

Communication

Highly Efficient 1-Iodination of Terminal Alkynes Catalyzed by Inorganic or Organic Bases

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Abstract: 1-Iodoalkynes are one type of the most reactive and the most practical intermediates in organic synthesis. Here, some facile and efficient methods for the 1-iodination of terminal alkynes are developed using N-iodosuccinimide (NIS) as an iodination reagent and some inexpensive mild bases as catalysts. K_2CO_3 and 4-dimethylaminopyridine (DMAP) have been proven to be the most suitable inorganic and organic bases, succeeding in 17 examples with excellent yields (up to 99%).

Keywords: base catalysis; terminal alkyne iodination; transition-metal-free; oxidant-free

1. Introduction

Owing to the unique structure of the carbon–carbon triple bond and the carbon–halogen bond, 1-halogenated alkynes are regarded as difunctional molecules and are widely used in organic synthesis [1,2]. Under the assistance of transition metal catalysts, 1-halogenated alkynes can form many key intermediates containing C–C, C–O, or C–N bonds and then transform into various highly functional compounds through coupling reactions [3,4]. Among all 1-halogenated alkynes, 1-iodoalkynes are the most reactive and the most practical building blocks; they have been attracting more and more attention in the organic chemistry domain.

To date, significant progress has been made in the synthesis of 1-iodized alkynes. As summarized in Table 1, many substances have been proven to be feasible iodine reagents, including elemental iodine [5–10], KI [11–13], NaI [14], ZnI_2 [15,16], tetrabutylammonium iodide (TBAI) [17,18], bis (*sym*-collidine)iodine (I) hexafluorophosphate [19], Cl_4 [20], hexamethylene bis (N-methylimidazolium) bis (dichloroiodate) ionic liquid (IL) [21], N-iodomorpholine [22], N-iodosuccinimide (NIS) [23–27], etc. Based on the concept of modern green synthetic chemistry, however, it is hard for the reactions using these iodine reagents to meet the requirements of cleanness, safety, economy, and environmental friendliness, especially when conducting large-scale production in industry. For example, elemental iodine is volatile and poisonous; N-iodomorpholine and $(collidine)_2I^+PF_6^-$ are of relatively high cost; KI and TBAI usually need transition metals or strong oxidants (tBHP, $Me_3SiOOSiMe_3$, $PhI(OAc)_2$, $KHSO_5$ (oxone), etc.) to activate; and Cl_4 and NIS are often used with strong bases or precious metals. Therefore, the development of mild and economic iodization methods for the synthesis of 1-iodized alkynes is still to be accomplished. In recent years, more and more researchers have begun to pay attention to NIS and have found it to be a promising iodine reagent since it delivers higher functional group tolerance and chemical regional selectivity. However, the reported catalysts for the iodination of alkynes by NIS were either strong bases like KOH [24] and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) [25] or precious metals like $Ph_3PAuNTf_2$ [23], $AgNO_3$ [24], $[Au(SiPr)(NEt_3)][HF_2]$ [26], and nano-Ag/g- C_3N_4 [27]. In light of this, our group has undertaken some exploration in this field. First, we found that $\gamma-Al_2O_3$ could mediate NIS' reaction with terminal alkynes in the presence of a 4 Å molecular sieve, developing a non-noble metal amphoteric oxide catalysis route [28].



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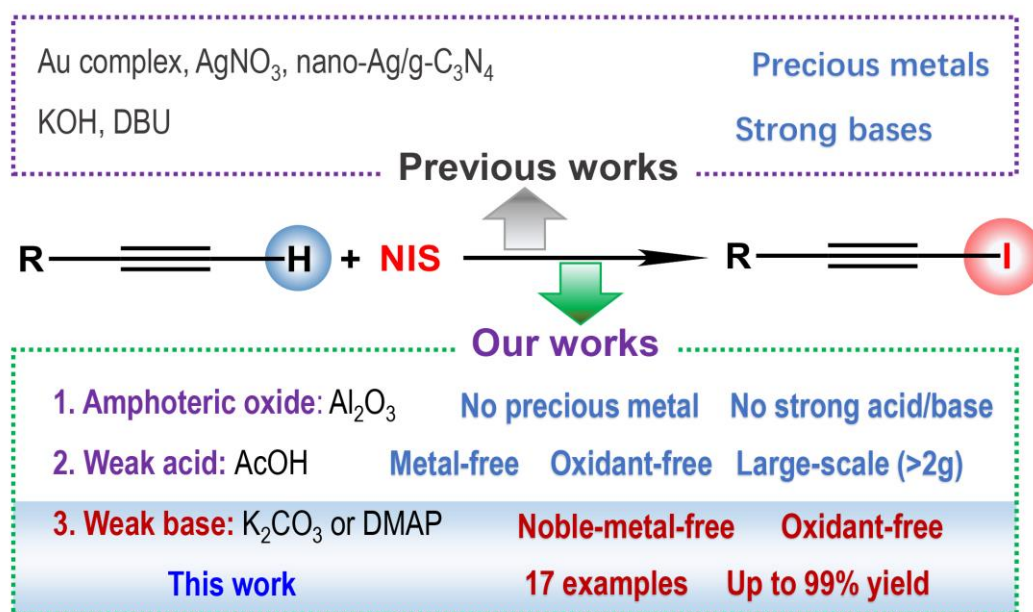


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Table 1. Reported methods for iodination of terminal alkynes.

Year	Iodine Source	Catalyst	Solvent/Condition	Ref.
1933	I ₂	—	Liquid NH ₃	Vaughn [5]
1988	I ₂	CuI, K ₂ CO ₃ or Na ₂ CO ₃ , TBAC	DMF	Jeffery [6]
1995	I ₂	EtMgBr	THF	Rao [7]
2007	I ₂	Cs ₂ CO ₃ , KOH	THF-HMPA	He [8]
2008	I ₂	DMAP	CH ₂ Cl ₂	Meng [9]
2009	I ₂	CuI, Et ₃ N, TBAB	H ₂ O	Chen [10]
2007	KI	CuI, Et ₃ N, PhI(OAc) ₂	MeCN	Yan [11]
2010	KI	tBHP	MeOH	Reddy [12]
2019	KI	CuSO ₄ · 5H ₂ O, BPDS	NaOAc buffer	Ferris [13]
2000	NaI	—	MeOH divided cell	Nishiguchi [14]
1991	CuI or ZnI ₂	Me ₃ SiOOSiMe ₃	THF	Casarini [15]
2018	ZnI ₂	TBN, Et ₃ N	CHCl ₃	Chen [16]
2017	TBAI	PhI(OAc) ₂	MeCN	Liu [17]
2017	TBAI	KHSO ₅	Water	Srujana [18]
1995	(collidine) ₂ I ⁺ PF ₆ [−]	—	CH ₂ Cl ₂	Brunel [19]
2001	Cl ₄	KOH, 18-crown-6	Benzene	Abele [20]
2013	HMBMIBDCI IL	DBU	THF	Nouzarian [21]
2009	N-iodomorpholine	CuI	THF	Hein [22]
2012	NIS	Ph ₃ PAuNTf ₂	CH ₂ Cl ₂	Starkov [23]
2013	NIS	AgNO ₃ or KOH	Acetone/H ₂ O or MeOH	Nösel [24]
2014	NIS	DBU	MeCN	Li [25]
2016	NIS	[Au(SIPr)(NEt ₃)] [HF ₂]	Toluene	Gómez-Herrera [26]
2017	NIS	Ag/g-C ₃ N ₄	Acetone	Shi [27]
2020	NIS	γ-Al ₂ O ₃ , 4 Å MS	MeCN	Our group [28]
2020	NIS	AcOH	MeCN	Our group [29]

Then, we noticed that AcOH could also efficiently activate the iodination of terminal alkynes with NIS, suggesting a metal-free acid catalysis method [29]. Herein, new methods for the iodination of terminal alkynes with NIS under K₂CO₃ and 4-dimethylaminopyridine (DMAP) are reported. Since these iodination methods are catalyzed by weak bases, they are good complements to our previous procedures, in which NIS was activated by amphoteric oxide and weak acid, as shown in Scheme 1.

**Scheme 1.** Catalysts for 1-iodination of terminal alkynes with NIS.

2. Results and Discussion

2.1. Screening of Reaction Conditions

2.1.1. Inorganic Alkali Activators

To screen out the potentially applicable inorganic base catalysts in industry, some familiar inexpensive weak bases— Na_2CO_3 , K_2CO_3 , NaHCO_3 and KHCO_3 —were selected as candidates for the 1-iodination of terminal alkynes with NIS. The results of the screening tests (Table 2) indicated that K_2CO_3 had a better catalytic effect on the reactions. In methanol, 1.5 mol% of K_2CO_3 (0.03 equiv.) could effectively activate NIS, reacting with phenylacetylene at 40 °C, obtaining 1-iodoalkyne (**1b**) with a yield of 97.6% in 10 min (Table 2, entry 18). In view of the fact that K_2CO_3 is almost insoluble in methanol, an equivalent amount of tetrabutylammonium bromide (TBAB) was added to promote the catalysis procedure. As expected, the yield increased to 99% in 10 min at 40 °C, and no new byproduct was generated. So, the optimum reaction conditions were selected as follows: phenylacetylene (2 mmol, 1.0 eq.); NIS (1.1 equiv.); K_2CO_3 (0.03 equiv.); TBAB (0.03 equiv.); CH_3OH (10 mL); 40 °C, 10 min.

Table 2. Screening of inorganic bases and condition optimization ^a.

$\text{1a} + \text{NIS} \xrightarrow[\text{Solvent, heat}]{\text{Inorganic base}} \text{1b}$

Entry	Inorganic Base	Base (Equiv.)	Solvent	T (°C)	T (Min)	Yield ^b (%)
1	—	0	MeCN	40	40	21.5 ^c
2	K_2CO_3	0.25	MeCN	40	40	30.6
3	Na_2CO_3	0.25	MeCN	40	40	28.4
4	NaHCO_3	0.25	MeCN	40	40	— ^d
5	KHCO_3	0.25	MeCN	40	40	— ^d
6	K_2CO_3	0.25	THF	40	40	— ^d
7	K_2CO_3	0.25	DMSO	40	40	80.3
8	K_2CO_3	0.25	DMF	40	40	84.0
9	K_2CO_3	0.25	MeOH	40	40	90.6
10	K_2CO_3	0.03	MeOH	40	40	92.5
11	K_2CO_3	0.06	MeOH	40	40	91.1
12	K_2CO_3	0.12	MeOH	40	40	89.3
13	K_2CO_3	0.5	MeOH	40	40	86.2
14	K_2CO_3	0.03	MeOH	20	40	87.5
15	K_2CO_3	0.03	MeOH	30	40	88.4
16	K_2CO_3	0.03	MeOH	50	40	94.7
17	K_2CO_3	0.03	MeOH	40	5	93.8
18	K_2CO_3	0.03	MeOH	40	10	97.6
19	K_2CO_3	0.03	MeOH	40	20	95.2
20	K_2CO_3	0.03	MeOH	40	30	94.0

^a Phenylacetylene (**1a**, 2 mmol); solvent (10 mL); NIS (1.1 equiv., 2.2 mmol). ^b Isolated yield. ^c Mixture of 1-iodoalkyne and other by products. ^d Hard to separate.

2.1.2. Organic Alkali Activators

The catalytic performance of Et_3N , DMAP, and DBU for target reaction was inspected under different conditions, as listed in Table 3. Based on our previous experience, CH_3CN and CH_3OH were selected as solvents. The results showed that 0.25 equivalent mole of Et_3N gave a yield of 87% in CH_3OH at 45 °C (Table 3, entry 7), 0.5 equivalent mole of Et_3N gave a yield of 83% in CH_3OH at 45 °C (Table 3, entry 16), and 0.25 equivalent mole of DMAP achieved a yield of 97% in CH_3CN at 45 °C (Table 3, entry 7). To obtain the highest yield, the optimum reaction conditions were selected as follows: phenylacetylene (2 mmol, 1.0 equiv.); NIS (1.1 equiv.); DMAP (0.25 equiv.); CH_3CN (10 mL); 45 °C, 4 h.

Table 3. Screening of organic bases and condition optimization ^a.

c1ccccc1C#C (2a) + NIS $\xrightarrow[\text{Solvent, heat}]{\text{Organic base}}$ c1ccccc1C#CI (2b)

Entry	Base (Equiv.)	Solvent	T (°C)	Yield ^b (%)
1	Et ₃ N (0.05)	CH ₃ CN	15	28
2	Et ₃ N (0.1)	CH ₃ CN	15	30
3	Et ₃ N (0.25)	CH ₃ CN	15	43
4	Et ₃ N (0.5)	CH ₃ CN	15	32
5	Et ₃ N (0.25)	CH ₃ OH	15	49
6	Et ₃ N (0.25)	CH ₃ OH	30	79
7	Et ₃ N (0.25)	CH ₃ OH	45	87
8	Et ₃ N (0.25)	CH ₃ OH	60	75
9	DBU (0.5)	CH ₃ CN	15	46
10	DBU (0.25)	CH ₃ CN	15	39
11	DBU (0.6)	CH ₃ CN	15	42
12	DBU (0.5)	CH ₃ CN	30	59
13	DBU (0.5)	CH ₃ CN	45	65
14	DBU (0.5)	CH ₃ OH	15	75
15	DBU (0.5)	CH ₃ OH	30	81
16	DBU (0.5)	CH ₃ OH	45	83
17	DMAP (0.5)	CH ₃ CN	15	71
18	DMAP (0.25)	CH ₃ CN	15	76
19	DMAP (0.1)	CH ₃ CN	15	68
20	DMAP (0.25)	CH ₃ CN	30	95
21	DMAP (0.25)	CH ₃ CN	45	97
22	DMAP (0.25)	CH ₃ CN	60	92
23	DMAP (0.25)	CH ₃ OH	45	85

^a Phenylacetylene (2a, 2 mmol); solvent (10 mL); NIS (1.1 equiv., 2.2 mmol). ^b Isolated yield.

2.2. Substrate Scope Analyses

To probe the versatility of the weak bases we proposed, 1-iodination of varying terminal alkynes is discussed, and the results are listed in Table 4. It can be seen that good-to-excellent yields are also obtained when the hydrogen on the benzene ring of phenylacetylene is substituted by an alkyl, haloalkyl, ester, nitrile, nitro, alkoxy, or halogen atom. In the case of the nitro-substituted phenylacetylene (Table 4, entry 6), the reaction gives 99% yield when catalyzed by inorganic weak base K₂CO₃. When the alkoxy is on position 2 or 4 of phenylacetylene (Table 4, entries 7 and 8), the yield can reach up to more than 90% under an inorganic or organic base catalyst. In the case of halogen F or Cl substitution (Table 4, entries 9–14), the position of the halogen atom causes a limited influence on the yields, and on the whole, inorganic base K₂CO₃ gives a higher yield than organic base DMAP. In addition, the present catalysts are applicable to the 1-iodination reaction of many other terminal alkynes that contain no benzene ring, such as straight-chain alkyne (Table 4, entry 15), ethynylthiophene (Table 4, entry 16), and ethynylpyridine (Table 4, entry 17). All the mentioned substrates can transfer into the corresponding 1-iodination products in satisfactory yields, suggesting that the catalysis strategies have good universality.

As for the reaction mechanism, we speculated that the NIS first formed an intermediate with the alkyne group through N atom; then, the alkali catalysts, K₂CO₃ or DMAP, took the acidic H away and, at the same time, promoted the removal of succinimide. The exact mechanism was still to be confirmed by further experiments.

Table 4. 1-Iodination of different terminal alkyne substrates.

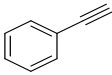
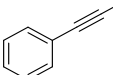
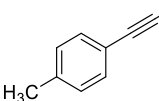
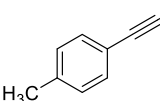
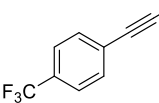
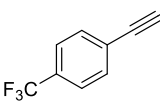
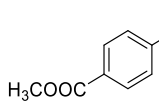
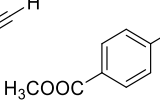
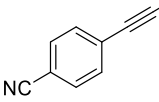
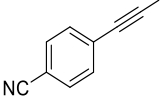
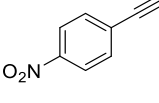
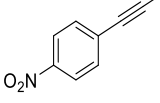
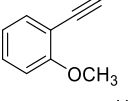
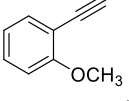
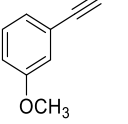
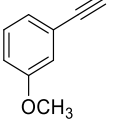
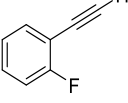
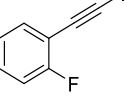
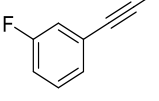
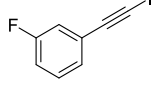
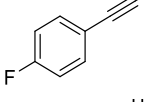
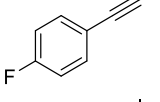
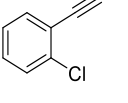
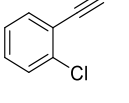
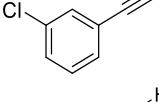
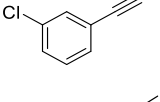
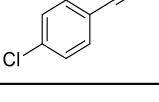
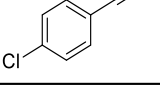
$\text{R}-\text{C}\equiv\text{CH} + \text{NIS} \xrightarrow[\text{Solvent, heat}]{\text{Base}} \text{R}-\text{C}\equiv\text{CI}$ 3a 3b				
Entry	Substrate	Product	Yield Under K ₂ CO ₃ ^a /%	Yield Under DMAP ^b /%
1			99	97
2			87	92
3			87	82
4			89	80
5			89	94
6			99	91
7			90	74
8			85	91
9			87	76
10			84	72
11			90	77
12			85	81
13			88	72
14			92	73

Table 4. Cont.

$\text{R}-\text{C}\equiv\text{C}-\text{H} + \text{NIS} \xrightarrow[\text{Solvent, heat}]{\text{Base}} \text{R}-\text{C}\equiv\text{C}-\text{I}$ 3a 3b				
Entry	Substrate	Product	Yield Under K ₂ CO ₃ ^a /%	Yield Under DMAP ^b /%
15			92	86
16			87	80
17			98	88

^a Substrates (**3a**, 2 mmol): NIS (1.1 equiv.); K₂CO₃ (0.03 equiv.); TBAB (0.03 equiv.); CH₃OH (10 mL); 40 °C, 10 min. ^b Substrates (**3a**, 2 mmol): NIS (1.1 equiv.); DMAP (0.25 equiv.); CH₃CN (10 mL); 45 °C, 4 h.

2.3. Characterization of Products

1-Iodo-2-phenylacetylene (3b-1): Yellow oily liquid. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.41–7.39 (m, 2H), 7.27–7.24 (m, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 132.42, 128.91, 128.35, 123.44, 94.25, 6.61.

1-(Iodoethynyl)-4-methylbenzene (3b-2): Colorless oily liquid. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.33 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 139.12, 132.31, 129.10, 120.46, 94.36, 21.66, 5.14.

1-(Iodoethynyl)-4-(trifluoromethyl)benzene (3b-3): White solid. m.p. 118–120 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.59–7.52 (m, 4H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 132.75, 130.62 (q, *J* = 32.8 Hz), 127.18, 125.34 (q, *J* = 3.8 Hz), 123.94 (q, *J* = 273.3 Hz), 92.96, 10.31.

Methyl 4-(iodoethynyl)benzoate (3b-4): White solid. m.p. 133–135 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.98 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 3.91 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 166.52, 132.41, 130.15, 129.54, 128.02, 93.58, 52.43, 10.60.

4-(Iodoethynyl)benzonitrile (3b-5): White solid. m.p. 171.0–171.6 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.60 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 2H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 132.99, 132.07, 128.18, 118.38, 112.24, 92.67, 13.20.

1-(Iodoethynyl)-4-nitrobenzene (3b-6): Light yellow powdery solid. m.p. 183.5–187.2 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.18 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 2H).

1-(Iodoethynyl)-2-methoxybenzene (3b-7): Light yellow oily liquid. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.40 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.31–7.27 (m, 1H), 6.92–6.86 (m, 2H), 3.88 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 160.97, 134.40, 130.29, 120.35, 112.50, 110.61, 90.41, 55.84, 9.60.

1-(Iodoethynyl)-3-methoxybenzene (3b-8): White solid. m.p. 50.3–51.5 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.24–7.20 (m, 1H), 7.05–7.02 (m, 1H), 6.97–6.96 (m, 1H), 6.90–6.87 (m, 1H), 3.79 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 159.26, 129.41, 124.96, 124.40, 117.15, 115.68, 94.16, 55.39, 6.39.

1-Fluoro-2-(iodoethynyl)benzene (3b-9): Light yellow oily liquid. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.45–7.41 (m, 1H), 7.33–7.28 (m, 1H), 7.11–7.04 (m, 2H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 163.83 (d, *J* = 253 Hz), 134.31 (d, *J* = 1.3 Hz), 130.62 (d, *J* = 8.0 Hz), 123.99 (d, *J* = 3.7 Hz), 115.61 (d, *J* = 20.8 Hz), 112.01 (d, *J* = 15.8 Hz), 87.48, 12.01 (d, *J* = 3.2 Hz).

1-Fluoro-3-(iodoethynyl)benzene (3b-10): Light yellow oily liquid. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.30–7.20 (m, 2H), 7.14–7.11 (m, 1H), 7.04–7.01 (m, 1H). ¹³C NMR (CDCl₃,

100 MHz): δ (ppm) 162.30 (d, J = 248 Hz), 129.94 (d, J = 8.7 Hz), 128.35 (d, J = 3.1 Hz), 125.19 (d, J = 9.5 Hz), 119.26 (d, J = 23 Hz), 116.40 (d, J = 21.3 Hz), 92.99 (d, J = 3.4 Hz), 8.40.

1-Fluoro-4-(iodoethynyl)benzene (3b-11): Light brown oily liquid. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 7.44–7.40 (m, 2H), 7.03–6.98 (m, 2H). ^{13}C NMR (CDCl_3 , 100 MHz): δ (ppm) 162.80 (d, J = 251.4 Hz), 134.35 (d, J = 8.6 Hz), 119.52 (d, J = 3.5 Hz), 115.65 (d, J = 22.3 Hz), 93.14, 6.44.

1-Chloro-2-(iodoethynyl)benzene (3b-12): Yellow oil. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 7.47 (dd, J = 7.6, 2.0 Hz, 1H), 7.39 (dd, J = 8.0, 1.2 Hz, 1H), 7.28–7.19 (m, 2H). ^{13}C NMR (CDCl_3 , 100 MHz): δ (ppm) 136.77, 134.26, 129.87, 129.31, 126.47, 123.29, 90.99, 12.50.

1-Chloro-3-(iodoethynyl)benzene (3b-13): Light brown oily liquid. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 7.42–7.41 (m, 1H), 7.33–7.29 (m, 2H), 7.26–7.22 (m, 1H). ^{13}C NMR (CDCl_3 , 100 MHz): δ (ppm) 134.12, 132.28, 130.52, 129.54, 129.21, 125.02, 92.81, 8.88.

1-Chloro-4-(iodoethynyl)benzene (3b-14): Pale yellow solid. m.p. 83.5–85.8 °C. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 7.36 (d, J = 8.8 Hz, 2H), 7.29 (d, J = 8.8 Hz, 2H). ^{13}C NMR (CDCl_3 , 100 MHz): δ (ppm) 135.04, 133.66, 128.73, 121.96, 93.10, 7.86.

1-Iodo-1-dodecyne (3b-15): Pale yellow oily liquid. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 2.35 (t, J = 7.0 Hz, 2H), 1.51–1.49 (m, 2H), 1.29–1.26 (m, 14H), 0.88–0.86 (m, 3H).

3-Iodothiophenylthiophene (3b-16): Pale yellow solid. m.p. 44.2–45.8 °C. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 8.53 (dd, J = 2.8, 1.2 Hz, 1H), 7.71 (dd, J = 5.0, 2.8 Hz, 1H), 7.68 (dd, J = 5.0, 1.2 Hz, 1H).

3-Iodothiophenylpyridine (3b-17): Yellowish brown powdery solid. m.p. 132.8–136.6 °C. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 8.67 (dd, J = 2.0, 1.2 Hz, 1H), 8.53 (dd, J = 4.8, 1.6 Hz, 1H), 7.71 (dt, J = 8.0, 2.0 Hz, 1H), 7.27–7.23 (m, 1H).

3. Material and Method

3.1. Instruments and Reagents

An AVANCE III HD 400 MHz NMR Spectrometer (Bruker, Fällanden, Switzerland), a RE-52A rotary evaporator (Shanghai Yarong Biochemical Instrument Factory, Shanghai, China), a Ze-7 hidden box UV analyzer (Shanghai Jiapeng Technology Co., LTD., Shanghai, China), and a YTR-3 melting point meter (Tianjing Tiantianfa Co., LTD., Tianjing, China) were used in the preparation and characterization of target compounds. All reagents are of analytical grade.

3.2. Synthesis of Iodide Alkynes

The terminal alkyne substrates (1.0 equiv., 2.0 mmol) were dissolved in a 50 mL round-bottomed flask with 10 mL organic solvent, followed by adding a certain amount of alkali and NIS (1.1 equiv., 2.2 mmol, 495.0 mg). The mixture was heated and stirred at a certain temperature, and the reaction was monitored via TLC. After the reaction, the reaction was quenched with saturated sodium thiosulfate aqueous solution. The reaction liquid was then extracted with ethyl acetate, washed with saturated salt water, dried with anhydrous sodium sulfate, and filtrated and concentrated via reduced-pressure distillation, obtaining the crude product. The crude product was finally separated and purified via silica gel column chromatography, using petroleum ether/ethyl acetate as the eluent. The optimal reaction conditions were as follows: (1) K_2CO_3 method: Substrates (2 mmol); NIS (1.1 equiv.); K_2CO_3 (0.03 equiv.); TBAB (0.03 equiv.); CH_3OH (10 mL); 40 °C, 10 min. (2) DMAP method: Substrates (2 mmol); NIS (1.1 equiv.); DMAP (0.25 equiv.); CH_3CN (10 mL); 45 °C, 4 h.

4. Conclusions

In summary, we have demonstrated two simple and efficient methods by which to prepare 1-iodide alkynes via the reaction of terminal alkynes with N-iodosuccinimide (NIS) using the inorganic weak base K_2CO_3 or the organic weak base DMAP as catalysts. The preparation methods are applicable to a variety of terminal alkynes, including aromatic or

substituted aromatic alkynes, aliphatic alkynes, ethynylthiophene, ethynylpyridine, and so on, affording good-to-excellent yields for the 17 substrates selected in the present work. Compared to the existing methods, which used precious metals, strong bases, or oxidants, our methods are safer, greener, more efficient, and more competitive in terms of preparation costs.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/catal14090610/s1>: ¹H NMR and ¹³C NMR spectra of the products can be found online.

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