INTRODUCTION

Carbonyl derivatives seize immense recognition in the area of synthetic organic chemistry due to their appearance in vital molecular scaffolds [1-4]. The traditionally used easy accessible approaches for their preparation refer to the hydration of alkynes [5]. The hydration protocol has customarily been accomplished by employing mercury based catalyst; whereas, by virtue of its affirmed hazardous characteristics restricts exercising the mercury complexes in chemical transformation [6]. In order to address the environmental benign concepts, in the past decades several research groups generously have contributed a series of surrogate protocols based upon transition-metal complexes. It has been well-investigated that multiple transition-metal based complexes namely Ir [7], Ag [8], Rh [9], Pd [10], Cu [11], Pt [12], Fe [13], Ru [14], Bi [15], Co [16], Au [8], Sn-W [17] could serve as the effective catalytic systems for this transformation to accomplish adeptly. Moreover, a metal-free mild and convenient protocol has been devised using catalytic amounts of trifluoromethane sulphonic acid and the reaction proceeds via Markovnikov-like hydration of alkynes [18].

In this regard, it is also remarkable that some of the Brønsted acid could perform well as catalyst to achieve this purpose [19,20]. Although, these reported approaches are quite well-competent for the preparation of carbonyl derivatives; whereas, many of these methods experience deviations from the ideal chemical transformations such as limited substrate tolerance, overload of aqueous acidic conditions and requirements of expensive transition metal complexes as catalyst (Scheme-I). Hence, the development of surrogate facile approaches may lead toward beneficial application in industrial and academic research. In this report, a simple and easy to perform mild approach is addressed for the preparation of acetophenone derivative by employing catalytic molecular iodine in the presence of N-methyl morpholine.

EXPERIMENTAL

All reagents and starting materials were availed from the commercial suppliers (Alfa-Aesar, Sigma-Aldrich, Merck, SD Fine chemicals, HI Media) and employed without prior purifi-

Scheme-I: Approaches toward hydration of alkynes
cation unless otherwise mentioned. Experiments were executed in 10 mL round bottom flask equipped with magnetic stirrer. Solvents utilized for extraction and purification purposes were thoroughly distilled prior to use. Thin-layer chromatography (TLC) was conducted on TLC plates purchased from Merck.

Products were identified by soaking in KMnO₄ staining solution followed by heating or with UV light (λ = 254 nm). The purified products were obtained by CombiFlash MPLC. All HRMS spectra are produced using 6545 QTOF LC/MS, Agilent instrument equipped with an auto sampler in EI-QTOF method in acetonitrile solvent. ¹H (¹³C) NMR spectra were obtained at 400 (100) MHz on a Brucker spectrometer employing CDCl₃ as solvent. The ¹H & ¹³C chemical shifts were referenced to residual solvent signals at δₑₛₑｃ 7.26/77.28 (CDCl₃) relative to TMS as internal standards.

**Synthesis of acetonophene derivatives (2a-q):** A 10 mL reaction flask was charged with terminal alkenes 1a-q (1.0 mmol), I2 (0.3 mmol) and N-methyl morpholine (1.0 mmol) in DMSO (2.0 mL) and then the reaction mixture was heated at 120 °C for 16 h. After completion of the reaction (progress was monitored by TLC; SiO₂, hexane/EtOAc = 9:1), the reaction mixture was quenched with saturated sodium thiosulphate solution, diluted with water (20 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was dried over anhydrous Na₂SO₄. Solvent was removed under reduced pressure and the remaining mixture was purified over silica gel column chromatography using hexane/EtOAc = 4:1 as an eluent to obtain the desired products 2a-q in high yields.

**Acetophenone (2a):** [21]: Colourless liquid, Rf = 0.7 (SiO₂, hexane/EtOAc = 9:1); yield: 103 mg (85%); ¹H NMR (600 MHz, CDCl₃): δ 7.97 (d, J = 8.0 Hz, 2H; 2H and 6H), 7.57 (t, J = 8.0 Hz, 1H; 4H), 7.47 (t, J = 8.0 Hz, 2H; 3H and 5H), 2.61 (s, 3H; 8H); ¹³C NMR (150 MHz, CDCl₃): δ 198.22 (C-9), 138.32 (C-1), 137.19 (C-3), 129.87 (C-5), 26.72 (C-8); HRMS (EI-QTOF, [M + H]+): calculated for C₁₀H₁₃O: 149.0966; found: 149.0673.

1-(4-Methoxyphenyl)ethan-1-one (2e) [21]: Rf = 0.7 (SiO₂, hexane/EtOAc = 9:1); yield: 123 mg (83%); ¹H NMR (600 MHz, CDCl₃): δ 7.99 (d, J = 8.5 Hz, 2H; 2H and 6H), 6.89 (d, J = 9 Hz, 2H; 2H and 6H), 4.07 (q, J = 6 Hz, 2H, 7H), 2.53 (s, 3H; 9H), 1.42 (t, J = 6 Hz, 3H, 8H); ¹³C NMR (150 MHz, CDCl₃): δ 196.65 (C-10), 162.88 (C-4), 135.30 (C-2 and C-6), 130.17 (C-1), 63.70 (C-7), 26.22 (C-9), 14.61 (C-8); HRMS (EI-QTOF, [M + H]+): calculated for C₁₀H₁₄O: 165.0916; found: 165.0758.

1-(3-Hydroxyphenyl)ethan-1-one (2h) [18]: Rf = 0.5 (SiO₂, hexane/EtOAc = 9:1); yield: 108 mg (79%); ¹H NMR (600 MHz, CDCl₃): δ 7.55 (t, J = 7.2 Hz, 1H, 5H), 7.50 (t, J = 7.8 Hz, 1H, 5H), 7.33 (t, J = 7.8 Hz, 2H, 2H ), 7.12 (dd, J = 8.4 Hz and 1.8 Hz, 1H, 4H), 6.30 (s, 1H, 7H), 2.60 (s, 3H, 8H); ¹³C NMR (150 MHz, CDCl₃): δ 199.28 (C-9), 156.41 (C-3), 138.31 (C-1), 129.87 (C-5), 120.98 (C-6), 120.82 (C-4), 114.73 (C-2), 26.72 (C-8); HRMS (EI-QTOF, [M + H]+): calculated for C₁₀H₁₄O: 170.0630; found: 170.0297.

1-(4-Hydroxyphenyl)ethan-1-one (2i) [25]: Rf = 0.5 (SiO₂, hexane/EtOAc = 9:1); yield: 115 mg (84%); ¹H NMR (600 MHz, CDCl₃): δ 7.94 (s, 1H, 7H), 7.81 (m, 2H, 2H and 6H), 6.92 (m, 2H, 2H and 5H), 2.58 (s, 3H, 8H); ¹³C NMR (150 MHz, CDCl₃): δ 191.33 (C-9), 160.80 (C-4), 131.09 (C-2 and C-6), 129.93 (C-1), 114.41 (C-3 and C-5), 26.72 (C-8); HRMS (EI-QTOF, [M + H]+): calculated for C₁₀H₁₄O: 170.0630; found: 170.0297.

1-(4-Chlorophenyl)ethan-1-one (2j) [21]: Rf = 0.65 (SiO₂, Hexane/EtOAc = 9:1); yield: 135 mg (87%); ¹H NMR (600 MHz, CDCl₃): δ 7.88 (d, J = 8.8 Hz, 2H, 2H and 6H), 7.43 (d, J = 9 Hz, 2H, 3H and 5H), 2.58 (s, 3H, 8H); ¹³C NMR (150 MHz, CDCl₃): δ 196.73 (C-9), 139.53 (C-4), 135.43 (C-1), 129.68 (C-2 and C-6), 128.85 (C-3 and C-5), 26.50 (C-8); HRMS (EI-QTOF, [M + H]+): calculated for C₁₀H₁₄ClO: 155.0264; found: 155.0365.

1-(3-Aminophenyl)ethan-1-one (2k) [23]: Rf = 0.45 (SiO₂, Hexane/EtOAc = 9:1); yield: 116 mg (85%); ¹H NMR (600 MHz, CDCl₃): δ 7.34 (d, J = 11.4 Hz, 1H, 6H), 7.25 (m, 2H, 2H and 5H), 6.87 (dt, J = 13.2 Hz, 1H, 4H), 3.81 (s, 2H, 7H), 2.49 (s, 3H, 8H); ¹³C NMR (150 MHz, CDCl₃): δ 193.17 (C-9),
144.72 (C-3), 136.33 (C-1), 127.48 (C-5), 121.01, 120.35, 114.62, 26.68; HRMS (EI-QTOF, \([M + H]^+\)): calculated for C8H10NO: 136.0762; found: 136.0487.

1-(Bromomethyl)phenylethan-1-one (2a) [18]: \(R_f = 0.65\) (SiO2, hexane/EtOAc = 9:1); yield: 161 mg (81%); \(^1^H\) NMR (600 MHz, CDCl3): \(\delta 7.89, J = 8.0\) Hz, 2H, 2H and 6H), 7.43 (d, \(J = 11.8\) Hz, 1H, 6H), 7.58 (m, 1H, 3H), 7.46 (t, \(J = 2.4\) Hz, 1H, 6H), 7.34 (d, \(J = 7.8\) Hz, 1H, 4H), 7.07 (dd, \(J = 7.8\) Hz, 1H, 5H), 2.58 (s, 3H, 8H); \(^1^C\) NMR (150 MHz, CDCl3): \(\delta 196.85\) (C-9), 139.58 (C-13), 143.5 (C-1), 131.9 (C-3 and C-5), 129.73 (C-2 or C-6), 128.90 (C-2 or C-6), 26.58 (C-8); HRMS (EI-QTOF, \([M + H]^+\)): calculated for C8H8BrO: 198.9759; found: 198.7846.

1-(4-Bromophenyl)ethan-1-one (2n) [24]: \(R_f = 0.65\) (SiO2, hexane/EtOAc = 9:1); yield: 161 mg (81%); \(^1^H\) NMR (600 MHz, CDCl3): \(\delta 7.89, J = 8.0\) Hz, 2H, 2H and 6H), 7.43 (d, \(J = 11.8\) Hz, 1H, 6H), 7.58 (m, 1H, 3H), 7.46 (t, \(J = 2.4\) Hz, 1H, 6H), 7.34 (d, \(J = 7.8\) Hz, 1H, 4H), 7.07 (dd, \(J = 7.8\) Hz, 1H, 5H), 2.58 (s, 3H, 8H); \(^1^C\) NMR (150 MHz, CDCl3): \(\delta 196.85\) (C-9), 139.58 (C-13), 143.5 (C-1), 131.9 (C-3 and C-5), 129.73 (C-2 or C-6), 128.90 (C-2 or C-6), 26.58 (C-8); HRMS (EI-QTOF, \([M + H]^+\)): calculated for C8H8BrO: 198.9759; found: 189.7846.

RESULTS AND DISCUSSION

Encouraged by the previous literature reports [1-20] and importance of the classical approach towards the hydration of terminal alkynes, we intended to commence with the standardization of the reaction conditions, and for this purpose the phenylacetylene (1a) has been selected as the initial reactants. The investigation on optimization of methods initiated by operating a reaction of 1a in the presence of catalytic amounts of 2-picolinic acid (10 mol%) and NaOtBu (1.0 equiv.) at 120 ºC for 16 h (Table-1, Entry 1). Unfortunately, the outcome of this conducted reaction revealed toward failure for the formation of desired product 2a and the reaction mixture remain complicated during chromatographic separation. The identical scenarios were experienced when the 2-picolinic acid was altered with catalytic amounts of thiourea (Table-1, Entry 2), vitamin-B1 (Table 1, Entry 3) and 3-nitropyridine (Table-1, Entry 4). Whereas, in all cases similar observation was noticed which does not favored the expected product formation (Table-1, Entries 1-4). Interestingly, it was remarkable that by replacing NaOtBu with pyridine (1.0 equiv.), the desired product 2a was generated in 10% yield, when the reaction was enforced by 3-nitropyridine (10 mol%) at 120 ºC for 16 h (Table-1, Entry 5). Under these conditions, TEMPO exhibited similar reactivity (Table-1, Entry 6), whereas catalytic molecular iodine (30 mol%) directed the transformation with the formation of product 2a in 33% yield (Table-1, Entry 7). It was also significant that a series of iodine and bromine based catalysts such as TBAI, NIS, KI, NBS and TBAB remain completely inactive to reinforce this transformation toward formation of product 2a (Table-1, Entries 8-12). Further, the effectiveness of the bases such as triethyamine (TEA), NaOtBu, K2CO3 and N-methyl morpholine was established (Table-1, Entries 13 - 16). Among these examined bases, N-methyl morpholine has exhibited maximum activities with the construction of the expected product 2a in 37% yield (Table-1, Entry 16). Therefore, the transformation was again verified with the influences of 2equiv. and 3 equiv. of N-methyl morpholine (Table-1, Entries 17 & 18). The tested reactions revealed the positive influences of the amounts of N-methyl morpholine toward successful conversion of starting material to product 2a with yields up to 85%. Next, the effects of molecular iodine as temperature of the reaction has been realized (Table-1, Entry 19 & 20). These reactions concluded that the variation in amounts of molecular iodine beyond 3.0 equiv. has no additional advantages in the outcome of reaction (Table-1, Entry 19); whereas, the reaction fails to proceed if the reaction is carried out below the temperature of 120 ºC. Finally, having comprehensive standardization experiments, it was remarkable that the highest yield (85%) of the product 2a can be achieved when the transformation is conducted using 30 mol% molecular iodine and 3.0 equiv. of N-methyl morpholine at 120 ºC for 16 h (Table-1, Entry 18) and these conditions are further considered as standard conditions.

With the investigated standard reaction protocol, the aptitude of designed chemical transformation employing an array of terminal alkyne derivatives 1a-q (Scheme-II) was also investigated. It has been perceived that the alkyne compounds embedded with electron-pushing functional groups 1b-i and electron-pulling substituents 1j-q, irrespective of their electronic nature endured propitiously under the nurtured conditions delivering the yields of corresponding products 2a-q ranging from 72-93%. It may be also observed that aryl acetylene molecule 1o embedded with trifluoromethyl group...
at ortho-position undergone slightly lower capability toward the formation of corresponding product 2o with 72% yield.

Having concluded with the satisfactory substrate variations under the devised standard method, we intended to realize the mechanistic overviews of the current protocol (Scheme-III). In the first step, base B enabled removal of acidic proton from terminal alkyne 1a could lead to the release of acetylide anion A, which upon iodination in the presence of molecular iodine may generate the terminal iodo-derivative C. The reaction between oxygen nucleophile from DMSO and intermediate C could result in the generation of intermediate D, which followed by hydrogen-shift and S-O bond cleavage produces α-iodocarbonyl derivative F. Finally, the intermediate F delivers the required compound 2a in the presence of I₂ and DMSO.

**Conclusion**

In summary, a metal-free molecular I₂ catalyzed hydration of terminal alkynes has been described. The reaction proceeded
via Markovnikov-type addition reaction with the excellent selectivity, functional group tolerance and yield of the desired products.

ACKNOWLEDGEMENTS

One of the authors, CCM thanks Science and Engineering Research Board (SERB), Govt. of India for financial support in the form of research grant ECR/2016/000337 and CRG/2020/004509. Thanks are also due to NIT Manipur, India for the financial and research support.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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