87% and 90%, respectively. Therefore, toluene is the best choice of solvent in this reaction.

With use of conditions optimized for the formation of **3a**, various *N*-tosylimines have been examined, and the representative results are shown in Table 2. It was found that the reactions of 1-phenylhex-2-yn-1-one with aromatic *N*-tosylimines afforded the corresponding products in good to excellent yields. Clearly, the substitutes on the aromatic *N*-tosylimines had an effect on the yields of the reactions. The substrate with an electron-withdrawing group on the aromatic ring gave a better yield than that of an electron-donating group on the aromatic ring. For example, when the substrates contained an electron-withdrawing group, such as fluoro, chloro, bromo, or nitro, on its phenyl

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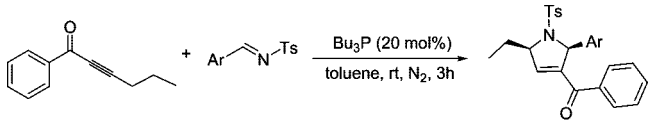
TABLE 2. Reactions of 1-Phenylhex-2-yn-1-one with Aromatic *N*-Tosylimines Catalyzed by Bu_3P



1 2 3

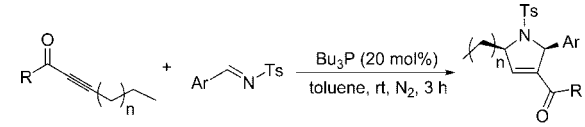
entry	Ar	product	yield (%)
1	C_6H_5	**3a**	90
2	4-BrC_6H_4	**3b**	90
3	4-ClC_6H_4	**3c**	93
4	4-FC_6H_4	**3d**	98
5	4-$NO_2C_6H_4$	**3e**	92
6	4-$CH_3C_6H_4$	**3f**	70
7	4-$MeOC_6H_4$	**3g**	64[a]
8	3-$NO_2C_6H_4$	**3h**	93
9	2-ClC_6H_4	**3i**	78
10	2-BrC_6H_4	**3j**	79
11	3, 4-$Cl_2C_6H_3$	**3k**	98
12	4-Me-3-$NO_2C_6H_3$	***3l***	90
13	4-Cl-3-$NO_2C_6H_3$	**3m**	99
14	1-naphthyl	**3n**	85
15	1-furanyl	**3o**	82
16	$C_6H_5CH_2CH_2$		NR[b]

[a] The reaction was stirred for 24 h. [b] NR = no reaction.

ring, the yields of the corresponding pyrrolidine products **3** were obtained in excellent yields. While the methoxyl group was on the para position of the benzene ring, the corresponding product **3g** was obtained in a 64% yield after prolonging the reaction time (24 h). However, when a fluoro or chloro group was on the ortho position of its benzene ring, the yield of the desired product was decreased obviously, which might be ascribed to steric hindrance. Notably, the multisubstituted benzene ring of *N*-tosylimines also reacted smoothly with 1-phenylhex-2-yn-1-one to give the desired products in almost quantitative yields. *N*-Tosyl furalimine was also converted to the corresponding product **3o** in 82% yields. However, it should be noted that no desired product was observed when aliphatic *N*-tosylimine was submitted to this reaction under our typical conditions.

To evaluate the scope of this reaction further, various alkynyl ketones were also tested under the standard conditions, and the results are summarized in Table 3. It was noted that aromatic alkynyl ketones could be converted to the corresponding annulation products **4** effectively, and the substrate with an electron-donating group on the aromatic ring gave a better yield than that of an electron-withdrawing group on the aromatic ring. For example, 1-(4-methoxyphenyl)hex-2-yn-1-one afforded the desired products **4f** and **4g** in almost quantitative yields, while a trace amount of the product **4d** was detected by TLC when 1-(4-nitrophenyl)hex-2-yn-1-one was used as substrate. The heteroaromatic alkynyl ketones, such as 1-(furan-2-yl)hex-2-yn-1-one and 1-(thiophen-2-yl)hex-2-yn-1-one, were submitted to this reaction, and the corresponding products **4k** and ***4l*** were obtained in 84% and 90% yields, respectively. However, when aliphatic alkynyl ketone was in place of aromatic alkynyl ketone, the reaction was complex and the desired product cannot be found (entry 13, Table 3). The aromatic alkynyl ketones containing long alkyl chains also gave the corresponding products in good yields. Treatment of 1-phenyloct-2-yn-1-one with *N*-tosylimines in the presence of Bu_3P (20 mol %) in toluene at room temperature for 4 h afforded the corresponding products **4m** and **4n** in 85% and 89% yields, respectively.

TABLE 3. Scope of Alkynyl Ketones in the Synthesis of Pyrrolidines 4



1 2 4

entry	R	*n*	Ar	product	yield (%)
1	4-BrC_6H_4	1	C_6H_5	**4a**	80
2	4-ClC_6H_4	1	C_6H_5	**4b**	61
3	4-FC_6H_4	1	C_6H_5	**4c**	67
4	4-$NO_2C_6H_4$	1	C_6H_5	**4d**	trace
5	4-$CH_3C_6H_4$	1	C_6H_5	**4e**	94
6	4-$MeOC_6H_4$	1	C_6H_5	**4f**	99
7	4-$MeOC_6H_4$	1	4-ClC_6H_4	**4g**	98
8	4-$CH_3C_6H_4$	1	4-BrC_6H_4	**4h**	92
9	4-BrC_6H_4	1	4-ClC_6H_4	**4i**	86
10	1-naphthyl	1	C_6H_5	**4j**	83
11	1-furanyl	1	C_6H_5	**4k**	84
12	1-thiophenyl	1	C_6H_5	***4l***	90
13	*n*-C_3H_7	1	C_6H_5		complex
14	C_6H_5	3	C_6H_5	**4m**	85[a]
15	C_6H_5	3	4-ClC_6H_4	**4n**	89[a]

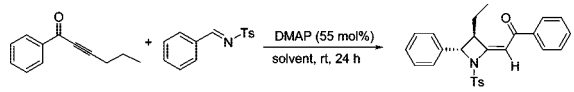
[a] The reaction was stirred for 4 h.

The structures of these products were determined by NMR spectroscopic data and X-ray diffraction. Interestingly, the stereochemistry of compounds **3** and **4** was determined to be the *syn* configuration for all cases in our reaction system as revealed by ^1H NMR analyses of the crude products. The *anti* isomer was not observed from the ^1H and ^{13}C NMR spectra. The ORTEP drawing of the product **3b** is shown in the Supporting Information.[14] Its relative configuration was firmly confirmed as the *syn* configuration. On the basis of these results, an efficient procedure for the synthesis of highly substituted pyrrolidines containing aromatic ketone groups has been developed. As the starting materials are readily obtained, and the reaction conditions are mild, this method presents a powerful diversity for the synthesis of highly functionalized pyrrolidines.

DMAP-Catalyzed [2+2] Annulation Reaction of Alkynyl Ketones with *N*-Tosylimines. In the reaction of alkynyl ketones with *N*-tosyl benzaldimine, when 4-(*N*,*N*-dimethylamino)pyridine (DMAP), in place of Bu_3P, was tested as a catalyst, a new cycloaddition reaction occurred. Treatment of 1-phenylhex-2-yn-1-one **1** with *N*-tosyl benzaldimine **2a** in the presence of 20 mol % of DMAP gave no desired product of pyrrolidine, but a 34% yield of azetidine **5a**. This compound was satisfactorily characterized by the spectra of NMR and HRMS. Recently, the preparation of functionalized azetidines from DABCO-catalyzed cyclization of activated allenes with *N*-tosylimine has been reported.[11e,12a] Inspired by these results, we anticipated that alkynyl ketones could also carry out the cyclization reaction instead of the activated allenes to produce highly substituted azetidines in the presence of DMAP. Thus, the reaction of 1-phenylhex-2-yn-1-one with *N*-tosyl benzaldimine **2a** catalyzed by DMAP

(14) The crystal data of **3b** have been deposited in CCDC with no. 682411. Empirical formula, $C_{416}H_{384}Br_{16}N_{16}O_{48}S_{16}$; formula weight, 8166.91; crystal color/habit, colorless/prismatic; crystal dimensions, 0.24 × 0.22 × 0.16 mm^3; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 39.435(5) Å, b = 15.399(2) Å, c = 15.384(2) Å, α = 90°, β = 99.734(3)°, γ = 90°, V = 9208(2) $Å^3$; space group, $P121/c1$; Z = 1; D_{calc} = 1.473 g/cm^3; F_{000} = 4192; diffractometer, Rigaku AFC7R; residuals, R 0.0663 and Rw 0.1228.

TABLE 4. Reactions of 1-Phenylhex-2-yn-1-one with 2a Catalyzed by DMAP (55 mol %)



entry	**1** (equiv)	**2a** (equiv)	solvent	yield (%)
1	1.0	1.0	CH_2Cl_2	34[a]
2	1.0	1.0	CH_2Cl_2	56
3	1.0	1.0	CH_2Cl_2	54[b]
4	1.0	1.5	CH_2Cl_2	61
5	1.5	1.0	CH_2Cl_2	66
6	2.0	1.0	CH_2Cl_2	65
7	1.5	1.0	CH_2Cl_2	66[c]
8	1.5	1.0	CH_2Cl_2	28[d]
9	1.5	1.0	Toluene	42
10	1.5	1.0	THF	18
11	1.5	1.0	CH_3CN	39
12	1.5	1.0	DMF	trace

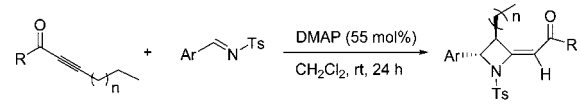
[a] 20 mol % DMAP was used. [b] 100 mol % DMAP was used. [c] At reflux. [d] At 0 °C.

was performed under various conditions and the results are shown in Table 4. The desired product **5a** was obtained in 56% yield when 55 mol % of DMAP was used and the yield of product was not improved with further increasing the amount of DMAP. The ratio of alkynyl ketone and *N*-tosylimine also has an effect on this reaction. A 66% yield of **5a** was obtained when 1.5 equiv of alkynyl ketone was added in this reaction. The yield was unsuccessfully improved at reflux conditions, but decreased sharply when the reaction was stirred at 0 °C. The choice of toluene and CH_3CN as solvent gave the desired product in 42% and 39% yields, respectively. THF and DMF gave a much lower yield of **5a**.

With the best reaction conditions in hand, various alkynyl ketones and *N*-tosylimines were submitted to the reaction under the optimal conditions, and the experimental results are summarized in Table 5. Clearly, the substitutes on the aromatic *N*-tosylimines have a slight effect on the yields of the reaction. The corresponding product **5g** was obtained in only 22% yield when the methoxyl group was on the para position of the benzene ring of *N*-tosylimine. The multisubstituted aromatic *N*-tosylimines also reacted smoothly with 1-phenylhex-2-yn-1-one to give azetidines in good yields. It should be noted that the reaction became disordered when *N*-tosyl furalimine or aliphatic *N*-tosylimine reacted with 1-phenylhex-2-yn-1-one (entries 13 and 14, Table 5). On the other hand, various aromatic alkynyl ketones could also be transformed to the desired azetidines **5** in the presence of *N*-tosyl benzaldimine and DMAP. When heteroaromatic alkynyl ketones were submitted to this reaction, the corresponding products **5t** and **5u** were obtained in 61% and 64% yields, respectively. The substrate with a long alkyl chain afforded the desire product **5w** in 68% yield. In many cases, the moderate yields obtained can be accounted for by the formation of any other byproducts, which cannot be isolated by column chromatography.

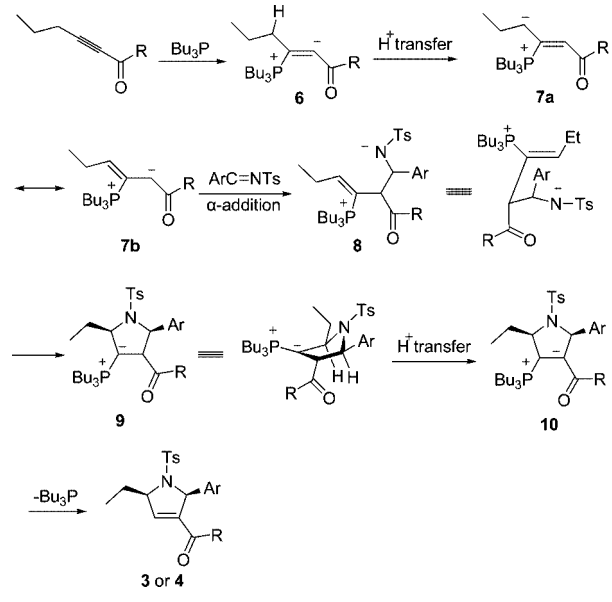
The structures of compounds **5** were determined as *anti* and *E* configuration by NMR spectroscopic data and X-ray diffraction. The *syn* isomer was also not observed from the ^1H and ^{13}C NMR spectra. The ORTEP drawing of the product **5s** is shown in the Supporting Information.[15] The presented procedure affords the synthesis of tetrasubstituted azetidines,

TABLE 5. Reactions of Alkynyl Ketones with Aromatic *N*-Tosylimines Catalyzed by DMAP



entry	R	*n*	Ar	product	yield (%)
1	C_6H_5	1	C_6H_5	**5a**	66
2	C_6H_5	1	4-BrC_6H_4	**5b**	67
3	C_6H_5	1	4-ClC_6H_4	**5c**	69
4	C_6H_5	1	4-FC_6H_4	**5d**	69
5	C_6H_5	1	4-$NO_2C_6H_4$	**5e**	70
6	C_6H_5	1	4-$CH_3C_6H_4$	**5f**	64
7	C_6H_5	1	4-$MeOC_6H_4$	**5g**	22
8	C_6H_5	1	2-ClC_6H_4	**5h**	65
9	C_6H_5	1	3-$NO_2C_6H_4$	**5i**	56
10	C_6H_5	1	3, 4-$Cl_2C_6H_3$	**5j**	66
11	C_6H_5	1	4-Me-3-$NO_2C_6H_3$	**5k**	52
12	C_6H_5	1	1-naphthyl	***5l***	75
13	C_6H_5	1	1-furanyl		complex
14	C_6H_5	1	$C_6H_5CH_2CH_2$		complex
15	4-BrC_6H_4	1	C_6H_5	**5m**	71
16	4-ClC_6H_4	1	C_6H_5	**5n**	62
17	4-FC_6H_4	1	C_6H_5	**5o**	63
18	4-$NO_2C_6H_4$	1	C_6H_5	**5p**	42
19	4-$CH_3C_6H_4$	1	C_6H_5	**5q**	58
20	4-$CH_3OC_6H_4$	1	C_6H_5	**5r**	49
21	4-BrC_6H_4	1	4-$NO_2C_6H_4$	**5s**	67
22	1-furanyl	1	C_6H_5	**5t**	61
23	1-thiophenyl	1	C_6H_5	**5u**	64
24	*n*-C_3H_7	1	C_6H_5	**5v**	trace
25	C_6H_5	3	C_6H_5	**5w**	68

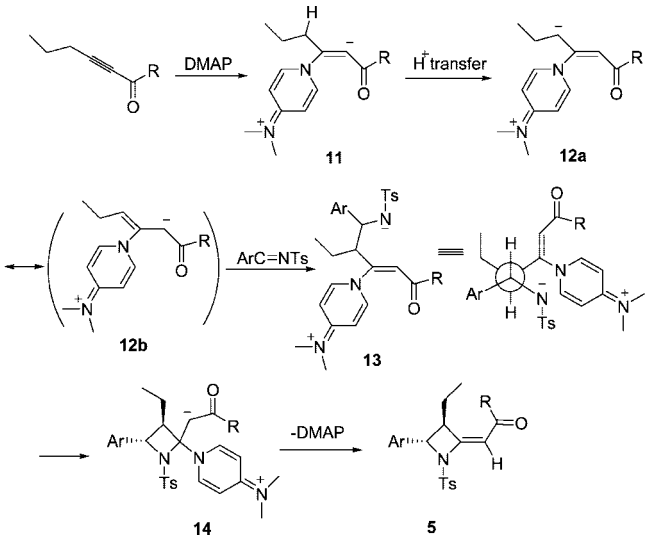
SCHEME 2. Plausible Mechanism for the Annulation Reaction of Alkynyl Ketone and *N*-Tosylimine Catalyzed by Bu_3P



which will lead to building blocks and potential intermediates with biological and pharmacological properties.

Reaction Mechanism. A plausible mechanism of these cycloaddition reactions is proposed in Schemes 2 and 3 on the basis of previous investigations.[9b,11,12] First, tri-*n*-butylphosphine and DMAP as nucleophilic triggers attack the β-carbon atom of the alkynyl ketone to generate the reactive dipolar intermediates **6** and **11**, respectively. In the case of Bu_3P, the intermediate **6** will be transformed to intermediate **7a** by proton transfer,

SCHEME 3. Plausible Mechanism for the Annulation Reaction of Alkynyl Ketone and *N*-Tosylimine Catalyzed by DMAP



followed by electron transfer to give intermediate **7b**. The intermediate **7b** adds to the *N*-tosylimine to give α-addition product **8**, which undergoes an intramolecular nucleophilic attack of the nitrogen anion (TsN^-) to the double bond (Michael type) to give intermediate **9**. At this point, the stereochemistry of the reaction is governed by the steric interaction between the tosyl and ethyl groups. At the same time, the stability of intermediate **9** also has a preference for the formation of the *syn* configuration with ethyl and aryl groups on equatorial positions. Finally, the proton transfer generates intermediate **10**, followed by elimination of Bu_3P to afford the desired product **3** or **4**. In the case of DMAP (Scheme 3), the intermediate **11** undergoes proton transfer to produce intermediate **12a**. The intermediate **12a** reacts with *N*-tosylimine via γ-addition to afford intermediate **13**, followed by an intramolecular Michael addition to give intermediate **14**. The formation of the trans configuration between ethyl and aryl groups might be due to the preferred conformation of intermediate **13** when the nitrogen anion (TsN^-) attacks the β-carbon of the carbon−carbon double bond. Then, the trans elimination (*E1cb* type) of DMAP from **14** affords product **5** with *E* configuration, and regenerates DMAP.

The different reactivity catalyzed by Bu_3P and DMAP has not been unequivocally established, but a plausible explanation is proposed according to the previous reports. Alkynyl ketones could be isomerized to (*E*,*E*)-diene ketones catalyzed by phosphine.[16] In the isomerization process, the key intermediate is similar to the enolate **7b**. So the allylic carbanion **7a** in the Bu_3P-catalyzed pathway prefers being transferred to the enolate **7b** as well, which may be the corresponding stabilized structure. Furthermore, the Bu_3P-catalyzed pathway also benefits from its ability to stabilize the ylide-like structure **9**.[17] In the DMAP-catalyzed pathway, the allylic carbanion **12a** is well stabilized by the pyridyl aromatic system due to its special feature, which might prevent or delay forming the enolate **12b**. Thus, the allylic carbanion **12a** could have enough time to react with *N*-tosylimine through γ-addition to give the desired product **5**. On the other hand, it has been reported that the reaction of activated allenes with *N*-tosylimine catalyzed by DMAP performs α-addition.[12] The enolate intermediate, like **12b**, generated by the reaction of activated allenes with DMAP is also stabilized by the pyridyl aromatic system, and prevents or delays the formation of allylic carbanion. Therefore, the similar reactions afford different products in the presence of Bu_3P and DMAP Lewis base promoters. However, the mechanistic details of these reactions need serious theoretical investigation.

Conclusions

We have described efficient cyclization reactions of alkynyl ketones and *N*-tosylimines by means of Bu_3P and DMAP promoters under mild conditions. The highly substituted pyrrolidine derivatives were produced through [3+2] annulation reactions catalyzed by Bu_3P with *syn* configuration in good to excellent yields. The DMAP-catalyzed [2+2] annulation reactions afforded tetrasubstituted azetidines with trans and *E* configuration in moderate to good yields. But it should be noted that aliphatic *N*-tosylimines and aliphatic alkynyl ketones are not suitable substrates for these two types of annulation reactions. These nitrogen heterocyclic compounds prepared from the reactions are important intermediates which exhibit interesting biological and pharmacological properties. Efforts are needed to elucidate the mechanistic details and the effects of Lewis base character on the reactions.

Experimental Section

General Procedure for the Reaction of Alkynyl Ketones with *N*-Tosylimines Catalyzed by Bu_3P. To a solution of alkynyl ketone (0.45 mmol) with *N*-tosylimine (0.3 mmol) in toluene (2 mL) was added tri-*n*-butylphosphine (16 μL, 0.06 mmol). The mixture was stirred at room temperature under nitrogen for 3 h. Then the solvent was removed in vacuo and the residue was purified by column chromatography on silica gel, using petroleum ether/ethyl acetate (5:1) as eluent, to give the pure product.

***syn*-(5-Ethyl-2-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrol-3-yl)(phenyl)methanone (3a):** white solid (116 mg, 90% yield); mp 92−94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.64−7.59 (m, 4H), 7.53−7.48 (m, 1H), 7.43−7.35 (m, 4H), 7.27−7.17 (m, 5H), 6.34 (s, 1H), 5.97 (s, 1H), 4.66−4.61 (m, 1H), 2.37 (s, 3H), 2.22−2.13 (m, 1H), 1.99−1.89 (m, 1H), 1.11 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 190.5, 143.7, 141.2, 140.0, 139.3, 137.4, 135.2, 133.0, 129.7, 129.0, 128.6, 128.4, 127.9, 127.9, 127.7, 70.3, 69.5, 30.1, 21.6, 10.7; IR (KBr) υ 1650, 1597 cm^{-1}; HRMS (EI) calcd for $C_{24}H_{20}NO_3S$ ($M^+ - C_2H_5$) 402.1164, found 402.1159.

General Procedure for the Reaction of Alkynyl Ketones with *N*-Tosylimines Catalyzed by DMAP. To a solution of alkynyl ketone (0.45 mmol) with *N*-tosylimine (0.3 mmol) in dry CH_2Cl_2 (2 mL) was added DMAP (21 mg, 0.165 mmol), and the resulting mixture was stirred at room temperature for 24 h. The solvent was removed in vacuo and the residue was purified by column

(15) The crystal data of **5s** have been deposited in CCDC with no. 688638. Empirical formula, $C_{26}H_{23}BrN_2O_5S$; formula weight, 555.43; crystal color/habit, colorless/prismatic; crystal dimensions, 0.26 × 0.18 × 0.04 mm^3; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 13.117(5) Å, b = 18.601(5) Å, c = 11.063 (5) Å, α = 90.000(5)°, β = 106.678(5)°, γ = 90.000(5)°, V = 2585.7(17) Å^3; space group, *P*21/*c*; Z = 4; D_{calc} = 1.427 g/cm^3; F_{000} = 1136; diffractometer, Gemini s ultra oxford diffraction; residuals, R 0.0447 and Rw 0.1147.

(16) (a) Trost, B. M.; Kazmaier, U. *J. Am. Chem. Soc.* **1992**, *114*, 7933. (b) Guo, C.; Lu, X. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1921. (c) Kazmaier, U. *Tetrahedron* **1998**, *54*, 1491. (d) Kwong, C. K.-W.; Fu, M. Y.; Lam, C. S.-L.; Toy, P. H. *Synthesis* **2008**, *15*, 2307.

chromatography on silica gel, using petroleum ether/ethyl acetate (10:1) as eluent, to afford the pure product.

(*E*)-2-(*anti*-3-Ethyl-4-phenyl-1-tosylazetidin-2-ylidene)-1-phenylethanone (5a): white solid (85 mg, 66% yield); mp 109−111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.98 (d, J = 7.2 Hz, 2H), 7.58−7.46 (m, 5H), 7.29−7.21 (m, 7H), 7.05 (d, J = 1.5 Hz, 1H), 4.94 (d, J = 3.0 Hz, 1H), 3.47−3.43 (m, 1H), 2.40 (s, 3H), 2.20−2.12 (m, 1H), 1.55−1.49 (m, 1H), 0.83 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 189.4, 163.7, 144.9, 139.1, 137.1, 135.1, 132.5, 129.8, 128.8, 128.8, 128.6, 128.0, 127.4, 127.1, 99.1, 72.3, 52.5, 22.3, 21.7, 10.5; IR (KBr) υ 1669, 1601 cm^{-1}; HRMS (EI) calcd for $C_{26}H_{25}NO_3S$ (M^+) 431.1555, found 431.1563.

Acknowledgment. We are grateful to the National Natural Science Foundation of China (20772116) and the Program of NCET (060551) for financial supports.

Supporting Information Available: Detailed experimental procedures and characterization data for all products; X-ray crystal data for **3b** and **5s**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO801687V

(17) Evans, C. A.; Miller, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 12394.