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Copper(II) Triflate Catalyzed Amination and Aziridination of 2-Alkyl Substituted 1,3-Dicarbonyl Compounds

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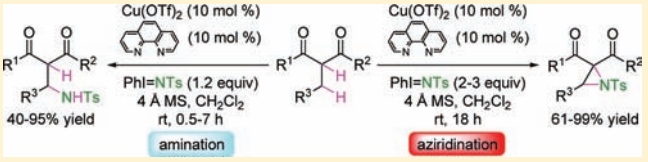
Supporting Information

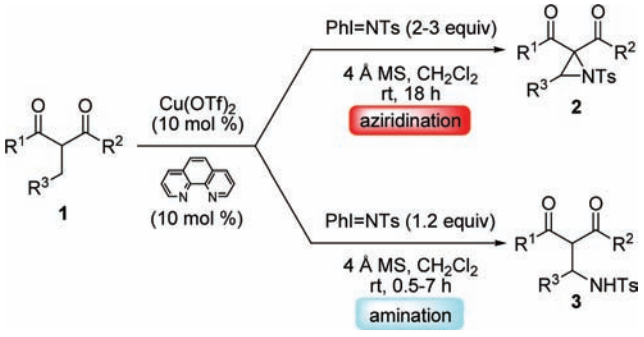
ABSTRACT: A method to prepare α-acyl-β-amino acid and 2,2-diacyl aziridine derivatives efficiently from $Cu(OTf)_2$ + 1,10-phenanthroline (1,10-phen)-catalyzed amination and aziridination of 2-alkyl substituted 1,3-dicarbonyl compounds with PhI=NTs is described. By taking advantage of the orthogonal modes of reactivity of the substrate through slight modification of the reaction conditions, a divergence in product selectivity was observed. In the presence of 1.2 equiv of the iminoiodane, amination of the allylic C—H bond of the enolic form of the substrate, formed in situ through coordination to the Lewis acidic metal catalyst, was found to selectively occur and give the β-aminated adduct. On the other hand, increasing the amount of the nitrogen source from 1.2 to 2−3 equiv was discovered to result in preferential formal aziridination of the C—C bond of the 2-alkyl substituent of the starting material and formation of the aziridine product.



INTRODUCTION

β-Amino acids and aziridines are immensely important targets in organic synthesis because of their ability to serve as building blocks in a wide variety of reactions.[1,2] They are also found as a substructure in numerous bioactive natural products and pharmaceutically interesting compounds. For this reason, establishing methods that can construct these two classes of nitrogen-containing compounds in an efficient manner and with control of substitution patterns from readily accessible substrates continues to be actively pursued. Herein, we report the synthesis of α-acyl-β-amino acid and 2,2-diacyl aziridine derivatives by copper(II)-catalyzed amination and azidirination of a common and readily available 2-alkyl substituted 1,3-dicarbonyl compound with PhI=NTs (Scheme 1). This divergence in product selectivity was found to be possible through slight modification of the reaction conditions.

Scheme 1. Synthesis of α-Acyl-β-amino Acid and 2,2-Diacyl Aziridine Derivatives from 2-Alkyl Substituted 1,3-Dicarbonyl Compounds



Within the field of transition-metal-mediated aminations and aziridinations of activated C—H and C=C bonds of alkanes and alkenes with iminoiodanes,[3−12] copper catalysis has come under renewed scrutiny due to its low cost and better biocompatibility when compared to other metal complexes.[4−6] For example, we recently reported one method for amide bond synthesis that relied on nitrene/imido insertion at the formyl C—H bond of aldehydes with PhI=NTs or $TsNClNa{\cdot}3H_2O$ (chloramine-T trihydrate) mediated by an in situ formed CuI + pyridine catalytic system or CuCl.[4b] As part of our efforts to further develop this type of synthetic approach for C—N bond formation,[7] we became interested in the potential chemical reactivity of readily available 2-alkyl substituted 1,3-dicarbonyl compounds. We reasoned that functionalization of the allylic C—H bonds of the pendant alkyl group of the enolic form of the substrate could be envisaged on in situ formation of a putative copper-enolate species.[8]

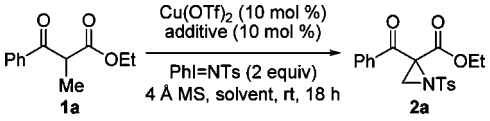
RESULTS AND DISCUSSION

Our studies began with the copper-catalyzed reactions of ethyl 2-methyl-3-oxo-3-phenylpropanoate **1a** and PhI=NTs (Table 1). While initial experiments with either CuI or CuCl gave <1 and 24% yield, respectively, when **1a** was treated with 10 mol % of $Cu(OTf)_2$, PhI=NTs (2 equiv), and 4 Å molecular sieves (MS) in CH_2Cl_2 at room temperature for 18 h, ethyl 2-benzoyl-1-tosylaziridine-2-carboxylate **2a** was obtained in 80% yield (entry 1). The structure of the nitrogen ring product was determined by ^1H NMR spectroscopy and X-ray crystallography of two closely related adducts (*vide infra*). Although geminal diacyl aziridines have been reported to exhibit a potent

Received: October 10, 2011
Published: April 1, 2012

   dx.doi.org/10.1021/ja301415k | J. Am. Chem. Soc. 2012, 134, 7344−7350

Table 1. Optimization of the Reaction Conditions[a]



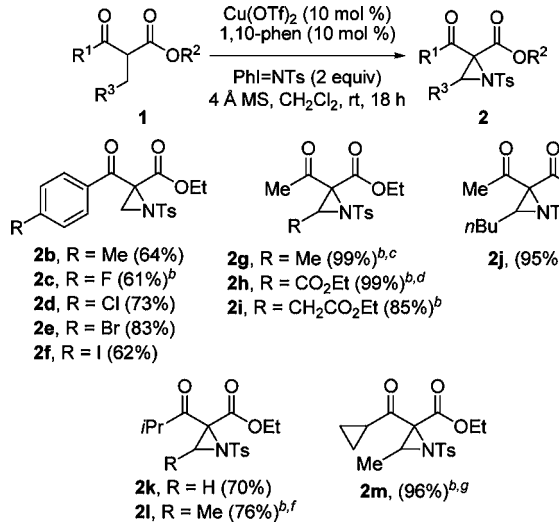
entry	additive	solvent	yield (%)[b]
1	–	CH_2Cl_2	80
2	1,10-phen	CH_2Cl_2	90
3	TMP	CH_2Cl_2	83
4	pyridine[c]	CH_2Cl_2	12
5	bipyridine	CH_2Cl_2	70
6	terpyridine	CH_2Cl_2	45
7	picolinic acid	CH_2Cl_2	70
8[d]	1,10-phen	CH_2Cl_2	74
9[e]	1,10-phen	CH_2Cl_2	98
10[f]	1,10-phen	CH_2Cl_2	60
11[g]	1,10-phen	CH_2Cl_2	43[h]
12	1,10-phen	PhMe	10
13	1,10-phen	MeCN	27
14	1,10-phen	DMSO	–[i]
15	1,10-phen	THF	–[j]
16[k]	1,10-phen	CH_2Cl_2	50
17[l]	1,10-phen	CH_2Cl_2	–[i]

[a]All reactions were carried out at room temperature and 4 Å MS (400 mg) in 2 mL of solvent for 18 h with catalyst/additive/**1a**/PhI=NTs molar ratio = 1:1:10:20. [b]Isolated yield. [c]Reaction conducted with 20 mol % of pyridine. [d]Reaction conducted with 5 mol % of $Cu(OTf)_2$ and 5 mol % of 1,10-phen. [e]Reaction conducted with 20 mol % of $Cu(OTf)_2$ and 20 mol % of 1,10-phen. [f]Reaction conducted with 1.5 equiv of PhI=NTs. [g]Reaction conducted in the absence of 4 Å MS. [h]Recovery of **1a** in 56% yield. [i]Trace amount of product detected on the basis of ^{1}H NMR analysis of the crude mixture. [j]Compound **4** obtained in 47% yield. [k]Reaction conducted with $PhI(OAc)_2$ (2 equiv) and $TsNH_2$ (2 equiv) in place of PhI=NTs. [l]Reaction conducted with $TsNNaCl{\cdot}3H_2O$ (2 equiv) in place of PhI=NTs.

range of bioactivities of current interest, synthetic methods to prepare this N-heterocycle have remained sparse.[13] In this regard, the unprecedented formation of **2a** via a mechanistically intriguing formal aziridination of a C—C bond prompted us to examine this transformation more closely to establish the reaction conditions (entries 2–17). This initially revealed that the addition of 10 mol % of a pyridyl-based additive, which could act as a ligand for the Cu(II) salt, to have a marked effect on the aziridination process (entries 2–7). An increase of 3 and 10% in product yield, respectively, was obtained when either 3,4,7,8-tetramethyl-1,10-phenanthroline (TMP) or 1,10-phen were employed (entries 2–3). On the other hand, lower product yields were furnished on repeating the reaction with pyridine, bipyridine, terpyridine, or picolinic acid (entries 4–7). Lower product yields were also afforded on lowering either the catalyst loading from 10 to 5 mol % or amount of PhI=NTs from 2 to 1.5 equiv (entries 8 and 10). By removing 4 Å MS from the reaction conditions, a similar outcome along with recovery of the 2-alkyl substituted β-ketoester substrate in 56% yield was found (entry 11). In contrast, a further slight increase in product yield to 98% was obtained when both the catalyst and 1,10-phen loading was increased from 10 to 20 mol % (entry 9). Changing the solvent from CH_2Cl_2 to MeCN, DMSO, or toluene was found to give either no reaction or **2a** in 10–27% yield (entries 12–14). The reaction with THF in place of CH_2Cl_2 as the solvent was the only exception, giving tetrahydro-*N*-tosylfuran-2-amine **4** as a byproduct in 47% yield (entry 15).[4d] Likewise, a low product yield of 50% or no reaction was observed on switching the nitrogen source from PhI=NTs to $PhI(OAc)_2$ + NH_2Ts or $TsNNaCl{\cdot}3H_2O$ (entries 16–17). On the basis of the above results, reaction of **1a** in the presence of 10 mol % of $Cu(OTf)_2$, 1,10-phen (10 mol %), PhI=NTs (2 equiv), and 4 Å MS in CH_2Cl_2 at room temperature for 18 h provided the optimal conditions.

To define the generality of the present procedure, we next turned our attentions to the reactions of a series of 2-alkyl substituted β-ketoesters, and the results are summarized in Table 2. Using the $Cu(OTf)_2$ + 1,10-phen system, these

Table 2. Copper(II)-Catalyzed Aziridination of 2-Alkyl Substituted β-Ketoesters[a]



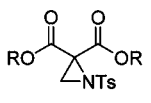
[a]All reactions were carried out at room temperature and 4 Å MS (400 mg) in 2 mL of CH_2Cl_2 for 18 h with $Cu(OTf)_2$/1,10-phen/**1**/PhI=NTs molar ratio = 1:1:10:20. Values in parentheses denote isolated product yields. [b]Reaction conducted with 3 equiv of PhI=NTs. [c]Product obtained as a 1.8:1 mixture of diastereomers. [d]Product obtained as a 1:1 mixture of diastereomers. [e]Product obtained as a 3.8:1 mixture of diastereomers. [f]Product obtained as a 1.7:1 mixture of diastereomers. [g]Product obtained as a 1.3:1 mixture of diastereomers.

experiments showed the conditions to be broad, and a variety of 2-acyl-1-tosylaziridine-2-carboxylates **2b–m** could be obtained in 61–99% yield. This hitherto included 2-alkyl substituted β-ketoesters containing benzoyl groups bearing either an electron-donating (**1b**, Me) or electron-withdrawing (**1c–f**, F, Cl, Br, I) group, showing that such moieties were well tolerated under the reaction conditions. A similar outcome was found when we examined the reactivity of 2-alkyl substituted β-ketoesters with a pendant acyl and alkyl group (**1g–j**), including ones containing a carboxylic ester (**1h–i**) or cyclopropane (**1m**) moiety. These reactions were found to proceed well and give the corresponding aziridine adducts **2g–m** in good to excellent yields. With the exception of **2i**, the trisubstituted products were also obtained as a mixture of diastereomers in *cis*/*trans* or *trans*/*cis* ratios of up to 3.8:1 in reactions where $R^3 \neq H$.

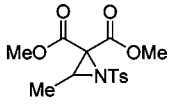
We next sought to evaluate the scope of this new methodology with respect to other types of 2-alkyl substituted 1,3-dicarbonyl compounds (Table 3). With this in mind, the reaction behavior of dimethyl 2-methylmalonate **1n** was first tested in the presence of 10 mol % of $Cu(OTf)_2$ and 10 mol % of 1,10-phen under the standard conditions and found that

dx.doi.org/10.1021/ja301415k | J. Am. Chem. Soc. 2012, 134, 7344–7350

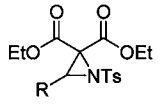
Table 3. Copper(II)-Catalyzed Aziridination of 2-Alkyl Substituted Malonates and 1,3-Diones[a]



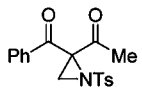
2n, R = Me (92%)
2o, R = Et (82%)
2p, R = Bn (60%)



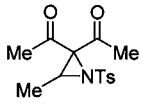
2q, (90%)[b]



2r, R = Me (81%)[b]
2s, R = Et (89%)[b]
2t, R = $(CH_2)_2Cl$ (90%)[b]



2u, (65%)



2v, (99%)[b]

[a]All reactions were carried out at room temperature and 4 Å MS (400 mg) in 2 mL of CH_2Cl_2 for 18 h with $Cu(OTf)_2$/1,10-phen/**1**/PhI═NTs molar ratio = 1:1:10:20. Values in parentheses denote isolated product yields. [b]Reaction conducted with 3 equiv of PhI═NTs.

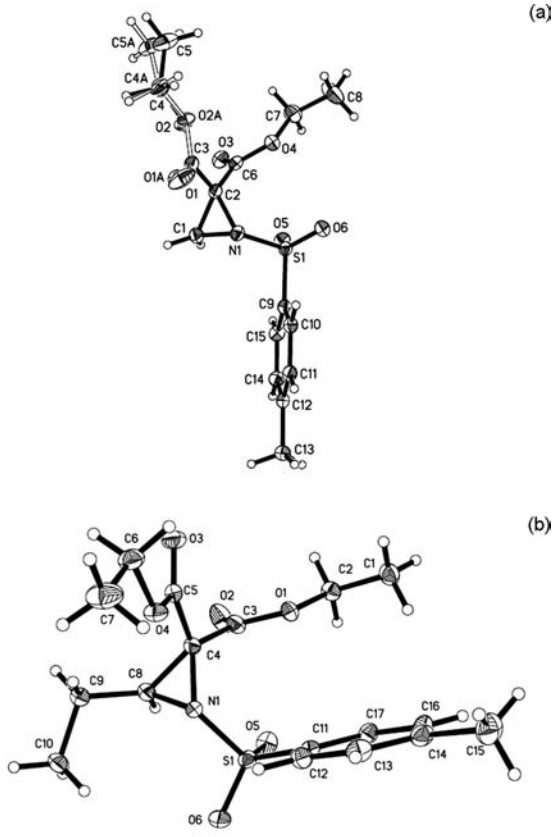
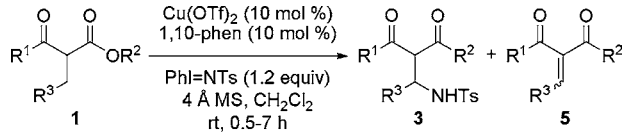


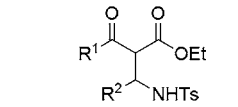
Figure 1. ORTEP drawings of (a) **2o** and (b) **2s** with thermal ellipsoids at 50% probability levels.[14]

dimethyl 1-tosylaziridine-2,2-dicarboxylate **2n** could be afforded in 92% yield. Under similar conditions, repetition of the reaction with other 2-alkyl substituted malonates **1o**−**t** gave the corresponding dialkyl and dibenzyl 1-tosylaziridine-2,2-dicarboxylates **2o**−**t** in 60−90% yield. This included one example where the C−Cl bond remained intact when a chlorine substituent (**2t**) was introduced. Likewise, treating the 2-alkyl substituted 1,3-diones **1u** and **1v** with the $Cu(OTf)_2$ + 1,10-phen catalyst system under the standard conditions afforded the corresponding 1,1′-(1-tosylaziridine-2,2-diyl)-1,3-diones **2u** and **2v** in 65 and 99% yield, respectively. In these latter reactions, the structure of the aziridine products was determined on the basis of X-ray crystallographic analysis of **2o** and **2s** (Figure 1).[14] Additionally, no other side products were detected by TLC and ^{1}H NMR analysis of the crude mixtures.

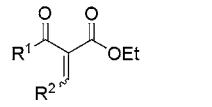
Further exploration of the reaction conditions found that the α-acyl-β-amino acid derivative **3** could be selectively formed in preference to the 2,2-diacyl aziridine **2** by simply reducing the amount of PhI═NTs from 2 to 1.2 equiv (Table 4). Under

Table 4. Copper(II)-Catalyzed Amination of 2-Alkyl Substituted β-Ketoesters 1g, 1l, and 1m, and Malonates 1q−t[a]

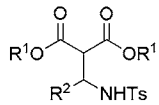




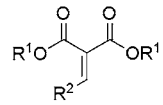
3g, $R^1 = R^2$ = Me (70%)[b]
3l, R^1 = *i*Pr, R^2 = Me (51%)[b]
3m, R^1 = *c*C_3H_5, R^2 = Me (40%)[b]



5l, R^1 = *i*Pr, R^2 = Me (40%)[c]
5m, R^1 = *c*C_3H_5, R^2 = Me (45%)[d]



3q, R^1 = Me, R^2 = Me (90%)
3r, R^1 = Et, R^2 = Me (95%)
3s, R^1 = Et, R^2 = Et (90%)
3t, R^1 = Et, R^2 = $(CH_2)_2Cl$ (82%)



5r, R^1 = Et, R^2 = Me (2%)
5t, R^1 = Et, R^2 = $(CH_2)_2Cl$ (16%)

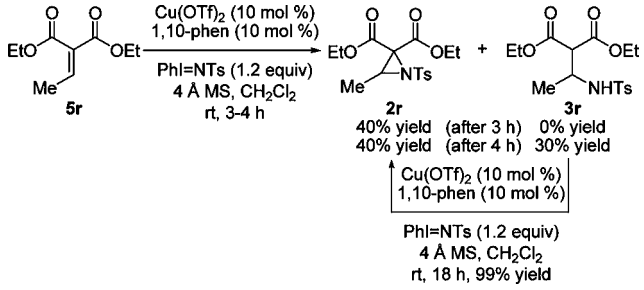
[a]All reactions were carried out at room temperature and 4 Å MS (400 mg) in 2 mL of CH_2Cl_2 with $Cu(OTf)_2$/1,10-phen/**1**/PhI═NTs molar ratio = 1:1:10:12 for 0.5−7 h; refer to Supporting Information for individual reaction times. Values in parentheses denote isolated product yields. [b]Product obtained as a 1:1 mixture of diastereomers. [c]Product obtained as a 4.4:1 mixture of regioisomers. [d]Product obtained as a 1.6:1 mixture of regioisomers and yield estimated on the basis of ^{1}H NMR analysis with CH_2Br_2 as the internal reference standard.

these slightly modified conditions, reactions of 2-alkyl substituted β-ketoesters **1g**, **1l**, and **1m** as representative examples with $Cu(OTf)_2$ (10 mol %) and 1,10-phen (10 mol %) gave the corresponding aminated products **3g**, **3l**, and **3m** in 40−70% yield and as a 1:1 mixture of diastereomers. A similar outcome was observed with **3q**−**t** obtained in excellent yields of 82−95% from the corresponding selected 2-alkyl substituted malonates **1q**−**t** under these latter conditions. In the case of reactions with **1l**, **1m**, **1r**, and **1t**, the corresponding alkene byproducts **5l**, **5m**, **5r**, and **5t** were also obtained in 2−45% yield.

In light of these latter results, we next performed a series of control experiments to gain a better understanding of the reaction mechanism (Schemes 2−6). In a first set of experiments, treating **5r** to the conditions depicted in Scheme 2 gave **2r** in 40% yield after 3 h. Repeating this transformation again for a longer reaction time of 4 h, on the other hand, gave the aziridine product along with compound **3r** in 40 and 30% yield, respectively. Conversion of the β-aminated adduct to **2r** in 99% yield was then accomplished by exposing **3r** once more to the same conditions for 18 h. This indicates that the aziridination process could proceed via a pathway involving

dx.doi.org/10.1021/ja301415k | J. Am. Chem. Soc. 2012, 134, 7344−7350

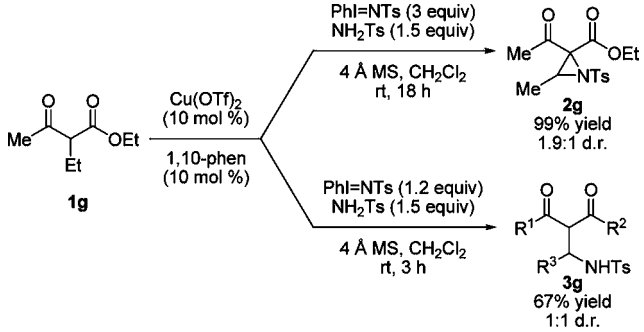
Scheme 2. Cu(OTf)$_2$-Catalyzed Reactions of 3r and 5r with PhI=NTs



either or both **3** and **5** as intermediates. It additionally suggests that the origin of the alkene could be due to the direct reaction of the enolate of **1** with PhI=NTs presumably via an addition−elimination process rather than from deamination of **3**.[13b] Formation of **5** in this manner would be consistent with our observations showing a marked increase in the amount of alkene obtained as the acidity of the substrate increased on going from 2-alkyl substituted malonates to β-ketoesters in Table 4. It would also explain the NH_2Ts and PhI detected by ^1H NMR analysis in the crude mixtures of these reactions.

The possibility that in situ formed NH_2Ts could then act as an inhibitor was also ruled out when we examined the reactions of **1g** with 1.2 or 3 equiv of PhI=NTs and 1.5 equiv of the aryl sulfonamide under the standard conditions (Scheme 3). In

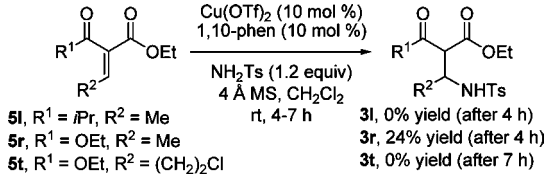
Scheme 3. Cu(OTf)$_2$-Catalyzed Reactions of 1g with PhI=NTs in the Presence NH_2Ts



both instances, this revealed the production of the corresponding aziridine and β-aminated adducts **2g** and **3g** in 99 and 67% yield and a diastereomeric ratio (d.r.) of 1.9:1 and 1:1, respectively, comparable to those furnished in the analogous reactions described in Tables 2 and 4.

In another set of experiments, the interactions of compounds **5l**, **5r**, and **5t** with 1.2 equiv of NH_2Ts and 10 mol % of the Cu(II) + 1,10-phen catalyst system in CH_2Cl_2 at room temperature for 4−7 h was next investigated (Scheme 4). In

Scheme 4. Cu(OTf)$_2$-Catalyzed Reactions of 5l, 5r, and 5t with NH_2Ts as the Nitrogen Source

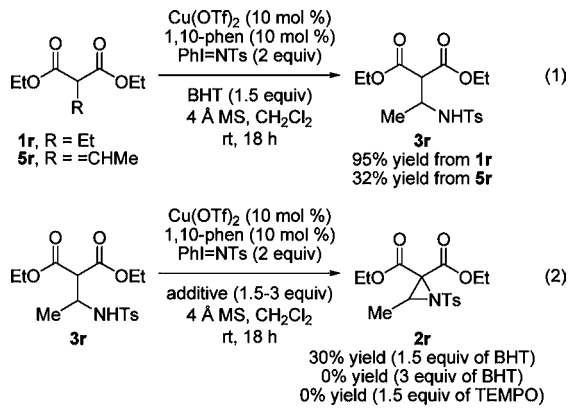


our hands, subjecting **5r** to these conditions was found to give **3r** in 24% yield. In contrast, the analogous reactions with **5l** and **5t** led to recovery of only the starting alkene in both instances. Added to this are our findings that showed **5m** to rapidly decompose in CH_2Cl_2 over a 30 min period to give a variety of side products that could not be identified by NMR analysis. These marked differences in reactivity to those observed for **1r**, **1l**, **1m**, and **1t** with PhI=NTs shown in Table 4 suggest a pathway involving 1,4-conjugate addition of the aryl sulfonamide to an in situ formed alkene to be unlikely. While this amination path cannot be completely ruled out, if operative, we posit that it is most probably limited to sterically unhindered 2-alkyl substituted malonates and, even then, at most provides a minor contribution to the overall yield.

On the other hand, the premise that the present C—N bond forming processes occur via Cu(II)-mediated transfer of the nitrene/imido group from PhI=NTs to the substrate is evident in two experiments examined in this work. First is the preferential amination of the α-C—H bond of THF to give compound **4** as a byproduct in the reaction of **1a** with PhI=NTs and the oxygen heterocycle as the solvent under the conditions described in Table 1, entry 15.[4d] Second is the markedly lower yield of **2a** and substantial recovery of the substrate observed when the analogous reaction was examined with CH_2Cl_2 as the solvent and in the absence of 4 Å MS (Table 1, entry 11). This would be consistent with competitive hydrolysis of the nitrene/imido donor due to residual amounts of H_2O present in the reaction mixture.[12]

In a final set of control experiments, we turned our attentions to the nature of the nitrene/imido transfer in the present Cu(II)-catalyzed reactions. In an earlier work, the use of the radical inhibitor butylhydroxytoluene (BHT) was demonstrated to implicate the possible involvement of radical species in Ag(I)-catalyzed amination of the C—H bond of alkanes with PhI=NTs.[9] With this in mind, the reactivities of compounds **1r**, **3r**, and **5r** in the presence of 1.5−3 equiv of BHT or 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) and 2 equiv of PhI=NTs were first compared (Scheme 5). This revealed a change in

Scheme 5. Cu(OTf)$_2$-Catalyzed Reactions of 1r, 3r, and 5r in the Presence of a Radical Scavenger



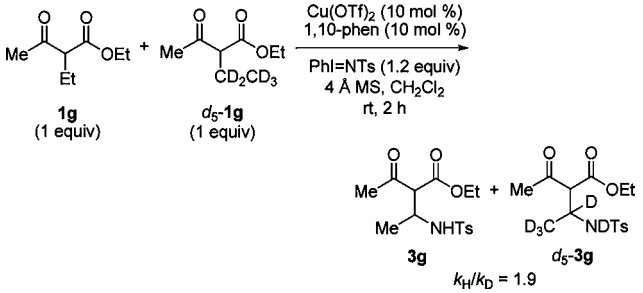
product selectivity in reactions with either **1r** or **5r** as the substrate, affording **3r** and not **2r** in 95 and 32% yield, respectively (Scheme 5, eq 1). In the latter case, this could be presumably due to decomposition of PhI=NTs to NH_2Ts by the metal catalyst,[3,12] followed by Cu(II)-mediated 1,4-conjugate addition of the aryl sulfonamide to the alkene,

dx.doi.org/10.1021/ja301415k | J. Am. Chem. Soc. 2012, 134, 7344−7350

reflecting our earlier findings depicted in Scheme 4. In contrast, reactions with **3r** showed the yield of aziridine **2r** to decrease as the ratio of [BHT]/[PhI=NTs] increased while replacing the phenol additive with TEMPO led to only recovery of the β-aminated substrate in near-quantitative yield (Scheme 5, eq 2). This trend would account for **3r** obtained from **1r** shown in Scheme 5, eq 1 not proceeding on to the aziridine product as the amount of PhI=NTs decreases due to the gradual formation of the β-aminated adduct. It would also be in good agreement with that reported in works describing Ag(I)-catalyzed C—H bond aminations.[9] Overall, these observations suggest that C—H bond amination of **1** to give **3** occurs via a concerted asynchronous pathway whereas formal aziridination of **3** or **5** to afford **2** proceeds through a radical-based mechanism. This latter argument in which the aziridine formation process occurs via radical species is additionally corroborated by the lack of stereoselectivity found in a number of reactions of substrates examined in Table 2.

To provide further support for our hypothesis, we next turned to measuring the deuterium kinetic isotope effect (KIE) for the present Cu(II)-catalyzed reactions with **1g** and d_5-**1g** as the test substrates under the conditions described in Scheme 6.

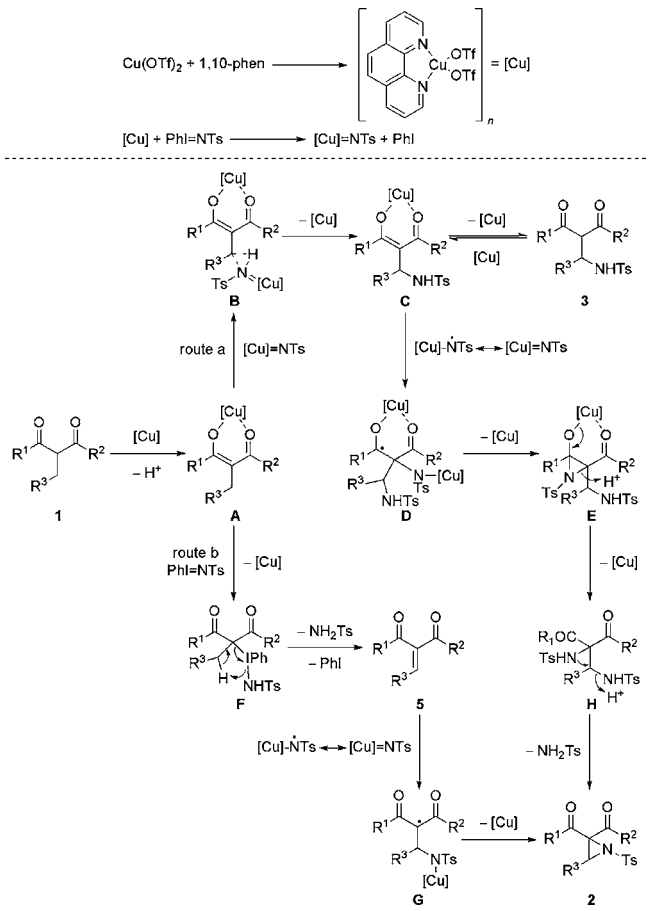
Scheme 6. Measurement of the Deuterium Kinetic Isotope Effect for the Cu(OTf)$_2$-Catalyzed Reactions of 1g and d_5-1g



Analysis by GC-MS gave a KIE value of 1.9 that suggested carbon−hydrogen bond cleavage might be the rate determining step. This value is in the same range as those previously reported for metal- and base-mediated concerted nitrene and carbene reactions, with KIE values of 1.2 to 2.1 depending on the catalyst and substrate employed.[15−17] By contrast, Fe(II)- and Ru(II)-based intermolecular C—H bond aminations, which are thought to occur by way of a H-atom abstraction/radical rebound pathway, afford KIE values of greater than 4.4.[7a,10]

Although highly speculative, the above results led us to put forward the mechanism outlined in Scheme 7 for the present Cu(II)-catalyzed amination and aziridination of 2-alkyl substituted 1,3-dicarbonyl compounds with PhI=NTs. This could involve the initial formation of a Cu-1,10-phen species, in either the monomeric or polymeric form, from reaction of Cu(OTf)$_2$ and 1,10-phen additive.[18] Further reaction of this Cu-1,10-phen complex with PhI=NTs generates the putative highly reactive [Cu]=NTs species.[19] At the same time, coordination of the Cu-1,10-phen complex to **1** could occur and give the copper-enolate species **A**. Subsequent rate-limiting transfer of the imido/nitrene group in [Cu]=NTs into the allylic C—H bond of this newly formed enolic form of the substrate via a direct insertion pathway is then thought to deliver **3** (route a in Scheme 7).[8] Under conditions where the [Cu]=NTs species can be rapidly reformed due to an excess

Scheme 7. Proposed Reaction Pathway for the Formation of α-Acyl-β-amino Acid and 2,2-Diacyl Aziridine Derivatives



amount of PhI=NTs, further transfer of the imido/nitrene group to the C=C bond of the copper-enolate of **3** via the carboradical **D** would give the aziridine **E**.[11] Presumably, the acid labile nature of the aziridin-2-ol intermediate results in ring opening to afford the diamine **H** that can undergo deaminative cyclization to provide **2**.[20] Alternatively, the copper-enolate species **A** could directly react with PhI=NTs to give the hypervalent iodine(III) adduct **F** (route b in Scheme 7).[13b] Deiodination of this newly formed intermediate would furnish **5**. Radical imido/nitrene transfer of the [Cu]=NTs species to the alkene intermediate via the carboradical **G** would then complete the aziridination process to deliver **2**.

CONCLUSIONS

In summary, we have exploited the intriguing reactivities of a diverse set of 2-alkyl substituted 1,3-dicarbonyl compounds in the presence of a Cu(II) salt as a catalyst and PhI=NTs to prepare α-acyl-β-amino acid and 2,2-diacyl aziridine derivatives. Complete control of product selectivity in the reaction was shown to be possible through slight modification of the reaction conditions. Further investigations are underway to examine the applications of this reaction to natural products synthesis and medicinal chemistry and will be reported in due course.

EXPERIMENTAL SECTION

General Considerations. All reactions were performed in oven-dried glassware under a nitrogen atmosphere at ambient temperature

dx.doi.org/10.1021/ja301415k | J. Am. Chem. Soc. 2012, 134, 7344−7350

unless otherwise stated. PhI=NTs was prepared following literature procedures.[21] Unless otherwise specified, all reagents and starting materials were purchased from commercial sources and used as received. Solvents were purified prior to use following literature procedures; CH_2Cl_2 and MeCN were purified prior to use by distilling over CaH_2, and pyridine was distilled over KOH. Analytical thin layer chromatography (TLC) was performed using a precoated silica gel plate. Visualization was achieved by UV−vis light (254 nm) followed by treatment with ninhydrin stain and heating. Flash chromatography was performed using silica gel using a gradient solvent system (EtOAc/*n*-hexane as eluent). Unless otherwise stated, ^1H and ^{13}C NMR spectra were measured on a 300 MHz spectrometer. Unless otherwise stated, chemical shifts (ppm) were recorded in $CDCl_3$ solution with tetramethylsilane (TMS) as the internal reference standard. ^1H NMR product yields were estimated with CH_2Br_2 as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), quin (apparent quintet), or m (multiplet). The number of protons (*n*) for a given resonance is indicated by *n*H, and coupling constants are reported as a *J* value in Hz. Low resolution mass spectra were determined on a mass spectrometer and reported as a ratio of mass to charge (*m*/*z*). High resolution mass spectra (HRMS) were obtained using an LC-HRMS mass spectrometer. Kinetic isotope measurements were conducted on a GC-MS mass spectrometer.

General Procedure for the Synthesis of 2-Alkyl 1,3-Dicarbonyl Compounds 1.[22] To a mixture of the 1,3-dicarbonyl compound (2.0 mmol) and iodoalkane (2.2 mmol) in *N*,*N*-dimethylformamide (5.0 mL) was added K_2CO_3 (1.5 mmol, 415 mg) at room temperature. The resulting reaction mixture was stirred at room temperature for 18 h or at 60 °C for 5 h. The reaction was then quenched with H_2O (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated to dryness. The residue was purified by flash column chromatography (32:1 → 19:1 *n*-hexanes/EtOAc as eluent) to give the title compound.

General Procedure for Cu(II)-Catalyzed Aziridination of 2-Alkyl 1,3-Dicarbonyl Compounds 1 to 2,2-Diacyl Aziridine Derivatives 2. To a mixture of $Cu(OTf)_2$ (0.05 mmol, 18.1 mg), 1,10-phen (0.05 mmol, 9.9 mg), and powdered 4 Å MS (400 mg) were added 2 mL of CH_2Cl_2. After the mixture was stirred for 1 h, PhI=NTs (1.0 mmol, 373 mg or 1.5 mmol, 560 mg) and **1** (0.5 mmol) were added. The reaction mixture was stirred for a further 18 h at room temperature, after which the mixture was filtered through Celite, washed with EtOAc (50 mL), evaporated to dryness, and purified by flash column chromatography (4:1 *n*-hexanes/EtOAc as eluent) to give the title compound.

General Procedure for Cu(II)-Catalyzed Amination of 2-Alkyl 1,3-Dicarbonyl Compounds 1 to α-Acyl-β-amino Acid Derivatives 3. To a mixture of $Cu(OTf)_2$ (0.05 mmol, 18.1 mg), 1,10-phen (0.05 mmol, 9.9 mg), and powdered 4 Å MS (400 mg) were added 2 mL of CH_2Cl_2. After the mixture stirred for 1 h, PhI=NTs (0.6 mmol, 224 mg) and **1** (0.5 mmol) were added. The reaction mixture was stirred at room temperature and monitored by TLC analysis. Upon completion, the mixture was filtered through Celite, washed with EtOAc (50 mL), evaporated to dryness, and purified by flash column chromatography (4:1 *n*-hexanes/EtOAc as eluent) to give the title compound.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures for control reactions, characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work is supported by a University Research Committee Grant (RG55/06) from Nanyang Technological University (NTU). A Nanyang President's Graduate Scholarship (to T.M.U.T.) from NTU is also gratefully acknowledged, and we thank Dr. Yongxin Li of this Division for providing the X-ray crystallographic data reported in this work.

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NOTE ADDED AFTER ASAP PUBLICATION

This paper was published ASAP on April 18, 2012, with incorrect graphics for Tables 1 and 4. The corrected version was reposted on April 19, 2012.