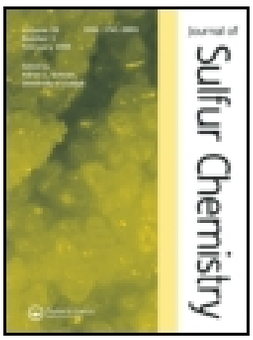


Journal of Sulfur Chemistry

ISSN: 1741-5993 (Print) 1741-6000 (Online) Journal homepage: https://www.tandfonline.com/loi/gsrp20

Silver iodide catalyzed the three-component reaction between terminal alkynes, carbon disulfide, and aziridines

A. Samzadeh-Kermani

To cite this article: A. Samzadeh-Kermani (2019): Silver iodide catalyzed the three-component reaction between terminal alkynes, carbon disulfide, and aziridines, Journal of Sulfur Chemistry, DOI: 10.1080/17415993.2019.1631316

To link to this article: https://doi.org/10.1080/17415993.2019.1631316

Published online: 25 Jun 2019.

JOURNAL OF SULFUR CHEMISTRY
https://doi.org/10.1080/17415993.2019.1631316

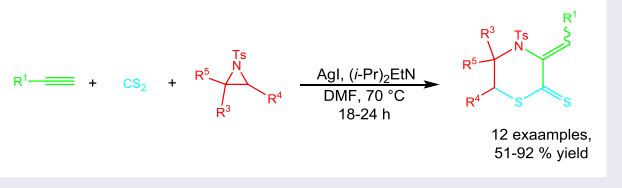
Silver iodide catalyzed the three-component reaction between terminal alkynes, carbon disulfide, and aziridines

A. Samzadeh-Kermani

Chemistry Department, Faculty of Science, University of Zabol, Zabol, Iran

ABSTRACT

A novel catalytic reaction involving terminal alkynes, carbon disulfide, and aziridines has been described. In this transformation, silver-acetylides react with carbon disulfide and aziridines to form 1,4-thiomorpholine molecules in good yields. The optimum conditions developed using silver iodide and $(i\text{-Pr})_2$EtN in DMF at 70°C.



ARTICLE HISTORY
Received 16 April 2019
Accepted 7 June 2019

KEYWORDS
Carbon disulfide; aziridine; terminal alkyne; silver salt; multicomponent reaction

1. Introduction

Terminal alkynes are valuable synthons in the synthesis of a wide range of organic molecules [1–3]. Conversion of terminal alkynes to the corresponding acetylides take place either in the presence of a strong base or using an appropriate catalyst system. The latter method takes advantage of simplicity, compatibility with a wide range of functional groups and protic solvents. Particularly, the nucleophilic additions of metal-acetylides to Michael acceptors serve as an efficient method for the synthesis of highly desirable C–C bond from the readily accessible substrates [4–9]. In last decade, the development of catalytic formations of metal-acetylides offers an opportunity for the expedient synthesis of complex molecules from such simple starting materials [10–12]. In most of these transformations, copper salts were selected as the catalysts of choice based on the cost, tolerability with functional groups, and efficiency [13–16]. It is worth mentioning that the oxidation states of copper salts have tiny effect on metal-acetylides formation. For instance, Carreira and co-workers reported the first nucleophilic additions of copper-acetylides into unsaturated carbonyl in aqueous reaction medium using Cu(II)/ascorbate as catalyst system [17]. Particularly notable is the use of copper-acetylide as an organometallic

CONTACT A. Samzadeh-Kermani drsamzadeh@gmail.com

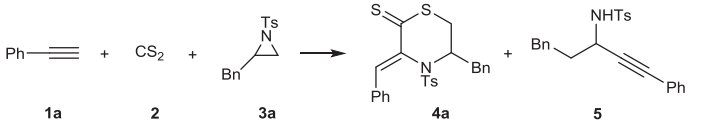
species in such protic reaction medium. Additionally, their reports on nucleophilic additions of copper-acetylides to carbonyl and imine moieties were without precedent [18,19]. Recently, Garcia-Tellado reported an enantioselective route for the synthesis of chiral propargylic amines based on the nucleophilic addition of metal-acetylides into α-imino esters [20]. The pioneering work of Medal in use of copper-acetylides with azides has also attracted much attentions owing to its compatibility toward synthesis of a variety of functional groups and heterocycles [21–25]. To our knowledge, Ghazanfarpour reported the first addition of copper-acetylides to carbon disulfide, allowing efficient access to 1,4-oxathiane skeletons [26]. Our group have also disclosed a reaction involving terminal alkynes, isothiocyanates, and oxiranes using silver salts as a catalyst [27]. Our recent report on the reaction of copper-acetylides, isothiocyanates, and aziridines leads to the formation of thiomorpholine derivatives in good yields [28]. Based on the above literatures and in continuation of our reports in synthesis of heterocycles [29,30], we became interested to explore the efficiency of silver-acetylides in a catalytic multicomponent reaction that uses carbon disulfide and aziridines.

2. Results and discussion

To develop the designed catalytic multicomponent reaction, phenyl acetylene (**1a**), carbon disulfide (**2**), and aziridine **3a** were chosen as reaction partners to optimize the reaction conditions (Table 1). Initial efforts using CuOTf and $(i\text{-Pr})_2$EtN to implement the proposed transformation were complicated by formation of compound **5** (entry 1), which might be arising from the competing attack of the copper-acetylide to 4-methyl-*N*-(3-phenylpropylidene)benzenesulfonamide derived from Meinwald rearrangement [31], of 2-benzyl-1-tosylaziridine (**3a**). Control experiments clearly revealed that common copper (I) and (II) salts were not efficient for the successful synthesis of the desired product **4** (entries 2–7). The yields of the desired product **4** and the by-product **5** could be modulated by using *N*-heterocyclic carbene copper(I) catalyst (IPr)CuCl (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) (entry 8). The study also showed that $Fe(OTf)_3$ and $In(OTf)_3$ were not efficient in carrying out this transformation (Table 1, entries 9 and 10). $Pd(OAc)_2$ and $AuCl_3$ were also examined but proved unsuitable catalysts (entries 11 and 12). Various silver salts were also examined to further optimize the reaction outcome (entries 14–18). Upon examination of silver salts, AgI has been found to be optimal (entry 14). An outcome we attributed to higher affinity of silver-acetylide to sulfur atom of CS_2 in comparison of oxygen in oxirane molecule. Particularly notable was that the use of silver salts as the catalyst of choice completely inhibited the formation of undesired product **5**. These results demonstrated that the insertion of carbon disulfide into silver-acetylide species proceeds significantly faster than that of aziridine to the silver-acetylide bond.

The control experiment revealed that an extremely low yield of **4a** was obtained without $(i\text{-Pr})_2$EtN, testifying to the vital roles of base in this catalytic system (entry 19). The reactions run with either K_2CO_3 or Cs_2CO_3 resulted in moderate conversions (entries 20 and 21), whereas no the desired product formation take place upon using *t*. BuOLi and instead 4-benzyl-3-tosylthiazolidine-2-thione was obtained in 69% yield (entry 22). To our surprise, polyethylene glycol (PEG) (a known solvent for activating of oxiranes and aziridines,[32]) was not good choice here (entries 23–25), as the by-product **5** was the main product upon using PEG as the solvent. It could be deduced that PEG activates aziridine

Table 1. Optimization of reaction conditions[a].



1a 2 3a 4a 5

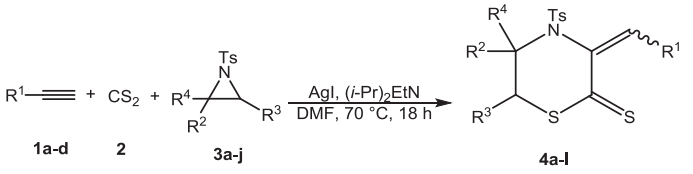
Entry	Catalyst	Base	Solvent	Yield **4a** (%)	Yield **5** (%)
1	CuOTf	$(i\text{-Pr})_2$EtN	DMF	29	35
2	Cu_2O	$(i\text{-Pr})_2$EtN	DMF	38	30
3	CuBr	$(i\text{-Pr})_2$EtN	DMF	43	26
4	CuCl	$(i\text{-Pr})_2$EtN	DMF	35	22
5	CuI	$(i\text{-Pr})_2$EtN	DMF	56	21
6	$Cu(OTf)_2$	$(i\text{-Pr})_2$EtN	DMF	25	58
7	$Cu(OAc)_2$	$(i\text{-Pr})_2$EtN	DMF	31	43
8	(IPr)CuCl	$(i\text{-Pr})_2$EtN	DMF	64	Traces
9	$Fe(OTf)_3$	$(i\text{-Pr})_2$EtN	DMF	–	–
10	$In(OTf)_3$	$(i\text{-Pr})_2$EtN	DMF	–	–
11	$Pd(OAc)_2$	$(i\text{-Pr})_2$EtN	DMF	49	–
12	$AuCl_3$	$(i\text{-Pr})_2$EtN	DMF	57	–
13	AgOAc	$(i\text{-Pr})_2$EtN	DMF	73	–
14	AgI	$(i\text{-Pr})_2$EtN	DMF	82	–
15	AgCl	$(i\text{-Pr})_2$EtN	DMF	75	–
16	$AgNO_3$	$(i\text{-Pr})_2$EtN	DMF	67	–
17	AgF	$(i\text{-Pr})_2$EtN	DMF	71	–
18	$AgBF_4$	$(i\text{-Pr})_2$EtN	DMF	87	–
19	AgI	–	DMF	Traces	–
20	AgI	K_2CO_3	DMF	43	–
21	AgI	Cs_2CO_3	DMF	60	–
22	AgI	LiO^{t}Bu	DMF	–[b]	–
23	AgI	$(i\text{-Pr})_2$EtN	PEG-200	–	53
24	AgI	$(i\text{-Pr})_2$EtN	PEG-400	–	70
25	AgI	$(i\text{-Pr})_2$EtN	PEG-600	–	38
26	AgI	$(i\text{-Pr})_2$EtN	–	Complicated	–
27	–	$(i\text{-Pr})_2$EtN	DMF	–	–

[a]Reaction conditions: **1a** (1.2 mmol), **2** (1.0 mL), **3a** (1.0 mmol), catalyst (0.1 mmol), base (1.5 mmol), ground 3 Å molecular sieves (250 mg) in solvent (3 mL) at 70°C for 18 h.
[b]4-Benzyl-3-tosylthiazolidine-2-thione was obtained in 69% yield.

and thereby the insertion of **3a** into silver(I) acetylide species proceeds faster than that of carbon disulfide to the silver(I) acetylide bond. The reaction conducted in neat condition formed a complicated mixture (Table 1, entry 26). As expected, reaction did not proceed at all with catalyst (Table 1, entry 27).

Having determined the optimized conditions, we set out to examine the scope of this transformation (Table 2). *N*-Tosyl aziridine bearing a benzyl group **3a** reacted smoothly and afforded the desired product in acceptable yield (entry 1). This transformation was sensitive to steric hindrance of substrate, as reaction conducted with 1,1-disubstituted aziridine **3b** formed only a moderate yield of **4b** (entry 2). Aziridine possessing alkyl group like *n*-butyl and *n*-hexyl were also appropriate substrates (entries 3 and 4). If a six-membered aziridine utilized as the aziridine source, the yield increased while, the aziridine prepared from cycloheptene gave only in moderate yield (entries 5–6). Additionally, the desired reaction did not proceed at all with cyclopentene aziridine **3 g**, most likely due to the interference of strain energy of the product (entry 7). The difference in reactivity was reflected in the case of phenyl-substituted aziridines where the internal position was exclusively attacked by the sulfur ion (entry 8). 2,3-Diphenyl-1-tosylaziridinealso was also successful in the preparation of thiomorpholine skeleton (Table 2, entry 9). The substrate

Table 2. Synthesis of functionalized thiomorpholines[a].



1a-d 2 3a-j 4a-l

Entry	Alkyne	R^1	Aziridine	R^2,R^3, R^4	Yield (%)
1	**1a**	Ph	**3a**	Bn, H, H	**4a**, 82
2	**1a**	Ph	**3b**	*n*-C_3H_7, H, CH_3	**4b**, 64
3	**1a**	Ph	**3c**	*n*-C_4H_9, H, H	**4c**, 86
4	**1a**	Ph	**3d**	*n*-C_6H_{13}, H, H	**4d**, 73
5	**1a**	Ph	**3e**	$-(CH_2)_4-$, H	**4e**, 89
6	**1a**	Ph	**3f**	$-(CH_2)_5-$, H	**4f**, 51
7	**1a**	Ph	**3g**	$-(CH_2)_3-$, H	–
8	**1a**	Ph	**3h**	H, Ph, H	**4 g**, 89[b]
9	**1a**	Ph	**3i**	Ph, Ph, H	**4 h**, 92
10	**1a**	Ph	**3j**	Ph, H, CH_3	**4i**, 72[b]
11	**1b**	*n*-Pr	**3a**	Bn, H, H	**4j**, 79[c]
12	**1c**	2-furyl	**3a**	Bn, H, H	**4k**, 90
13	**1d**	TMS	**3a**	Bn, H, H	**4 l**, 80[d]

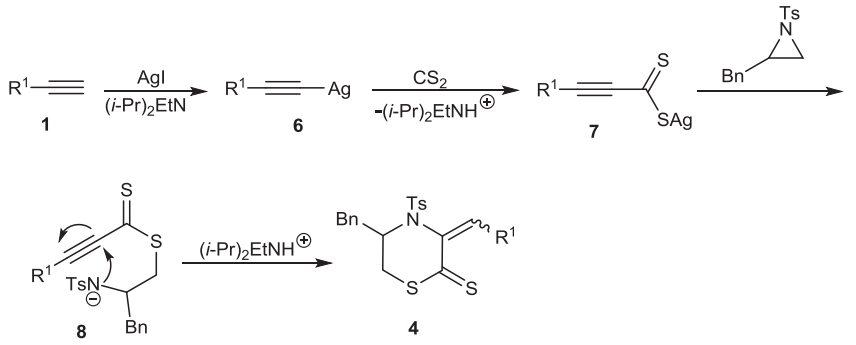
[a]For all entries except stated otherwise: **1** (1.2 mmol), **2** (1.0 mL), **3** (1.0 mmol), AgI (0.1 mmol), $(i\text{-Pr})_2$EtN (1.5 mmol), ground 3 Å molecular sieves (250 mg) in DMF (3 mL) at 70°C for 18 h.
[b]The yield of benzylic- attacked product.
[c]Reaction mixture was stirred for 22 h.
[d]Reaction mixture was stirred at 90°C for 22 h.

possessing both alkyl- and phenyl- substituents **3j** was also tolerated (entry 10). In this reaction, we could not find the other plausible regio-isomers at all. It is noteworthy that 1-pentyne (**1b**), as an aliphatic alkyne, afforded the targeted product in acceptable yield (entry 11). Not only phenyl- and alkyl- substituted terminal alkynes but also 2-ethynylfuran (**1c**) engaged proficiently in this catalytic reaction to furnish compound **4k** (entry 12). To our delight, trimethylsilylacetylene (**1d**) could also react to form the desired thiomorpholine motif in good yield (entry 15).

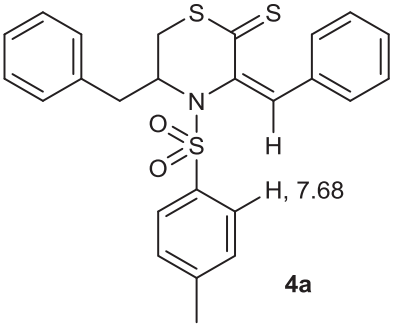
The structures of the products were confirmed by spectroscopic analyses including ^{1}H-NMR, ^{13}C-NMR, FT-IR, Mass spectroscopy, and elemental analysis. The ^{1}H-NMR spectrum of **4a** exhibited a characteristic (AB)X spin system for the CH_2-CH H-atoms, together with a singlet for the vinyl group. The ^{13}C-NMR spectrum of **4a** exhibited 25 signals and the mass spectrum of **4a** displayed the molecular ion peak at $m/z = 465$.

Mechanistically, silver iodide coordinates with the triple bond lowering acidity of the terminal C–H bond. The abstraction of the terminal proton easily by $(i\text{-Pr})_2$EtN leads to the formation of silver acetylide **6**. Silver acetylide reacts with the carbon disulfide (**2**) to form the corresponding ((3-phenylprop-2-ynethioyl)-λ^3-sulfaneylidene)silver **7**. It could be deduced that the activation of **3a** with silver cation weakened the carbon–nitrogen bond in aziridine and produced an activated species which is attacked by anionic adduct **7**. While silver iodide system exhibited somewhat Lewis acidic character, the reaction did not proceed through the S_N1-like route as no products arising from Meinwald rearrangement are detected by crude reaction mixture analyses.

The adduct then attacked on aziridine **3** to give **8**. The *N*-tosyl anion of propargylic skeleton **8** participated in the nucleophilic addition to the triple bond by intramolecular *6-exo* cyclization to give **4** (Scheme 1).



Scheme 1. Plausible mechanism for the formation of thiomorpholine derivatives.



Scheme 2. Configurational study with homonuclear NOE.

The stereochemistry of *exo*-cyclic double bond was determined by homonuclear NOE experiment. This kind of experiment concerns substrates which have spatially close protons. Experiments emphasize significant homonuclear NOE between the involved protons, suggesting the exact Z -configuration in compounds **4a** (Scheme 2). When the signal appeared at 7.68 ppm was irradiated the intensity of the vinylic hydrogens increased. This result indicated that these two kind of protons are spatially enough close to affect their signal intensity.

3. Conclusion

In summary, we have developed a novel catalytic multicomponent reaction between *in situ* generated silver-acetyilides, carbon disulfide, and aziridines. The study showed that the choice of catalyst and the reaction medium had great impact in furnishing the desired transformation with good success. Of the metal precatalysts examined, silver salts exhibited unique reactivity and selectivity in this transformation as no product arising from the direct attack of acetyilide on aziridine are detected in reaction mixture analysis. We found that the efficiency as well as regio-selectivity of the ring opening reaction of aziridines is sensitive to electronic and steric properties of substrates. This silver-catalyzed reaction demonstrates good functional group tolerance and acceptable yields.

4. Experimental

Commercially available reagents were used without further purification. *N*-Ts Aziridines were prepared using the literature procedures [33]. All the solvents were purchased from PALACHEM Chemical Industries. Solvents were dried over molecular sieves 3 Å or 4 Å before the use. Molecular sieves were activated in vacuum oven at 200°C for 14 h and stored under vacuum at 100 °C in the presence of P_4O_{10}. The copper (I) salts were typically weighted into smaller vials containing about 500 mg of reagent in a glovebox and sealed. The smaller containers were transferred outside the glovebox, stored in a desiccator while being utilized and kept for no more than 2 weeks outside the glovebox. All reactions were carried out in Schlenk tube (25 mL) using oven-dried and/or flame dried glassware under a pure and dry argon atmosphere with magnetic stirring. All reactions were monitored by TLC analyses were performed on Silica gel 60 (Merck, item number 116835). Plates were visualized using UV light (254 nm) and/or iodine. Column chromatography was performed on silica gel 60 (particle size 63–200 μm) (Merck, item number 7734-3) on a glass column. Melting points (mp) were recorded with Electrothermal-9100 apparatus and were determined in capillary tubes and are uncorrected. ^{1}H-NMR spectra were recorded with Bruker DRX-500 AVANCE instrument; at 500 MHz (using TMS, as a reference), and ^{13}C NMR were recorded at 125 MHz (using the $CDCl_3$ triplet as reference) in $CDCl_3$ as solvent at ambient temperature. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, br = broad, t = triplet, q = quartet, m = multiplet). Chemical shifts were reported as (δ) in parts per million (ppm) and Coupling constants *J* values are given in Hz. Mass data were recorded with EIMS (70 eV): Finnigan-MAT-8430 mass spectrometer, in m/z. IR spectra were recorded with Shimadzu IR-460 FTIR spectrometer as KBr pellets or neat. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer. The results agreed favorably with the calculated values.

4.1. General procedure for the preparation of compounds 4

An oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was charged with terminal alkyne (1.2 mmol), AgI (0.1 mmol) and ground 3 Å molecular sieves (250 mg) in DMF (3 mL). After stirring at 25°C for 30 min, carbon disulfide (1.0 mL) and aziridine (1.0 mmol) were added under an Ar atmosphere. Stirring was continued at 70°C temperature until the starting material was completely consumed (TLC monitoring, 16 h). Afterwards, the mixture was quenched with sat.aq NH_4Cl (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and evaporated under reduced pressure to dryness. The crude product obtained was further purified by column chromatography (silica gel, hexane:EtOAc 3:1) to give the pure product.

4.1.1. 5-Benzyl-3-benzylidene-4-tosylthiomorpholine-2-thione (4a, $C_{25}H_{23}NO_2S_3$)

Yellow powder; M.P: 113–115°C. Yield: 0.38 g (82%). IR (KBr) (ν_{max}, cm^{-1}): 3032, 2978, 1541, 1364, 1311, 1115. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 2.36 (3 H, s, Me), 2.80 (1 H, *dd*, ^2J = 12.0 Hz, ^3J = 11.8 Hz, CH), 3.01 (1 H, *dd*, ^2J = 12.0 Hz, ^3J = 5.8 Hz, CH), 3.23 (1 H, *dd*, ^2J = 11.9 Hz, ^3J = 7.5 Hz, CH), 3.40 (1 H, *dd*, ^2J = 11.9 Hz, ^3J = 5.5 Hz, CH),

4.02–4.11 (1 H, m, CH), 5.62 (1 H, s, CH), 7.17–7.33 (6 H, m, 6 CH), 7.35–7.45 (4 H, m, 4 CH), 7.56 (2 H, d, ^3J = 6.1 Hz, 2 CH), 7.68 (2 H, d, ^3J = 6.3 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 22.8 (Me), 39.1, 43.5 (CH_2), 63.2, 111.3, 125.1, 125.8 (CH), 127.1 (2 CH), 128.0 (2 CH), 128.3 (2 CH), 129.1 (2 CH), 129.4 (2 CH), 130.5 (2 CH), 132.7, 135.1, 135.6, 138.6, 140.0, 226.5 (C). MS: *m/z* (%) = 465 (M^+, 1), 310 (11), 155 (34), 128 (59), 91 (100), 77 (62), 54 (42). Anal. Calcd (%) for (465.64): C, 64.49, H, 4.98, N, 3.01, S, 20.66. Found: C, 64.70, H, 5.21, N, 3.26, S, 20.74.

4.1.2. 3-Benzylidene-5-methyl-5-propyl-4-tosylthiomorpholine-2-thione (4b, $C_{22}H_{25}NO_2S_3$)

Yellow oil. Yield: 0.28 g (64%). IR (KBr) (ν_{max}, cm^{-1}): 3041, 2983, 1536, 1372, 1314, 1122. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 0.84 (3 H, t, ^3J = 6.5 Hz, Me), 1.41–1.53 (4 H, m, 2 CH_2), 1.55 (3 H, s, Me), 2.40 (3 H, s, Me), 3.11 (1 H, *d*, ^2J = 10.1 Hz, CH), 3.34 (1 H, *d*, ^2J = 10.1 Hz, CH), 5.71 (1 H, s, CH), 7.30–7.45 (5 H, m, 5 CH), 7.61 (2 H, d, ^3J = 6.5 Hz, 2 CH), 7.70 (2 H, d, ^3J = 6.6 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 15.8 (Me), 16.0 (CH_2), 22.5, 25.0 (Me), 41.8, 49.2 (CH_2), 64.9 (C), 113.0, 128.1 (CH), 127.9 (2 CH), 128.9 (2 CH), 129.9 (2 CH), 131.2 (2 CH), 132.5, 135.0, 135.8, 139.5, 225.8 (C). MS: *m/z* (%) = 431 (M^+, 1), 276 (17), 187 (25), 155 (53), 91 (42), 77 (100), 54 (63). Anal. Calcd (%) for (431.63): C, 61.22, H, 5.84, N, 3.25, S, 22.28. Found: C, 61.45, H, 6.02, N, 3.41, S, 22.41.

4.1.3. 3-Benzylidene-5-butyl-4-tosylthiomorpholine-2-thione (4c, $C_{22}H_{26}NO_2S_3$)

Yellow oil. Yield: 0.37 g (86%). IR (KBr) (ν_{max}, cm^{-1}): 3025, 2987, 1530, 1342, 1311, 1116. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 0.81 (3 H, t, ^3J = 6.0 Hz, Me), 1.29–1.54 (6 H, m, 3 CH_2), 2.40 (3 H, s, Me), 2.96 (1 H, *dd*, ^2J = 11.2 Hz, ^3J = 10.4 Hz, CH), 3.14 (1 H, *dd*, ^2J = 11.2 Hz, ^3J = 5.6 Hz, CH), 3.49–3.58 (1 H, m, CH), 5.63 (1 H, s, CH), 7.27–7.45 (5 H, m, 5 CH), 7.57 (2 H, d, ^3J = 6.5 Hz, 2 CH), 7.69 (2 H, d, ^3J = 6.8 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 14.2, 22.9 (Me), 25.1, 26.2, 33.0, 41.1 (CH_2), 62.5, 113.2, 126.2 (CH), 127.9 (2 CH), 128.8 (2 CH), 129.4 (2 CH), 130.3 (2 CH), 132.7, 134.1, 134.6, 139.0, 224.1 (C). MS: *m/z* (%) = 490 (M^+, 1), 276 (14), 187 (50), 155 (43), 77 (100), 54 (48). Anal. Calcd (%) for (431.63): C, 61.22, H, 5.84, N, 3.25, S, 22.28. Found: C, 61.53, H, 6.05, N, 3.43, S, 22.35.

4.1.4. 3-Benzylidene-5-hexyl-4-tosylthiomorpholine-2-thione (4d, $C_{24}H_{29}NO_2S_3$)

Yellow oil. Yield: 0.34 g (73%). IR (KBr) (ν_{max}, cm^{-1}): 3018, 2967, 1540, 1362, 1314, 1122. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 0.79 (3 H, t, ^3J = 6.2 Hz, Me), 1.23–1.38 (8 H, m, 4 CH_2), 1.57 (2 H, m, CH_2), 2.40 (3 H, s, Me), 2.86 (1H, *dd*, ^2J = 12.0 Hz, ^3J = 6.0 Hz, CH), 3.19 (1H, *dd*, ^2J = 12.3 Hz, ^3J = 9.1 Hz, CH), 3.57–3.67 (1 H, m, CH), 5.60 (1 H, s, CH), 7.28–7.41 (5 H, m, 5 CH), 7.58 (2 H, d, ^3J = 6.2 Hz, 2 CH), 7.69 (2 H, d, ^3J = 6.7 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 13.7, 23.1 (Me), 24.5, 27.8, 29.1, 33.2, 35.6, 44.1 (CH_2), 65.2, 113.1, 126.9 (CH), 127.9 (2 CH), 128.5 (2 CH), 129.1 (2 CH), 130.7 (2 CH), 132.5, 134.5, 135.6, 139.1, 224.1 (C). MS: *m/z* (%) = 459 (M^+, 1), 304 (16), 302 (36), 155 (56), 91 (36), 77 (100), 54 (53). Anal. Calcd (%) for (459.68): C, 62.71, H, 6.36, N, 3.05, S, 20.92. Found: C, 62.90, H, 6.54, N, 3.21, S, 20.98.

4.1.5. 3-Benzylidene-4-tosyloctahydro-2H-benzo[b][1,4]thiazine-2-thione (4e, $C_{22}H_{23}NO_2S_3$)

Yellow powder; M.P: 198–200°C. Yield: 0.38 g (89%). IR (KBr) (ν_{max}, cm^{-1}): 3032, 2981, 1541, 1347, 1321, 1108. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 1.26–2.18 (8 H, m, 4 CH_2), 2.41 (3 H, s, Me), 2.55–2.64 (1 H, m, 1 CH), 3.01–3.11 (1 H, m, CH), 5.60 (1 H, s, CH), 7.30–7.44 (5 H, m, 5 CH), 7.59 (2 H, d, ^3J = 6.2 Hz, 2 CH), 7.68 (2 H, d, ^3J = 6.5 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 22.5 (Me), 25.8, 26.4, 29.1, 30.3 (CH_2), 43.5, 60.1, 112.1, 126.9 (CH), 127.9 (2 CH), 128.9 (2 CH), 129.6 (2 CH), 131.2 (2 CH), 132.2, 134.9, 135.1, 139.0, 226.1 (C). MS: *m/z* (%) = 429 (M^+, 1), 274 (13), 185 (54), 155 (37), 91 (35), 77 (100), 54 (47). Anal. Calcd (%) for (429.61): C, 61.51, H, 5.40, N, 3.26, S, 22.39. Found: C, 61.77, H, 5.64, N, 3.51, S, 22.51.

4.1.6. 3-Benzylidene-4-tosyloctahydrocyclohepta[b][1,4]thiazine-2(3H)-thione (4f, $C_{23}H_{25}NO_2S_3$)

Yellow powder; M.P: 185–187°C; Yield: 0.23 g (51%). IR (KBr) (ν_{max}, cm^{-1}): 3046, 2978, 1646, 1548, 1346, 1312, 1110. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 1.32–2.19 (10 H, m, 5 CH_2), 2.40 (3 H, s, Me), 2.44–2.52 (1 H, m, 1 CH), 2.91–3.02 (1 H, m, CH), 5.60 (1 H, s, CH), 7.30–7.44 (5 H, m, 5 CH), 7.57 (2 H, d, ^3J = 6.2 Hz, 2 CH), 7.68 (2 H, d, ^3J = 6.5 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 23.1 (Me), 25.4, 26.9, 27.4, 30.1, 32.6 (CH_2), 49.1, 67.1, 113.1, 126.37 (CH), 127.9 (2 CH), 128.9 (2 CH), 129.7 (2 CH), 131.0 (2 CH), 132.9, 134.8, 136.2, 139.2, 225.7 (C). MS: *m/z* (%) = 443 (M^+, 1), 288 (25), 197 (61), 155 (43), 77 (100), 54 (39). Anal. Calcd (%) for (443.64): C, 62.27, H, 5.68, N, 3.16, S, 21.68. Found: C, 62.51, H, 5.88, N, 3.34, S, 21.82.

4.1.7. 3-Benzylidene-6-phenyl-4-tosylthiomorpholine-2-thione (4g, $C_{24}H_{21}NO_2S_3$)

Pale yellow powder; M.P: 137–139°C. Yield: 0.40 g (89%). IR (KBr) (ν_{max}, cm^{-1}): 3026, 2971, 1541, 1338, 1315, 1122. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 2.41 (3 H, s, Me), 4.03 (1 H, dd, ^3J = 11.0 Hz, ^3J = 6.7 Hz, CH), 4.48 (1 H, dd, ^2J = 12.1 Hz, ^3J = 5.1 Hz, CH), 4.65 (1 H, dd, ^2J = 12.1 Hz, ^3J = 9.0 Hz, CH), 5.60 (1 H, s, CH), 7.17–7.26 (3 H, m, 3 CH), 7.29–7.43 (7 H, m, 7 CH), 7.58 (2 H, d, ^3J = 6.1 Hz, 2 CH), 7.69 (2 H, d, ^3J = 6.5 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 22.8 (Me), 51.1, 64.7, 112.7, 126.4, 126.7 (CH), 127.5 (2 CH), 128.2 (2 CH), 128.6 (2 CH), 129.4 (2 CH), 129.9 (2 CH), 131.2 (2 CH), 132.1, 134.1, 135.2, 138.2, 139.1, 223.7 (C). MS: *m/z* (%) = 451 (M^+, 4), 296 (22), 294 (57), 155 (44), 77 (100), 54 (48). Anal. Calcd (%) for (451.62): C, 63.83, H, 4.69, N, 3.10, S, 21.30. Found: C, 64.05, H, 4.87, N, 3.33, S, 21.52.

4.1.8. 3-Benzylidene-5,6-diphenyl-4-tosylthiomorpholine-2-thione (4h, $C_{30}H_{25}NO_2S_3$)

Pale yellow powder; M.P: 188–190°C. Yield: 0.37 g (91%). IR (KBr) (ν_{max}, cm^{-1}): 3067, 2975, 1578, 1344, 1289, 1102. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H = 2.38 (3 H, s, Me), 4.01 (1 H, d, ^3J = 7.2 Hz, CH), 5.12 (1 H, d, ^3J = 7.2 Hz, CH), 5.78 (1 H, s, CH), 7.18–7.55 (17 H, m, 17 CH), 7.6 (2 H, d, ^3J = 6.9 Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 23.7 (Me), 50.3, 69.2, 112.7, 125.2, 126.5 (CH), 127.0 (2 CH), 127.2 (2 CH), 128.1 (CH), 128.2 (2 CH), 128.6 (2 CH), 129.1 (2 CH), 129.5 (2 CH), 129.6 (2 CH), 131.3 (2 CH), 132.4, 134.3, 136.2, 138.2, 139.8, 140.2, 144.8, 222.6 (C). MS: *m/z* (%) = 527 (M^+, 6), 450 (9), 373 (19),

155 (51), 131 (69), 77 (100). Anal. Calcd (%) for (527.72): C, 68.28, H, 4.78, N, 2.65, S, 18.23. Found: C, 68.41, H, 4.84, N, 2.80, S, 18.44.

4.1.9. 3-Benzylidene-6-methyl-6-phenyl-4-tosylthiomorpholine-2-thione (4i, $C_{25}H_{23}NO_2S_3$)

Yellow powder; M.P: 167–169°C. Yield: 0.33 g (72%). IR (KBr) (ν_{max}, cm^{-1}): 3051, 2973, 1551, 1346, 1312, 1112. ^1H NMR (500.1 MHz, $CDCl_3$): $\delta_H = 1.82$ (3 H, s, Me), 2.42 (3 H, s, Me), 4.19 (1 H, d, $^2J = 10.1$ Hz, CH), 4.41 (1 H, d, $^2J = 10.1$ Hz, CH), 5.01 (1 H, s, CH), 7.28–7.46 (10 H, m, 10 CH), 7.60 (2 H, d, $^3J = 6.2$ Hz, 2 CH), 7.68 (2 H, d, $^3J = 6.5$ Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta_C = 23.5$, 28.1 (Me), 55.9 (C), 68.1 (CH_2), 112.1, 126.3 (CH), 126.5 (2 CH), 127.1 (CH), 127.9 (2 CH), 128.4 (2 CH), 128.6 (2 CH), 129.8 (2 CH), 130.4 (2 CH), 132.1, 134.1, 136.2, 139.0, 151.2, 225.2 (C). MS: *m/z* (%) = 465 (M^+, 2), 278 (17), 192 (56), 155 (57), 91 (43), 77 (100). Anal. Calcd (%) for (465.64): C, 64.49, H, 4.98, N, 6.87, S, 20.66. Found: C, 64.60, H, 5.22, N, 7.09, S, 20.76.

4.1.10. 5-Benzyl-3-butylidene-4-tosylthiomorpholine-2-thione (4j, $C_{22}H_{25}NO_2S_3$)

Yellow powder; M.P: 83–85°C. Yield: 0.34 g (79%). IR (KBr) (ν_{max}, cm^{-1}): 3025, 2961, 1553, 1341, 1319, 1108. ^1H NMR (500.1 MHz, $CDCl_3$): $\delta_H = 0.85$ (3 H, t, $^3J = 6.0$ Hz, Me), 1.48–1.60 (2 H, m, CH_2), 2.33–2.41 (2 H, m, CH_2), 2.44 (3 H, s, Me), 2.76 (1 H, *dd*, $^2J = 12.1$ Hz, $^3J = 5.7$ Hz, CH), 2.91 (1 H, *dd*, $^2J = 12.1$ Hz, $^3J = 8.7$ Hz, CH), 3.11 (1 H, *dd*, $^2J = 9.8$ Hz, $^3J = 5.8$ Hz, CH), 3.31 (1 H, *dd*, $^2J = 9.8$ Hz, $^3J = 8.0$ Hz, CH), 3.76–3.85 (1 H, m, CH), 4.76 (1 H, t, $^3J = 6.5$ Hz, CH), 7.19–7.30 (5 H, m, 5 CH), 7.39 (2 H, d, $^3J = 6.2$ Hz, 2 CH), 7.68 (2 H, d, $^3J = 6.3$ Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta_C = 15.0$, 22.1 (Me), 25.4, 28.1, 40.1, 43.7 (CH_2), 65.1, 108.2, 126.1 (CH), 127.9 (2 CH), 128.9 (2 CH), 129.4 (2 CH), 131.3 (2 CH), 134.1, 134.7, 139.0, 139.3, 224.1 (C). MS: *m/z* (%) = 431 (M^+, 1), 276 (18), 274 (50), 155 (43), 91 (100), 77 (55). Anal. Calcd (%) for (431.63): C, 61.22, H, 5.84, N, 3.25, S, 22.28. Found: C, 61.46, H, 6.07, N, 3.46, S, 22.43.

4.1.11. 5-Benzyl-3-(furan-2-ylmethylene)-4-tosylthiomorpholine-2-thione (4k, $C_{23}H_{21}NO_3S_3$)

Yellow powder; M.P: 100–102°C. Yield: 0.51 g (90%). IR (KBr) (ν_{max}, cm^{-1}): 3035, 2978, 1647, 1548, 1341, 1308, 1111. ^1H NMR (500.1 MHz, $CDCl_3$): $\delta_H = 2.40$ (3 H, s, Me), 2.70 (1 H, dd, $^2J = 10.8$ Hz, $^3J = 6.0$ Hz, CH), 2.88 (1 H, *dd*, $^2J = 10.8$ Hz, $^3J = 9.0$ Hz, CH), 3.11 (1 H, dd, $^2J = 12.0$ Hz, $^3J = 4.9$ Hz, CH), 3.29 (1 H, *dd*, $^2J = 12.0$ Hz, $^3J = 8.5$ Hz, CH), 3.67–3.78 (1 H, m, CH), 5.67 (1 H, s, CH), 6.64 (1 H, t, $^3J = 6.0$ Hz, CH), 6.90 (1 H, d, $^3J = 6.0$ Hz, CH), 7.17–7.34 (5 H, m, 5 CH), 7.39 (2 H, d, $^3J = 6.7$ Hz, 2 CH), 7.68 (2 H, d, $^3J = 6.2$ Hz, 2 CH), 7.81 (1 H, d, $^3J = 6.1$ Hz, CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 22.1 (Me), 40.1, 44.5 (CH_2), 65.1, 97.9, 113.4, 114.7, 125.7 (CH), 127.7 (2 CH), 128.3 (2 CH), 129.4 (2 CH), 129.7 (2 CH), 134.5, 136.7, 137.2, 138.8 (C), 145.2 (CH), 148.1, 226.7 (C). MS: *m/z* (%) = 455 (M^+, 1), 300 (19), 221 (35), 155 (52), 91 (100), 67 (51). Anal. Calcd (%) for (455.61): C, 60.63, H, 4.65, N, 3.07, S, 21.11. Found: C, 60.82, H, 4.78, N, 3.26, S, 21.34.

4.1.12. 5-Benzyl-4-tosyl-3-((trimethylsilyl)methylene)thiomorpholine-2-thione (4l, $C_{22}H_{27}NO_2S_3Si$)

Yellow oil. Yield: 0.37 g (80%). IR (KBr) (ν_{max}, cm^{-1}): 3041, 2971, 1641, 1547, 1326, 1309, 1107. ^1H NMR (500.1 MHz, $CDCl_3$): $\delta_H = 0.03$ (9 H, s, 3 Me), 2.40 (3 H, s, Me), 2.69 (1 H, dd, $^2J = 11.8$ Hz, $^3J = 6.7$ Hz, CH), 2.88 (1 H, dd, $^2J = 11.8$ Hz, $^3J = 4.5$ Hz, CH), 3.11 (1 H, dd, $^2J = 11.0$ Hz, $^3J = 7.0$ Hz, CH), 3.38 (1 H, dd, $^2J = 11.0$ Hz, $^3J = 4.7$ Hz, CH), 4.03–4.12 (1 H, m, CH), 4.63 (1 H, s, CH), 7.188–7.34 (5 H, m, 5 CH), 7.34 (2 H, d, $^3J = 6.5$ Hz, 2 CH), 7.68 (2 H, d, $^3J = 6.2$ Hz, 2 CH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 1.5 (3 Me), 23.4 (Me), 40.1, 43.5 (CH_2), 64.1, 103.2, 126.1 (CH), 128.2 (2 CH), 128.9 (2 CH), 129.1 (2 CH), 129.3 (2 CH), 134.2, 138.1, 139.2, 152.3, 224.7 (C). MS: m/z (%) = 461 (M^+, 1), 306 (22), 221 (34), 155 (46), 91 (100), 77 (68). Anal. Calcd (%) for (461.73): C, 57.23, H, 5.89, N, 3.03, S, 20.83, Si, 6.08. Found: C, 57.42, H, 6.05, N, 3.21, S, 20.97, Si, 6.22.

Disclosure statement

No potential conflict of interest was reported by the author.

References

[1] Li H, Liu J, Yan B, et al. New domino approach for the synthesis of 2,3-disubstituted benzo[b]furans via copper-catalyzed multi-component coupling reactions followed by cyclization. Tetrahedron Lett. 2009;50:2353–2357.
[2] Yoo WJ, Lia CJ. Copper-catalyzed four-component coupling between aldehydes, amines, alkynes, and carbon dioxide. Adv Synth Catal. 2008;350:1503–1506.
[3] Patil NT, Raut VS. Cooperative catalysis with metal and secondary amine: synthesis of 2-substituted quinolines via addition/cycloisomerization cascade. J Org Chem. 2010;75:6961–6964.
[4] Pappo R, Collins PW. Synthesis of prostaglandin analogs by novel 1,4 addition reactions. Tetrahedron Lett. 1972;13:2627–2630.
[5] Bruhn M, Brown CH, Collins PW, et al. Synthesis and properties of 16-hydroxy analogs of PGE_2. Tetrahedron Lett. 1976;17:235–238.
[6] Schwartz J, Carr DB, Hansen RT, et al. Nickel-catalyzed conjugate addition of alkynyl groups to alpha, beta-unsaturated ketones. J Org Chem. 1980;45:3053–3061.
[7] Sinclair JA, Molander GA, Brown HC. Conjugate addition of B-1-alkynyl-9-borabicyclo[3.3.1]-nonanes to alpha, beta-unsaturated ketones. A convenient synthesis of gamma, delta-acetylenic ketones. J Am Chem Soc. 1977;99:954–956.
[8] Kim S, Lee JM. Trialkylsilyl triflate promoted conjugate addition of alkynylzinc compounds to α,β-enones. Tetrahedron Lett. 1990;31:7627–7630.
[9] Hooz J, Layton RB. Reaction of diethylalkynylalane reagents with conjugated enones. 1,4 addition of acetylene units to simple: alpha, beta-unsaturated ketones. J Am Chem Soc. 1971;93:7320–7322.
[10] Zhang X, Zhang WZ, Shi LL, et al. Ligand-free Ag(I)-catalyzed carboxylative coupling of terminal alkynes, chloride compounds, and CO_2. Tetrahedron. 2012;68:9085–9089.
[11] Ranjan A, Mandal A, Yerande SG, et al. Asymmetric alkynylation/hydrothiolation cascade: enantioselective synthesis of thiazolidine-2-imines from imine, acetylene and isothiocyanate. Chem Commun. 2015;51:14215–14218.
[12] Guo M, Li D, Zhang Z. Novel synthesis of 2-oxo-3-butynoates by copper-catalyzed cross-coupling reaction of terminal alkynes and monooxalyl Chloride. J Org Chem. 2003;68:10172–10174.
[13] Meldal M, Tornøe CW. Cu-Catalyzed Azide−alkyne Cycloaddition. Chem Rev. 2008;108:2952.
[14] Hein JE, Tripp JC, Krasnova LB, et al. Copper(I)-catalyzed cycloaddition of organic azides and 1-iodoalkynes. Angew Chem Int Ed. 2009;48:8018–8021.

[15] Kolb HC, Finn MG, Sharpless KB. Click chemistry: diverse chemical function from a few good reactions. Angew Chem Int Ed. 2001;40:2004–2021.
[16] Himo F, Lovell T, Hilgraf R, et al. Copper(I)-catalyzed synthesis of Azoles. DFT study predicts unprecedented reactivity and intermediates. J Am Chem Soc. 2005;127:210–216.
[17] Knöpfel TF, Carreira EM. The first conjugate addition reaction of terminal alkynes catalytic in copper: conjugate addition of alkynes in water. J Am Chem Soc. 2003;125:6054–6055.
[18] Fischer C, Carreira EM. Direct addition of TMS-acetylene to aldimines catalyzed by a simple, commercially available Ir(I) complex. Org Lett. 2001;3:4319–4321.
[19] Frantz DE, Fassler R, Carreira EM. Facile enantioselective synthesis of propargylic alcohols by direct addition of terminal alkynes to aldehydes. J Am Chem Soc. 2000;122:1806–1807.
[20] Lu Y, Johnstone TC, Arndtsen BA. Hydrogen-bonding asymmetric metal catalysis with α-amino acids: a simple and tunable approach to high enantioinduction. J Am Chem Soc. 2009;131:11284–11285.
[21] Yavari I, Ghazanfarpour-Darjani M, Nematpour M. Copper-catalyzed tandem synthesis of 2-(sulfonylimino)alkanamides from N-sulfonylketenimines and alkyl isocyanides. Tetrahedron let. 2015;56:2416–2417.
[22] Khalaj M, Ghazanfarpour-Darjani M, Barat-Seftejani F, et al. Novel catalytic three-component reaction between a terminal alkyne, sulfonyl azide, and o-methyl oxime. Synlett. 2017;28:1445–1448.
[23] Ramanathana D, Pitchumani K. Copper(I)-Y zeolite-catalyzed regio- and stereoselective [2+2+2] cyclotrimerization cascade: an atom- and step-economical synthesis of pyrimido[1,6-a]quinolone. J Org Chem. 2015;80:10299–10308.
[24] Lu P, Wang Y. The thriving chemistry of ketenimines. Chem Soc Rev. 2012;41:5687–5705.
[25] Chauhan DP, Varma SJ, Vijeta A, et al. A 1,3-amino group migration route to form acrylamidines. Chem Commun. 2014;50:323–325.
[26] Ghazanfarpour-Darjani M, Babapour-Kooshalshahi M, Mousavi-Safavi SM, et al. Copper-catalyzed domino addition–cyclization reaction between terminal alkynes, carbon disulfide, and oxiranes. Synlett. 2016;27:259–261.
[27] Samzadeh-Kermani A. Silver salt catalyzed synthesis of 1,4-oxathian-3-imine derivatives. Tetrahedron. 2016;72:5301–5304.
[28] Samzadeh-Kermani A. Copper catalyzed synthesis of thiomorpholine derivatives: A new entry of multicomponent reaction between terminal alkynes, isothiocyanates, and aziridines. J Heterocyclic Chem. 2019. doi:10.1002/jhet.3418
[29] Samzadeh-Kermani A. Synthesis of benzyl hydrazine derivatives via amination of benzylic C(sp3)–H bonds with dialkyl azodicarboxylates. New J Chem. 2018;42:4766–4772.
[30] Samzadeh-Kermani A. Copper-catalyzed C–N bond formation using dialkyl azodicarboxylate as the amination reagent. Tetrahedron Lett. 2016;57:463–465.
[31] Meinwald J, Labana SS, Chadha MS. Peracid reactions. III.1 The oxidation of Bicyclo [2.2.1]heptadiene2. J Am Chem Soc. 1963;85:582–585.
[32] Kumaraswamy G, Ankamma K, Pitchaiah A. Tandem epoxide or aziridine ring opening by azide/copper catalyzed [3+2] cycloaddition: efficient synthesis of 1,2,3-triazolo α-hydroxy or α-tosylamino functionality motif. J Org Chem. 2007;72:9822–9825.
[33] Ando T, Kano D, Minakata S, et al. Iodine-catalyzed aziridination of alkenes using Chloramine-T as a nitrogen source. Tetrahedron. 1998;54:13485–13494.