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Tetrahedron 62 (2006) 3798–3808
Tetrahedron

Thermal cyclization of 1,2-dialkynylimidazoles to imidazo[1,2-*a*]pyridines

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Received 14 November 2005; accepted 26 November 2005

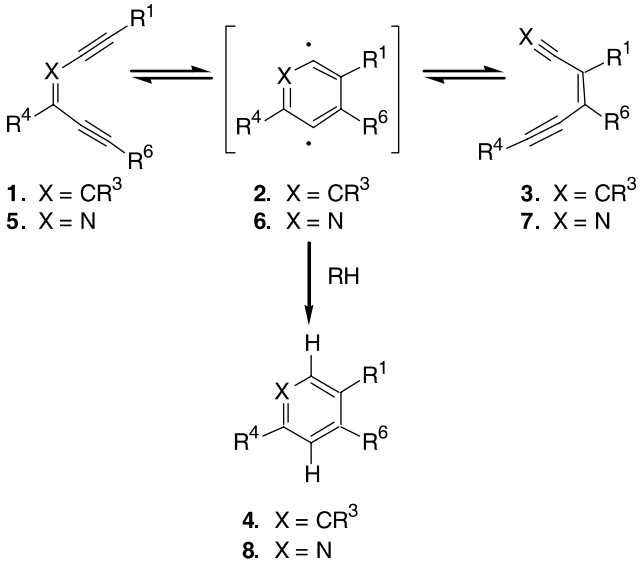
Available online 20 February 2006

Abstract—Thermolysis of 1,2-dialkynylimidazoles in chlorinated solvents leads to 5-chloroimidazo[1,2-*a*]-pyridine products, which are also formed in DMF containing 1 equiv of HCl. Deuterium labeling of the starting dialkynylimidazoles indicates that reaction may proceed by multiple pathways, depending upon conditions and substituents. Dialkynylimidazoles can also give rise to 5-diethylamino-substituted imidazopyridines when the thermolysis is carried out in the presence of diethylamine.

1. Introduction

The enediyne structural moiety (**1**, Scheme 1) is present in several naturally occurring anticancer antibiotics like calicheamicin,[1] dynemicin A[2] and C-1027.[3] A Bergman cyclization[4] of these enediynes generates 1,4-benzenoid diradicals (**2**, Scheme 1) that abstract hydrogen atoms from the sugar-phosphate backbone of DNA (**2**→**4**, Scheme 1) thus inducing DNA cleavage and cell death.[5] The isolation of the enediyne antitumor antibiotics has led to a search for alternative diradical-generating cyclizations that might be incorporated in the design of improved DNA-cleavage agents.[6] This search has led to the examination of aza-enediynes, or *C*,*N*-dialkynyl imines (**5**, Scheme 1) as potential precursors of 2,5-didehydropyridine diradicals (**6**, Scheme 1).[7]

The incorporation of an *N*-alkynylimine (ynimine) moiety in the aza-enediynes **5** has a profound effect on their cyclization chemistry. First, the cyclization barrier for aza-enediynes is substantially lower than for comparable enediynes, such that sterically unencumbered aza-enediynes undergo cyclization at room temperature and below.[7] Second, whereas the Bergman cyclization of hex-3-ene-1,5-diyne in the absence of hydrogen atom donors is thermoneutral (i.e., **1**→**3**, R^1–R^6=H), the aza-Bergman rearrangement of aza-enediynes to β-alkynylacrylonitriles (**5**→**7**) is exothermic by ca. 40 kcal/mol.[7] This



Scheme 1. Bergman cyclization of enediynes and aza-Bergman cyclization of aza-enediynes.

thermochemical driving force is accompanied by a very low kinetic barrier for the collapse of 2,5-didehydropyridine **6** to nitrile **7**.[7,8] As a result, the elusive 2,5-didehydropyridine intermediate **6** derived from aza-Bergman cyclization of aza-enediynes **5** does not enter into hydrogen atom abstraction or radical cyclization reactions; despite some effort,[7,8,9,10] there has been no success in trapping **6** to give pyridine-containing products **8** from the thermolysis of aza-enediynes under neutral conditions. Based on computational studies, it has been proposed that the didehydropyridine

Keywords: Aza-enediynes; Cyclization; Thermal rearrangement; Carbenes; β-Chloroenamines.
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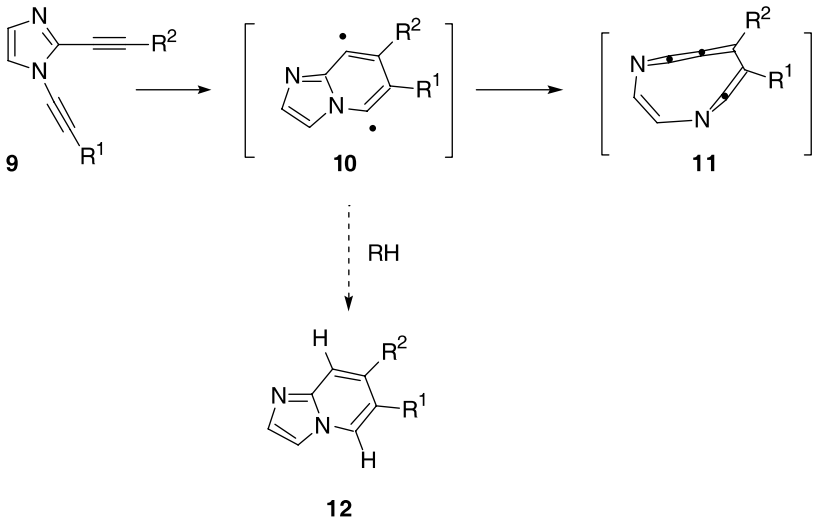
doi:10.1016/j.tet.2005.11.084



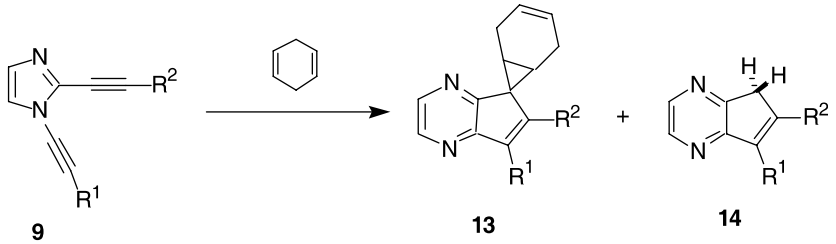
Scheme 2. Proposed aza-Bergman cyclization of 1,2-dialkynylimidazoles.

intermediate **6** derived from these aza-enediynes is selectively reactive only under acidic conditions,[8] such as occur in tumor tissue. This increased reactivity is due to an increase in the barrier for collapse of the protonated didehydropyridine, along with a more favorable singlet–triplet gap for this diradical.[10,11] However, the reactivity of the ynimine functionality of aza-enediynes can preclude this approach to trap **6**. Under aqueous acidic conditions, aza-enediyne **5** ($R^1=R^4=$Ph, $R^6=$H) undergoes addition of water across the ynimine triple bond. The resulting *N*-acyl-*C*-alkynylimine cyclizes to an oxazolyl carbene.[9]

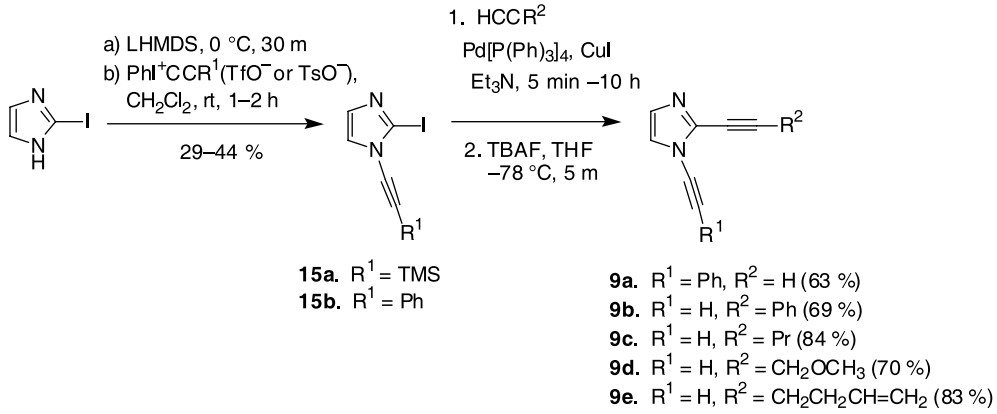
In our continuing studies of aza-Bergman cyclizations, we considered the previously unknown 1,2-dialkynyl imidazoles (**9**, Scheme 2) as heterocyclic aza-enediyne analogs.[12] It was presumed that aza-Bergman cyclization of these aza-enediyne analogs would give rise to 5,8-didehydroimidazo[1,2-*a*]pyridine intermediates **10**, collapse of which to **11** (Scheme 2) would be disfavored relative to the facile collapse of didehydropyridines **6** to nitriles **7** (Scheme 1). Trapping of **10** by hydrogen atom abstraction, perhaps facilitated by protonation as in the case of aza-enediynes, would lead to the imidazopyridines **12** (Scheme 2). In addition to these considerations, the dialkynylimidazoles might have other advantages over simple acyclic aza-enediynes, such as increased hydrolytic stability and enforcement of the desired stereochemical arrangement of the alkyne groups, resulting from formal replacement of the imine functionality with the imidazole ring.

Despite these predictions, initial studies of the thermolysis of these dialkynylimidazoles did not lead to imidazopyridine products. Instead, mild thermolysis (75–100 °C) of **9** (R^1 or $R^2=$H) in 1,4-cyclohexadiene led to the isolation of cyclopentapyrazines **13** and **14** (Scheme 3),[12,13] both presumably arising from the corresponding cyclopentapyrazine carbene. The cyclization of disubstituted dialkynylimidazoles (e.g., **9**, $R^1=R^2=$Ph) required more forcing conditions, and did not afford isolable products.[12]

In this report, we present the results of studies that began as an effort to optimize reaction conditions for this fascinating rearrangement of dialknylimidazoles to cyclopentapyrazine carbenes, particularly in an effort to trap these carbenes in an intramolecular sense to afford polycyclic pyrazines.[14] Examining the effect of varying the solvent on this rearrangement led to the isolation of 5-chloroimidazo[1,2-*a*]-pyridine products from reactions carried out in a variety of chlorinated solvents. This cyclization of dialkynylimidazoles to 5-chloroimidazopyridines can also be accomplished in DMF containing HCl. While the transformation is general, there is a very pronounced substituent effect on both the rate of the reaction and the regiochemical outcome. We have employed deuterium labeling of the starting dialkynylimidazoles to provide insight into the mechanism of the transformation and these substituent effects. These studies indicate that reaction may proceed by multiple pathways, depending upon conditions and substituents. Finally, we note that dialkynylimidazoles can also give rise



Scheme 3. Formation of cyclopentapyrazines from 1,2-dialkynylimidazoles.



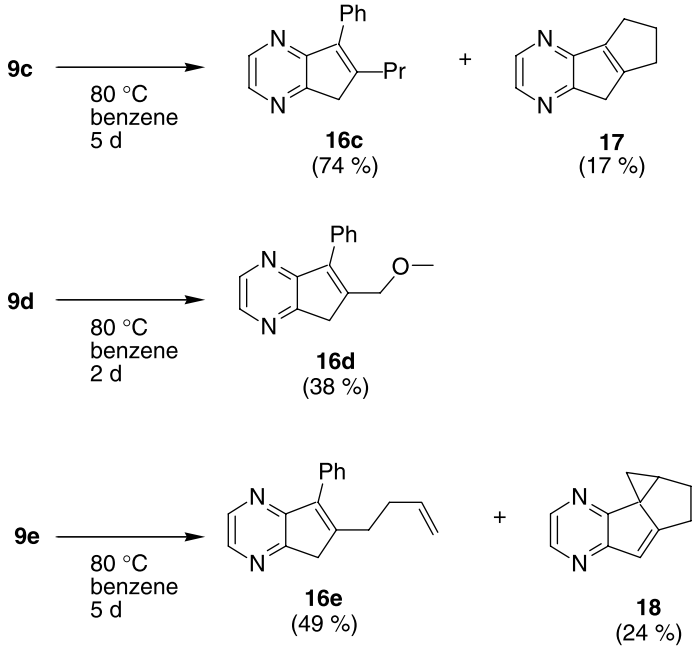
Scheme 4. Synthesis of 1,2-dialknylimidazoles.

to 5-(diethylamino)-substituted imidazopyridines when the thermolysis is carried out in the presence of diethylamine.

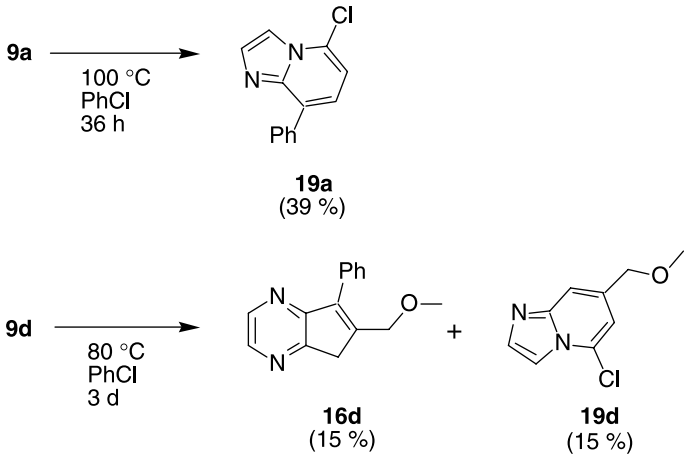
2. Results and discussion

Prior to embarking upon this exploration of thermal chemistry of dialkynylimines, we required the synthesis of these *N*-alkynyl heterocycles. A recent review on the synthesis of *N*-alkynyl heterocycles has appeared.[15] As there were no previous examples of *N*-alkynylimidazoles, we explored various routes to these *N*-alkynyl heterocycles.[12] We found that a variety of dialkynylimidazoles can be prepared by a two-step sequence (Scheme 4). In the first step, the lithium anion of the imidazole is allowed to react with an alkynyl iodonium tosylate or triflate to afford the *N*-alkynyl-2-iodoimidazoles **15a**,**b** in moderate yield. Subsequent Sonogashira[16] coupling of these 2-iodoimidazoles with a variety of terminal acetylenes proceeds in good yield. The desired mono-substituted dialkynylimidazoles are obtained after protodesilylation with TBAF during work-up (Scheme 4).

The dialkynylimidazoles **9c**–**e** contain substitutents that can participate in intramolecular carbene C–H insertion or olefin addition reactions. Thermolysis of these dialkynylimidazoles in benzene was expected to lead to polycyclic pyrazine products. In the event, modest yields of tricycle **17** and tetracycle **18** were obtained, along with the products of formal benzene C–H insertion by the carbene (**16c**–**e**), which were the major products in all cases (Scheme 5).[14] The propensity of the carbene derived from these dialkynylimidazoles to undergo addition to benzene led us to explore alternative solvents for these intramolecular trapping reactions. While we eventually found that **17** and **18** can be obtained as the major products in high yield from thermolyses carried out in hexafluorobenzene,[14] products apparently derived from an alternative cyclization mode were observed from thermolyses carried out in chlorinated solvents.



Scheme 5. Thermolysis of 1,2-dialkynylimidazoles in benzene leads to inter- and intramolecular carbene trapping products.



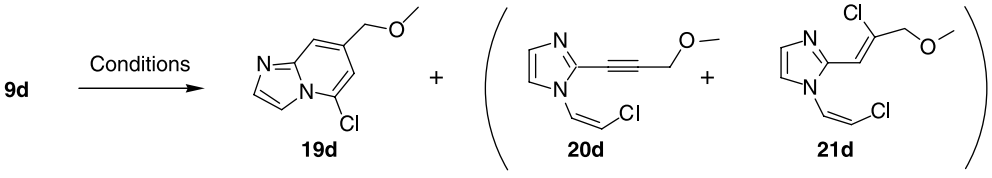
Scheme 6. Thermolysis of 1,2-dialkynylimidazoles in chlorobenzene.

In a previous communication, we reported that thermolysis of **9a** in chlorobenzene afforded the 5-chloroimidazopyridine **19a** (Scheme 6).[12] Examination of the structure of chloroimidazopyridine **19a** reveals that it is not related to the potential intermediate 5,8-didehydroimidazopyridine **10** (Scheme 2) through any straight-forward process, such as hydrogen- and chlorine-atom abstraction from chlorobenzene solvent. The 5-chloroimidazopyridine **19d**, which could be formed from intermediate **10** through chlorine- and hydrogen-atom abstraction, was obtained from thermolysis of **9d** in chlorobenzene, along with the phenyl substituted cyclopentapyrazine **16d** (Scheme 6), the same product obtained in benzene as solvent (Scheme 5). No products of intramolecular C–H insertion were observed. The structures of both **19a** and **19d** were assigned based upon 2D NMR (COSY, NOESY, and HMBC) experiments.

Due to the wide-spread interest in imidazo[1,2-*a*] pyridines[17,18] and the interesting mechanistic implications of the formation of **19a**,**d** from dialkynylimidazoles **9a**,**d**, we set out to optimize the conditions for this cyclization starting with dialkynylimidazole **9d** (Table 1). Thermolysis of **9d** in a variety of chlorinated solvents (chlorobenzene, dichloromethane, 1,2-dichloroethane) affords chloroimidazopyridine **19d** in moderate yield (entries 1–3), with the best yields obtained in 1,2-dichloroethane. With the exception of chlorobenzene, in which the cyclopentapyrazine **16d** is also produced, no other products were observed in ^{1}H NMR spectra of the reaction mixtures prior to chromatographic purification. The remainder of the reaction mixture was a polar, tarry material, presumably polymeric.

In order to address the potential role of HCl generated from these chlorinated solvents in the cyclization, reactions were performed in the presence of added excess tetramethylammonium chloride and trifluoroacetic acid in dichloromethane (entry 4). Although this reaction proceeded to completion more quickly than those performed in the absence of added proton and chloride ion sources, no imidazopyridine product was obtained; instead, the *N*-(2-chlorovinyl)imidazoles **20d** and **21d** were isolated. The (*Z*)-stereochemistry of the *N*-(2-chlorovinyl)groups of **20d** and **21d** was assigned based on the observed ^{1}H NMR coupling constants for the vinylic protons, and, in the case of **21d**, NOESY data, which also confirmed the (*Z*)-stereochemical arrangement of the 2-(2-chloro-3-methoxypropenyl)substituent. Although contrary to the normal regiochemistry of ynamine additions, the addition of nucleophiles to the 2-position of *N*-ethynylpyrrole[19] and *N*-alkynylbenzotriazoles[20] is known. In the latter case, the stereochemistry of the addition is also the same that we observe here, leading to exclusively the (*Z*)-isomers.

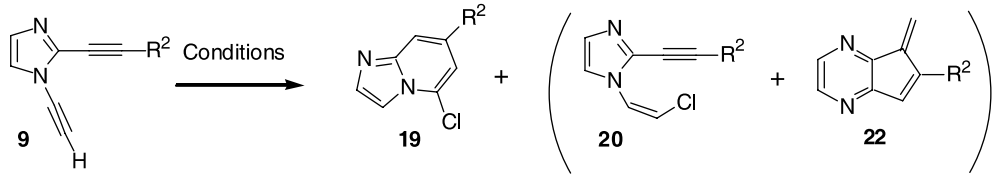
Table 1. Optimization of the cyclization of dialkynylimidazole **9d**



Entry	Reaction conditions	Yield of **19d** [a]	Other products (yield)[a]
1	PhCl, 80 °C, 3 days	15%	**16d** (15%)
2	CH_2Cl_2, 80 °C, 4 days	19%	nd[b]
3	$Cl(CH_2)_2Cl$, 80 °C, 4 days	31%	nd[b]
4	Me_4NCl (3 equiv), TFA (3 equiv), CH_2Cl_2, 80 °C, 12 h	nd[b]	**20d** (10%), **21d** (36%)
5	HCl_{aq} (1.2 equiv) DMF, 80 °C, 14 h	64%	**20d** (9%)
6	HCl_{aq} (4 equiv), DMF, 80 °C,12 h	nd[b]	**21d** (84%)
7	Me_4NCl (1 equiv), TFA (1 equiv), DMF, 80 °C, 4 h	71%	**20d** (8%)

[a] Isolated yield.
[b] Not detected.

Table 2. Cyclization of dialkynylimidazoles under various reaction conditions



Entry	Series	R^2	Reaction conditions		
			CH_2Cl_2, 80 °C	HCl_{aq} (1 equiv), DMF, 80 °C	Me_4NCl (1 equiv), TFA (1 equiv), DMF, 80 °C
			Product (yield)		
1	**b**	Ph	**19b** (18%)[a], **22b** (7%)[a]	**20b** (69%)[b]	nd
2	**c**	Pr	**19c** (12%)[c], **22c** (14%)[c]	**19c** (14%)[d], **20c** (56%)[d]	**19c** (35%)[e], **20c** (40%)[e]
3	**d**	CH_2OCH_3	**19d** (19%)[f]	**19d** (64%)[g], **20d** (9%)[g]	**19d** (71%)[h], **20d** (8%)[h]

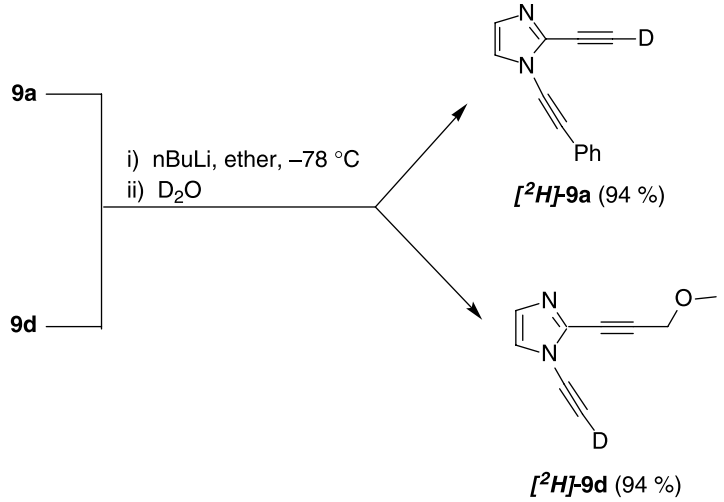
[a] Reaction time=31 days.
[b] Reaction time=68 h.
[c] Reaction time=31 days.
[d] Reaction time=56 h.
[e] Reaction time=56 h.
[f] Reaction time=4 days.
[g] Reaction time=14 h.
[h] Reaction time=4 h.

Good yields of **19d** are obtained from reactions carried out with 1 equiv of HCl (entry 5) or 1 equiv each of tetramethylammonium chloride and trifluoroacetic acid (entry 7) in DMF; however, excess HCl in DMF leads again to the formation of the *N*-chlorovinylimidazole **21d** (entry 6), which is obtained in high yield under these conditions.

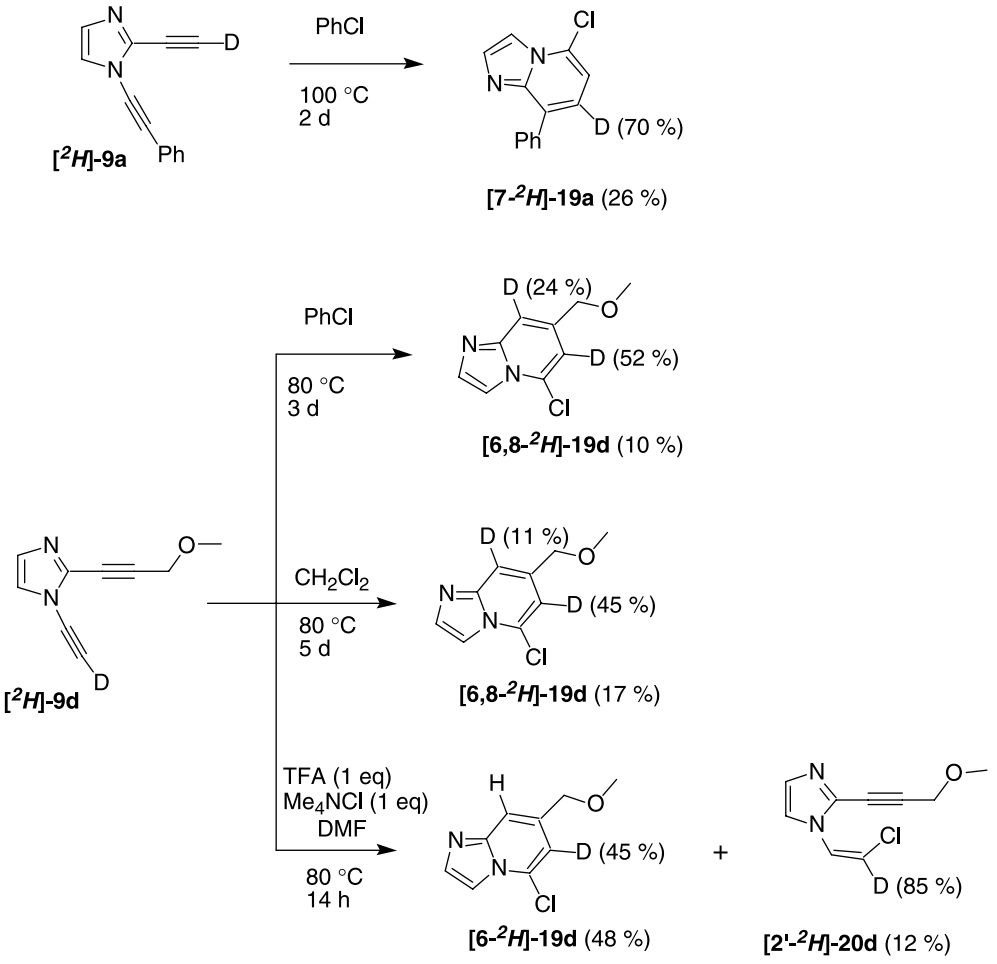
In order to examine the generality of the cyclization of dialkynylimidazoles to chloroimidazopyridines, two additional dialkynylimidazoles were subjected to the optimized cyclization reactions conditions in DMF and thermolysis in dichloromethane (Table 2). The phenyl-substituted analog **9b** affords only the *N*-chlorovinylimidazole **20b** in DMF containing 1 equiv of HCl, and a mixture of chloroimidazopyridine **19b** and the methylenylcyclopentapyrazine **22b** in dichloromethane (entry 1). In both cases, the reaction times were excessive, up to 31 days for the case of thermolysis in dichloromethane. Similarly, the reaction times required for consumption of the propyldialkynylimidazole **9c** were also very long (entry 2), but moderate yields of chloroimidazopyridine **19c** were obtained in DMF, accompanied by the *N*-chlorovinylimidazole **20c**, which was the major product. Thermolysis of **9c** in dichloromethane eventually afforded low yields of the **19c** and the methylenylcyclopentapyrazine **22c** (entry 2).

From the above results, it is apparent that the dialkynylimidazole substituents affect both the facility and efficiency of the cyclization to chloroimidazopyridines. In order to probe this effect in more detail, and to provide some insight into the mechanism of this transformation, the deuterated dialkynylimidazoles [^2H]-**9a** and [^2H]-**9d** were prepared (Scheme 7). Deprotonation of the dialkynylimidazoles with *n*-BuLi in ether followed by D_2O quench afforded these deuterated dialkynylimidazoles in good yield and isotopic purity of >95%, as determined by ^1H NMR.

Thermolysis of [^2H]-**9a** in chlorobenzene afforded the deuterated chloroimidazopyridine **19a** with 70% isotopic

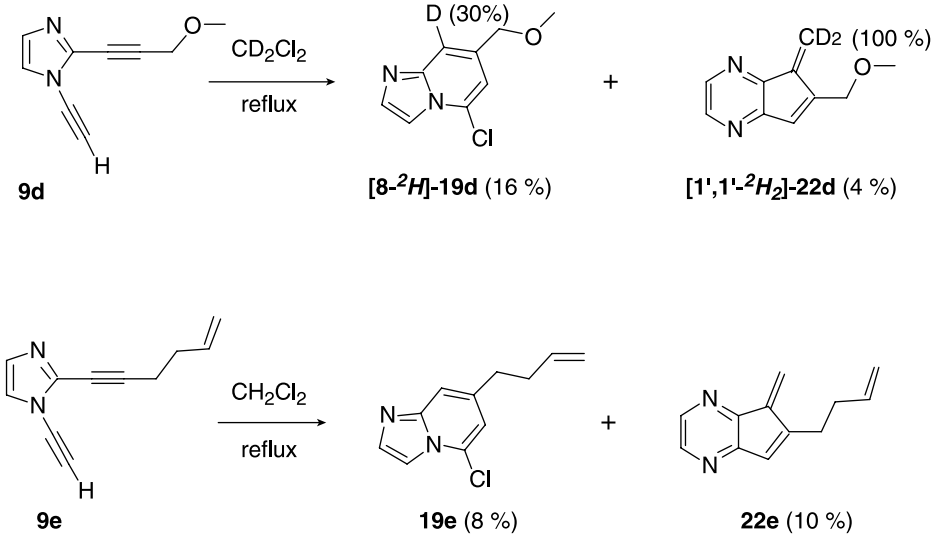


Scheme 7. Preparation of deuterated 1,2-dialkynylimidazoles.

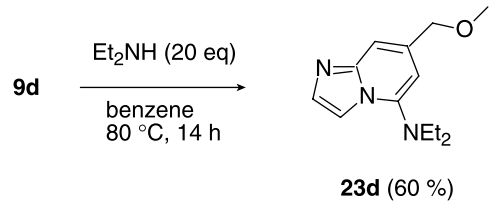


Scheme 8. Thermolysis of deuterated 1,2-dialkynylimidazoles.

label at the 7-position (Scheme 8). In contrast, thermolysis of [^2H]-**9d** in chlorobenzene leads to the isolation of chloroimidazopyridine **19d** in which the deuterium label is both at the 6- (major) and 8- (minor) positions (Scheme 8). A similar result is obtained when [^2H]-**9d** is subjected to thermolysis in dichloromethane. This is not the case for cyclization of [^2H]-**9d** in DMF in the presence of tetramethylammonium chloride and TFA, which leads to chloroimidazopyridine with deuterium label only at the 6-position, along with the deuterated-*N*-(2-chlorovinyl)imidazole. There is significant loss of deuterium label in all these cases, particularly in the case of chloroimidazopyridine **19d** from cyclization in DMF.



Scheme 9.

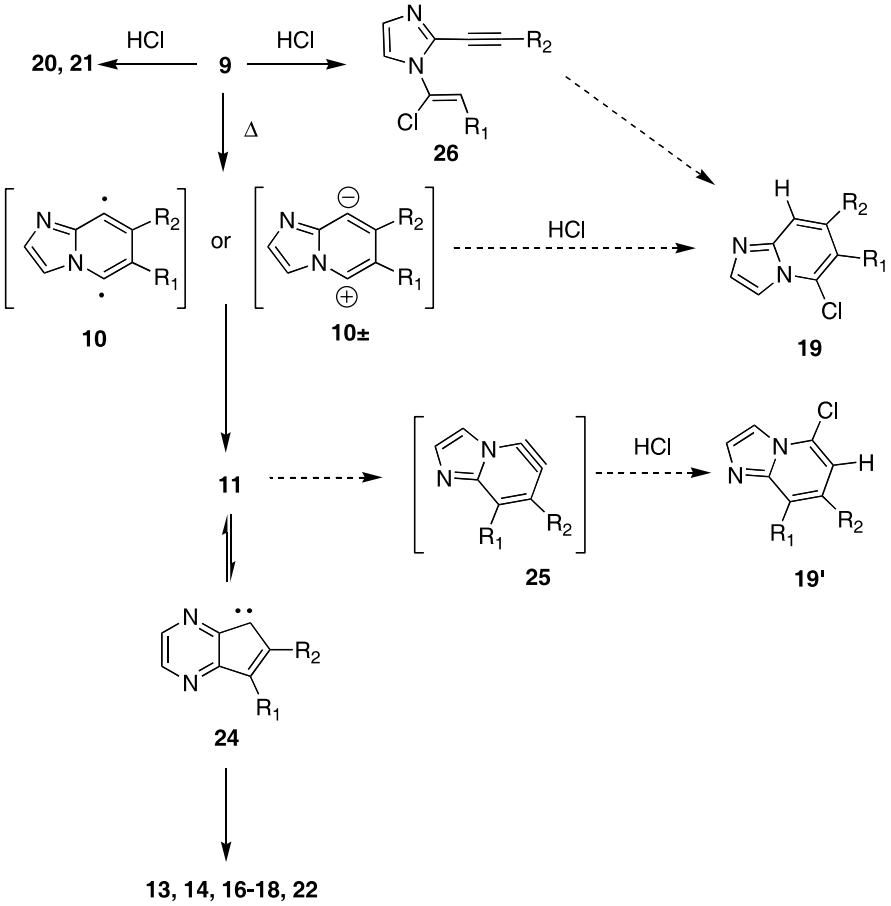


Scheme 10.

These deuterium labeling results reflect a difference in the cyclization of **9b** when compared to **9d** in chlorinated solvents, as well as a difference in the cyclization carried out in chlorinated solvents versus that in DMF in the presence of acid and chloride ion. The deuterium label originating from the 2-ethynyl substituent of [^2H]-**9a** is found exclusively at the 7-position in the product imidazopyridine; however, in no case did we observe products derived from dialkynylimidazoles in which an alkyl or aryl substituent from the 2-alkynyl moiety of the imidazole was found at the imidazopyridine 7-position. This indicates that either there is a regiospecific migration of the deuterium in [^2H]-**9a** to the 7-position of the product that does not occur for non-hydrogen substituents, or there are two different pathways involved in this cyclization—the pathway leading to [7-^2H]-**19a** from [^2H]-**19a**, which also accounts for the minor 8-deuterated products derived from [^2H]-**9d**, and a separate pathway leading to [6-^2H]-**19d** from [^2H]-**9d**. If this is the case, it is the later pathway that predominates in the cyclization of [^2H]-**9d** carried out in DMF. It is interesting to note that this pathway can be rationalized by the trapping of aza-Bergman cyclization product **10**, as the closed-shell, zwitterionic form, by HCl, although there are other mechanistic schemes that also account for these results (see below).

We also carried out the thermolysis of **9d** in deuterated dichloromethane (Scheme 9). In this case, the product imidazopyridine contains deuterium only at the 8-position, although the efficiency of deuterium incorporation is low. We also isolated a small amount of the methylenylcyclopentapyrazine **22d** in which the exocyclic methylene group was deuterated. In order to address the potential role of diradical **10** (Scheme 2) in these cyclization reactions, the butenyl analog **9e** was also subjected to thermolysis in dichloromethane. No products corresponding to radical cyclization of diradical **10** onto the butenyl side chain were observed, instead, low yields of the chloroimidazopyridine **19e** and methylenylcyclopentapyrazine **22e** were isolated (Scheme 9).

Interestingly, this cyclization of dialkynylimidazoles to imidazopyridines is also observed when a benzene solution of **9d** is heated in the presence of excess diethylamine, which affords the 5-(diethylamino)imidazopyridine **23b** in good yield (Scheme 10). However, under the same reaction conditions, no imidazopyridines were obtained from **9a–c**. Analysis of the crude reaction products in these cases demonstrated that the exclusive products were those of diethylamine addition to the *N*-alkynyl substituents.



Scheme 11.

The resulting enamines were unstable to chromatographic purification and were not isolated.

We have previously proposed a mechanism for the formation of the cyclopentapyrazine carbene **24** via cyclization of the cyclic cumulene **11**, which is derived from the dialkynylimidazole **9** by collapse of the aza-Bergman cyclization intermediate **10** (Scheme 11).[12,13] Perhaps the most striking mechanistic observation about the cyclization of dialkynylimidazoles to imidazo[1,2-*a*]-pyridines is that while certain products (**19** in Scheme 11) can be formally derived from trapping of **10**, or its corresponding zwitterion **10**$\pm$ (e.g., **19b–e**), other products (e.g., **19a**) cannot. Instead, these products (**19′** in Scheme 11) appear to be derived from a 5,6-didehydroimidazo-pyridine intermediate[12,13] (**25**, Scheme 11). Deuterium labeling studies support this distinction, in that the 2-ethynyl substituent of [^2H]-**9a** (R_2=D) maps to the imidazopyridine 7-position. While **19b–e** might also be derived from the same 5,6-didehydroimiazolopyridine intermediate, the deuterium labeling studies with [^2H]-**9d** map the *N*-ethynyl substituent (R^1=D) predominantly to the imidazopyridine 6-position, which is commensurate with either trapping of intermediate **10**$\pm$, or addition of HCl to the *N*-alkynyl substituent in the 'normal' ynamine regiochemical sense to give **27**, followed by cyclization (Scheme 11). In the presence of excess HCl, addition to the *N*-ethynyl substituent occurs in the opposite regiochemical sense to afford the β-chloroenamines **20** and **21** (Scheme 11). Some of the deuterium label of [^2H]-**9d** is found in the product imidazopyridine at the 8-position. This scrambling may simply reflect a competition between pathways involving **10**$\pm$ (or **27**) and the 5,6-didehydro intermediate **25**.

3. Conclusions

Dialkynylimidazoles **9** have been investigated as aza-enediyne analogs which, upon aza-Bergman cyclization, might lead to 5,8-didehydroimidazo[1,2-*a*]pyridine diradical intermediates **10** (Scheme 1). Previous work had shown that thermolysis of dialkynylimidazoles in cyclohexadiene or benzene led instead to products apparently derived from a cyclopentapyrazine carbene intermediate, which has been proposed[12,13] to be derived from the ring-opened form of **10** (Scheme 11). In an attempt to optimize this carbene-generating reaction for intramolecular cascade cyclizations, we have found that thermolysis of **9** in chlorinated solvents affords 5-chloroimidazo[1,2-*a*]pyridines, which can also be obtained from reactions carried out in DMF with 1 equiv of either aqueous HCl or trifluoroacetic acid and tetramethyl-ammonium chloride. In addition to providing access to these synthetically important halogenated imidazo-pyridines, this cyclization is mechanistically interesting due to the potential involvement of the diradical **10**, or its closed-shell, zwitterionic form.

In summary, the results presented here demonstrate the many-faceted chemistry of aza-enediynes such as 1,2-dialkynyl-imidazoles. Unlike enediyne chemistry, which is dominated by reactive diradicals derived from Bergman cyclization, no such reactive diradicals have been observed from thermal cyclization of aza-enediynes. In the case of dialkynylimidazoles, cyclization to imidazopyridine products is observed; however, the mechanism for this transformation is apparently complex, and further investigation is required.

4. Experimental

4.1. General

All reactions were carried out under argon in oven-dried glassware with magnetic stirring. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. THF, ether, and benzene were distilled from sodium/benzophenone immediately prior to use. Dichloromethane and chlorobenzene were distilled from CaH_2 immediately prior to use. Diethylamine was distilled from CaH_2 and stored over KOH, and 1,4-cyclohexadiene was distilled immediately prior to use. DMF was dried over $CaSO_4$ overnight before distillation under reduced pressure. Unless otherwise noted, organic extracts were dried with Na_2SO_4, filtered through a fritted glass funnel, and concentrated with a rotary evaporator (20–30 mmHg). R_f values are reported for analytical thin-layer chromatography (TLC) performed on EM Reagent 0.25 mm silica gel 60-F plates with UV light visualization. Flash chromatography was performed with EM Reagent silica gel (230–400 mesh) using the mobile phase indicated. Melting points (open capillary) are uncorrected. Unless otherwise noted, ^1H and ^{13}C NMR spectra were determined in $CDCl_3$ on a spectrometer operating at 300 and 75 MHz, respectively, and are reported in ppm using solvent as internal standard (7.26 ppm for ^1H and 77.0 ppm for ^{13}C). All mass spectra were obtained in the positive mode by chemical ionization using methane as the ionizing gas.

4.2. General procedure for N-alkynylation

4.2.1. 2-Iodo-1-(2-(trimethylsilyl)ethynyl)-1*H*-imidazole 15a. To a solution of 2-iodoimidazole[21] (900 mg, 4.64 mmol) in 36 ml of dry THF at 0 °C was added LiHMDS (1 M in hexanes, 4.74 ml). After stirring at 0 °C for 30 min, the solution was transferred via cannula to a solution of 2-(trimethylsilyl)ethynyl(phenyl)iodonium trifluoromethanesulfonate[22] (3.2 g, 7.11 mmol) in 36 ml CH_2Cl_2. After stirring at room temperature for about 2 h, the solvent was removed in vacuo and the residue washed with H_2O. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried, and evaporated. The residue was purified by flash chromatography (0–20% EtOAc/hexanes) to afford **15a** (585 mg, 44% yield) as a cream-colored solid: mp 84–86 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J=2 Hz, 1H), 6.98 (d, J=1.6 Hz, 1H), 0.28 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.1, 125.2, 94.1, 90.3, 77.9, −0.3; HRMS *m/z* 290.9814 (calculated 290.9816, $C_8H_{12}N_2SiI$).

4.2.2. 2-Iodo-1-phenylethynylimidazole 2b. Following the general procedure above, and using phenyl(phenylethynyl)-iodinium tosylate,[23] 135 mg (29% yield) of **2b** was obtained as a light yellow oil: ^1H NMR δ 7.07 (d, J=1.5 Hz, 1H), 7.32 (d, J=1.5 Hz, 1H), 7.36–7.41 (m, 3H), 7.54–7.57 (m, 2H); ^{13}C NMR δ 74.4, 78.5, 94.1, 120.8, 125.4, 128.5,

129.2, 131.6, 132.4; HRMS *m/z* 294.9743 (calculated 294.9732, $C_{11}H_8N_2I$).

4.3. General procedure for the preparation of 1,2-dialkynylimidazoles 9

In a glove box, a reaction flask was charged with **15a** (150 mg, 0.52 mmol), $Pd(PPh_3)_4$ (30 mg, 0.026 mmol), and CuI (10 mg, 0.05 mmol). Dry Et_3N (7 ml) was added, and the terminal alkyne (0.6 mmol) was slowly added to the reaction mixture, which was heated to 50 °C for 15 min. The reaction mixture was filtered and the solid washed with Et_2O. The filtrate was evaporated, and the residue was purified by flash chromatography (0–10% EtOAc/hexanes) to afford the silylated dialkynylimidazole. To this material in THF (16 ml) at −78 °C was added a solution of TBAF (112 mg, 0.43 mmol) in THF, and the mixture was stirred at −78 °C for 5 min. The solvent was removed in vacuo and the residue purified by flash chromatography (0:30% EtOAc/hexanes) to afford the dialkynylimidazole **9**.

4.3.1. 2-Ethynyl-1-phenylethynyl-1*H*-imidazole (9a). Following the general procedure above, 17 mg of **9a** (63% yield) was obtained as a white solid: mp 107–108 °C; ^{1}H NMR δ 7.51–7.54 (m, 2H), 7.36–7.39 (m, 3H), 7.19 (d, J=1.5 Hz, 1H), 7.15 (d, J=1.5 Hz, 1H), 3.40 (s, 1H); ^{13}C NMR δ 134.5, 132.0, 129.9, 129.4, 128.8, 122.8, 121.2, 82.5, 77.3, 73.7, 72.2; HRMS *m/z* 193.0762 (calculated 193.0766, $C_{13}H_9N_2$).

4.3.2. 1-Ethynyl-2-(2-phenylethynyl)-1*H*-imidazole (9b). Following the general procedure above, 70 mg of **9b** (69% yield) was obtained as a white solid: mp 69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.57 (m, 2H), 7.40–7.34 (m, 3H), 7.16 (d, J=1.6 Hz, 1H), 7.06 (d, J=1.6 Hz, 1H), 3.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 132.0, 129.7, 129.5, 128.4, 122.4, 121.1, 93.9, 77.2, 70.9, 61.9; HRMS *m/z* 193.0764 (calculated 193.0766, $C_{13}H_9N_2$).

4.3.3. 1-Ethynyl-2-(pent-1-ynyl)-1*H*-imidazole (9c). Following the general procedure above, 93 mg of **9c** (84% yield) was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, J=1.6 Hz, 1H), 6.95 (d, J=1.6 Hz, 1H), 3.12 (s, 1H), 2.44, (t, J=7.2 Hz, 2H), 1.65 (quintet, J=7.2 Hz, 2H), 1.04 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.9, 129.0, 121.7, 96.0, 71.1, 69.2, 61.3, 21.5, 21.2, 13.4; HRMS *m/z* 159.0928 (calculated 159.0922, $C_{10}H_{11}N_2$).

4.3.4. 1-Ethynyl-2-(3-methoxyprop-1-ynyl)-1*H*-imidazole (9d). Following the general procedure above, 111 mg of **9d** (70% yield) was obtained as a white solid: mp 100–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, J=1.2 Hz, 1H), 7.01 (d, J=1.6 Hz, 1H), 4.36 (s, 2H), 3.45 (s, 3H), 3.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.9, 129.7, 122.8, 90.4, 74.7, 70.9, 62.3, 60.1, 58.0; HRMS *m/z* 161.0708 (calculated 161.0715, $C_9H_9N_2O$).

4.3.5. 1-Ethynyl-2-hex-5-en-1-ynyl-1*H*-imidazole (9e). Following the general procedure above using hex-1-en-5-yne,[24] 57 mg (83% yield) of **9e** was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, J=1.5 Hz, 1H), 6.94 (d, J=1.5 Hz, 1H), 5.87 (ddt, J=17.2, 10.4, 6.4 Hz, 1H), 5.10 (dq, J=16.8, 1.6 Hz, 1H), 5.03 (dq, J=10.2, 1.2 Hz, 1H), 3.12 (s, 1H), 2.54 (t, J=7.2 Hz, 2H), 2.36 (q, J=7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 135.7, 129.1, 121.8, 116.1, 95.2, 71.0, 69.4, 61.4, 32.0, 19.1; HRMS *m/z* 171.0925 (calculated 171.0922, $C_{11}H_{11}N_2$).

4.4. General procedure for thermolysis of dialkynylimidazoles in benzene and chlorinated solvents

4.4.1. 7-Phenyl-6-propyl-5*H*-cyclopentapyrazine (16c) and 5,6,7,8-tetrahydropentaleno[2,1-*b*]pyrazine (17). A solution of **9c** (36 mg, 0.228 mmol) in benzene (7 ml) in a sealed vial purged with argon was heated for 5 days at 80 °C. Periodically, the reaction vial was allowed to cool, carefully opened under a stream of argon, sampled for TLC analysis, resealed and returned to the heating bath. Upon the disappearance of **9c** by TLC, the solvent was evaporated and the residue purified by flash chromatography (0–15% EtOAc/hexanes) to afford 40 mg (74% yield) of **16c** as a yellow oil and 6 mg (17% yield) of **17** as a tan solid. Compound **16c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J=2.5 Hz, 1H), 8.19 (d, J=3 Hz, 1H), 7.48–7.45 (m, 4H), 7.38–7.34 (m, 1H), 3.53 (d, J=0.5 Hz, 2H), 2.64 (t, J=7.5 Hz, 2H), 1.65 (sextet, J=7 Hz, 2H), 0.95 (t, J=7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 158.2, 151.4, 141.9, 138.5, 138.2, 132.8, 129.3, 128.5, 127.7, 39.2, 31.7, 22.8, 14.2; HRMS *m/z* 237.1389 (calculated 237.1392, $C_{16}H_{16}N_2$). Compound **17**: mp 90–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J=3.2 Hz, 1H), 8.11 (d, J=3.2 Hz, 1H), 3.33–3.32 (m, 2H), 2.80–2.72 (m, 4H), 2.43 (quintet, J=6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 158.9, 155.8, 146.7, 141.0, 137.3, 38.3, 35.3, 30.8, 27.1; HRMS *m/z* 159.0918 (calculated 159.0922, $C_{10}H_{11}N_2$).

4.4.2. 6-Methoxymethyl-7-phenyl-5*H*-cyclopentapyrazine (16d). Following the general procedure above with **9d** in benzene, 18 mg (38% yield) of **16d** was obtained as a white-pink solid: mp 115–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J=2.8 Hz, 1H), 8.29 (d, J=3.2 Hz, 1H), 7.54–7.48 (m, 4H), 7.44–7.40 (m, 1H), 4.50 (s, 2H), 3.73 (s, 2H), 3.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 157.2, 146.3, 142.0, 140.0, 139.4, 131.9, 129.2, 128.5, 128.3, 68.9, 58.7, 38.4; HRMS *m/z* 239.1182 (calculated 239.1184, $C_{15}H_{14}N_2O$).

4.4.3. 6-(But-3-enyl)-7-phenyl-5*H*-cyclopenta[*b*]pyrazine (16e) and cyclopropane 18. Following the general procedure above with **9e** in benzene, 18 mg (49% yield) of **16e** was obtained as a beige crystalline solid along with 6 mg (24% yield) of **18** as a yellow-brown oil. Compound **16e**: mp 77–79 °C; ^{1}H NMR δ 8.34 (d, J=3 Hz, 1H), 8.22 (d, J=3 Hz, 1H), 7.50–7.46 (m, 4H), 7.41–7.37 (m, 1H), 5.82 (ddt, J=17.1, 10.2, 6.6 Hz, 1H), 5.09–4.08 (m, 2H), 3.57 (s, 2H), 2.80 (t, J=7.8 Hz, 2H), 2.41 (q, J=7.8 Hz, 2H); ^{13}C NMR δ 158.5, 158.0, 150.4, 141.9, 138.6, 138.51 137.2, 132.6, 129.2, 128.5, 127.8, 115.7, 39.3, 33.3, 28.9; HRMS (CI) *m/z* 249.1390 (calculated 249.1392, $C_{17}H_{17}N_2$). Compound **18**: ^{1}H NMR δ 8.24 (d, J=2.7 Hz, 1H), 8.04 (d, J=2.7 Hz, 1H), 6.66 (br s, 1H), 2.66–2.57 (m, 2H), 2.55–2.45 (m, 2H), 2.42–2.31 (m, 1H), 2.22 (dd, J=8.1, 3.9 Hz, 1H), 1.68 (t, J=4.5 Hz, 1H); ^{13}C NMR δ 164.9, 160.8,

159.6, 140.8, 136.7, 118.1, 44.8, 33.4, 29.3, 21.9, 19.4; HRMS *m/z* 171.0924 (calculated 171.0922, $C_{11}H_{11}N_2$).

4.4.4. 5-Chloro-8-phenyl-imidazo[1,2-*a*]pyridine, (19a). Following the general procedure above with **9a** in chlorobenzene, 13 mg (39% yield) of **19a** was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (d, 1H, J=7.6 Hz, H6), 7.30 (d, 1H, J=8 Hz, H7), 7.40–7.44 (m, 1H, *para*-H), 7.48–7.52 (m, 2H, *meta*-H), 7.78 (d, 1H, J=1.2 Hz, H2), 7.85 (d, 1H, J=1.2 Hz, H3), 7.93–7.96 (m, 2H, *ortho*-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 112.1 (C2), 112.4 (C6), 123.3 (C7), 125.1 (C8), 128.6 (*para*-C), 128.7 (*ortho*-C), 129.0 (*meta*-C), 129.2 (C5), 133.9 (C3), 135.9 (*ipso*-C), 144.8 (C9); HRMS (CI) *m/z* 229.0530 (calculated 229.0533, $C_{13}H_{10}N_2Cl$).

4.4.5. 5-Chloro-7-phenyl-imidazo[1,2-*a*]pyridine (19b). Following the general procedure above starting with **9b** in CH_2Cl_2, 6 mg (18% yield) of **19b** was obtained as a tan solid along with 2 mg (7% yield) of **22b**. Compound **19b**: mp 102–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (t, J=1 Hz, 1H), 7.77 (s, 1H), 7.74 (d, J=1 Hz, 1H), 7.65–7.63 (m, 2H), 7.51–7.47 (m, 2H), 7.44–7.34 (m, 1H), 7.21 (d, J=1.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 138.2, 137.9, 134.4, 129.2, 128.6, 126.8, 126.4, 112.9, 111.9, 111.1; HRMS *m/z* 229.0532 (calculated 229.0533, $C_{13}H_{10}ClN_2$). Compound **22b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J=2.8 Hz, 1H), 8.35 (d, J=2.8 Hz, 1H), 7.87–7.84 (m, 2H), 7.52–7.47 (m, 3H), 7.33 (s, 1H), 4.51 (d, J=10.8 Hz, 1H), 4.18 (d, J=10.8 Hz, 1H); HRMS (CI) *m/z* 207.0920 (calculated 207.0922, $C_{14}H_{11}N_2$).

4.4.6. 5-Chloro-7-propyl-imidazo[1,2-*a*]pyridine (19c). Following the general procedure above starting with **9c** in CH_2Cl_2, 6 mg (12% yield) of **19c** was obtained as a yellow oil along with 6 mg (14% yield) of **22c**. Compound **19c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.64 (s, 1H), 7.36 (s, 1H), 6.76 (s, 1H), 2.63 (t, J=7.6 Hz, 2H), 1.69 (sextet, J=6 Hz, 2H), 0.97 (t, J=6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 140.5, 133.4, 125.7, 114.0, 113.8, 110.8, 37.3, 23.4, 13.6; HRMS *m/z* 195.0689 (calculated 195.0689, $C_{10}H_{12}ClN_2$). Compound **22c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J=3 Hz, 1H), 8.26 (d, J=3 Hz, 1H), 6.78 (t, J=2 Hz, 1H), 4.37 (d, J=10.8 Hz, 1H), 3.96 (d, J=10.8 Hz, 1H), 2.55–2.27 (m, 2H), 1.88–1.77 (m, 2H), 1.104 (t, J=8 Hz, 3H); HRMS (CI) *m/z* 173.1083 (calculated 173.1078, $C_{11}H_{13}N_2$).

4.4.7. 5-Chloro-7-(methoxymethyl)-imidazo[1,2-*a*]-pyridine (19d). Following the general procedure above with **9d** in chlorobenzene, 7 mg (15% yield) of **19d** was obtained as yellow oil along with 8.5 mg (15% yield) of **16d**. Compound **19d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H, H3), 7.68 (s, 1H, H2), 7.49 (s, 1H, H8), 6.92 (d, J=1 Hz, 1H, H6), 4.46 (s, 2H, CH_2O), 3.40 (s, 3H, CH_3O); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.1 (C9), 136.0 (C7), 134.1 (C3), 126.3 (C5), 113.9 (C8), 111.6 (C6), 111.4 (C2), 73.1 (CH_2O), 53.4 (CH_3O); HRMS (CI) *m/z* 197.0489 (calculated 197.0482, $C_9H_9ClN_2O$).

4.4.8. 7-(But-3-enyl)-5-chloro-imidazo[1,2-*a*]pyridine (19e). Following the general procedure above with **9e** in CH_2Cl_2, 2 mg (8% yield) of **19e** was obtained as a yellow oil along with 2.5 mg (10% yield) of **22e**. Compound **19e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.66 (s, 1H), 7.42 (d, J=0.9 Hz, 1H), 6.80 (d, J=0.9 Hz, 1H), 5.83 (ddt, J=16.8, 10.5, 6 Hz), 5.09–5.00 (m, 2H), 2.77 (t, J=7.2 Hz, 2H), 2.41 (q, J=7.2 Hz, 2H); HRMS (CI) *m/z* 207.0689 (calculated 207.0689, $C_{11}H_{12}N_2Cl$). Compound **22e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, J=2.4 Hz, 1H), 8.27 (d, J=2.4 Hz, 1H), 6.81 (s, 1H), 5.93 (m, 1H), 5.19 (dt, J=17.4, 1 Hz, 1H), 5.09 (dt, J=10.5, 1 Hz, 1H), 4.37 (d, J=9.9 Hz, 1H), 3.70 (d, J=9.9 Hz, 1H), 2.6–2.4 (m, 4H); HRMS (CI) *m/z* 185.1074 (calculated 185.1079, $C_{12}H_{13}N_2$).

4.5. General procedure for thermolysis in DMF

4.5.1. (*Z*)-1-(2-Chlorovinyl)-2-(3-methoxyprop-1-ynyl)-1*H*-imidazole (20d) and 2-[(*Z*)-2-chloro-3-methoxyprop-1-enyl]-1-[(*Z*)-2-chlorovinyl]-1*H*-imidazole (21d). To a solution of **9d** (25 mg, 0.155 mmol) in dry, degassed DMF (5 ml) was added tetramethylammonium chloride (48 mg, 0.44 mmol) and TFA (32 µl, 0.44 mmol). The mixture was stirred at 80 °C overnight. Upon disappearance of **9d** (by TLC), the solvent was evaporated and the residue diluted with CH_2Cl_2 (5 ml) and washed with satd $NaHCO_3$ solution (2×5 ml) and brine (5 ml). The organic extracts were combined, dried and the solvent evaporated. The residue was purified by flash chromatography (0–70% EtOAc/hexanes) to afford 3 mg (10% yield) of **20d** as a yellow oil and 13 mg (36% yield) of **21d** as a yellow oil. Compound **20d**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.87 (d, J=1.6 Hz, 1H), 7.26 (d, J=6.8 Hz, 1H), 7.10 (br s, 1H), 6.02 (d, J=6.2 Hz, 1H), 4.35 (s, 2H), 3.42 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 132.1, 130.4, 123.4, 119.7, 108.6, 91.1, 75.3, 60.4, 58.1; HRMS *m/z* 197.0483 (calculated 197.0482, $C_9H_{10}ClN_2O$). Compound **21d**: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.52 (d, J=1 Hz, 1H), 7.20 (br s, 1H), 6.98 (d, J=6 Hz, 1H), 6.63 (t, J=1.5 Hz, 1H), 6.18 (d, J=6 Hz, 1H), 4.14 (d, J=1.5 Hz, 2H), 3.42 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 142.4, 136.1, 129.9, 123.9, 119.5, 113.3, 112.3, 76.1, 58.7; HRMS *m/z* 233.0235 (calculated 233.0242, $C_9H_{11}Cl_2N_2O$).

4.5.2. (*Z*)-1-(2-Chlorovinyl)-2-(2-phenylethynyl)-1*H*-imidazole (20b). Following the general procedure above with **9b** and employing 1.2 equiv of conc HCl in place of Me_4NCl and TFA, 18 mg (69% yield) of **20b** was obtained as a yellow oil: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.92 (d, J=1.5 Hz, 1H), 7.58–7.55 (m, 2H), 7.41–7.32 (m, 4H), 7.19 (d, J=1.5 Hz, 1H), 6.00 (d, J=6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.6, 131.8, 130.03, 129.5, 128.5, 123.0, 121.2, 119.2, 107.9, 94.5, 77.7; HRMS (CI) *m/z* 229.0533 (calculated 229.0531, $C_{10}H_{12}ClN_2$)

4.5.3. (*Z*)-1-(2-Chlorovinyl)-2-(pent-1-ynyl)-1*H*-imidazole (20c). Following the general procedure above with **9b** and employing 1.2 equiv of conc HCl in place of Me_4NCl and TFA, 20 mg (56% yield) of **20c** was obtained as a yellow oil along with 5 mg (14% yield) of **19c**. Compound **20c**: ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.84 (d, J=1.5 Hz, 1H), 7.25 (d, J=6.6 Hz, 1H), 7.03 (d, J=1.2 Hz, 1H), 5.96 (d, J=6 Hz, 1H), 2.45, (t, J=6.9 Hz, 2H), 1.67 (quintet, J=7.5 Hz, 2H), 1.04 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 133.5, 129.9, 123.5, 118.9, 107.4, 96.6, 70.1, 22.1, 21.6,

13.7; HRMS (CI) *m/z* 195.0686 (calculated 195.0689, $C_{10}H_{12}ClN_2$).

4.6. General procedure for deuteration of dialkynylimidazoles

4.6.1. [^2H]-1-Ethynyl-2-(3-methoxyprop-1-ynyl)-1*H*-imidazole ([^2H]-9d). A solution of **9d** (101 mg, 0.63 mmol) in dry ether (7 ml) was cooled to −78 °C using a dry-ice acetone bath and a 1.4 M solution of *n*-BuLi in hexanes (0.495 ml, 0.69 mmol) was added slowly drop wise. The resultant suspension was stirred for 15 min and 3 ml of D_2O was added. The reaction mixture was allowed to slowly warm to room temperature over 0.5–1 h and extracted with CH_2Cl_2. The organic extracts were combined, dried, and purified by flash chromatography (5–10% Et_2O/hexanes) to yield 95 mg (94%) of [^2H]-**9d** as a light brown oil. Isotopic purity > 95% by ^1H NMR: ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, J= 1.6 Hz, 1H), 7.01 (d, J=1.2 Hz, 1H), 4.36 (s, 2H), 3.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 129.6, 122.5, 90.2, 74.5, 70.4, 61.6 (t, J_{C-D}=40.5 Hz), 59.9, 57.8; HRMS (CI) *m/z* 162.0774 (calculated 162.0777, $C_9H_8N_2DO$).

4.6.2. [^2H]-2-Ethynyl-1-phenylethynyl-1*H*-imidazole ([^2H]-9a). Following the procedure above starting with **9a**, 59 mg (94% yield) of [^2H]-**9a** was obtained as light brown solid. Isotopic purity was >95% by ^1H NMR: mp 108.5–109 °C; ^1H NMR (300 MHz, CD_2Cl_2) δ 7.57–7.52 (m, 2H), 7.42–7.37 (m, 3H), 7.24 (d, J=1.5 Hz, 1H), 7.05 (d, J=1.2 Hz, 1H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 134.3, 132.0, 121.9, 129.5, 128.9, 123.2, 121.2, 82.1 (t, J=39 Hz), 77.5, 73.6, 71.9 (t, J=7.5 Hz); HRMS (CI) *m/z* 194.0826 (calculated 194.0828, $C_{13}H_8N_2D$).

4.6.3. Diethyl-(7-methoxymethyl-imidazo[1,2-*a*]pyridin-5-yl)-amine (23d). A solution of **9d** (22 mg, 0.138 mmol) in benzene (1.8 ml) and diethylamine (285 μl, 2.76 mmol) was heated at 80 °C for 14 h. The reaction mixture was allowed to cool, the solvent was evaporated, and the residue was purified by flash chromatography (3:0:7–3:1:6 hexanes/CH_3OH/CH_2Cl_2) to afford 20 mg (60% yield) of **23d** as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.60, (s, 1H, H3), 7.57 (s, 1H, H2), 7.30 (s, 1H, H8), 6.36 (s, 1H, H6), 4.49 (s, 2H, CH_2O), 3.39 (s, 3H, CH_3O), 3.19 (q, J=7 Hz, 4H, CH_2N), 1.11 (t, J=7 Hz, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0 (C9), 144.2 (C5), 136.6 (C7), 133.0 (C2), 110.12 (C3), 110.0 (C8), 102.0 (C6), 74.2 (CH_2O), 58.2 (CH_3O), 44.8 (CH_2N), 12.1 (CH_3); HRMS (CI) *m/z*, 234.1599 (calculated 234.1606, $C_{13}H_{20}N_3O$).

Acknowledgements

This work was supported by a grant from the Robert Welch Foundation (F-1298).

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