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Ring-Closing Metathesis Reactions on Azinium Salts: Straightforward Access to Quinolizinium Cations and Their Dihydro Derivatives

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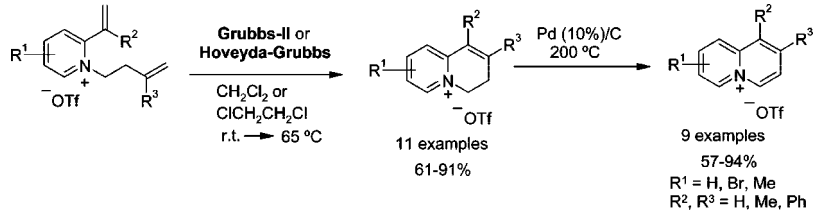

The ring-closing metathesis reaction of 1-butenyl-2-vinylpyridinium salts and 2-butenyl-1-vinylpyridinium salts using Grubbs second generation and Hoveyda−Grubbs catalysts proved to be an efficient approach to 3,4-dihydro- and 1,2-dihydroquinolizinium salts and the corresponding quinolizinium derivatives by an improved thermal oxidation in the presence of Pd/C without solvent. A comparative study showed that the quinolizinium system was obtained in better yields through the 3,4-dihydroquinolizinium route, thus allowing the synthesis of quinolizinium derivatives or improvements in the yields of some examples reported previously.

Introduction

Azinium and azolium salts are representative models of heteroaromatic cations. Some of these systems have been known since the emergence of heterocyclic chemistry as they have a wide range of applications that include (inter alia) a variety of biological activities,[1] their use as reagents for organic synthesis,[2] their role as viologens[3] or in chromophores that have fluorescent,[4] nonlinear optical (NLO)[5] and DNA intercalating[6] properties, and more recently their use as ionic liquids.[7] In addition, these salts are easily obtained by simple alkylation of an azine or an azole.

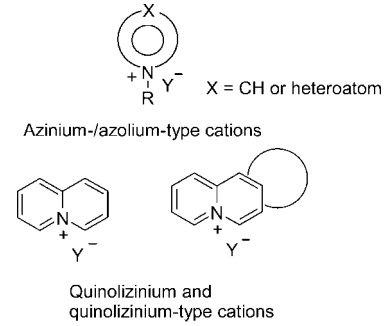

FIGURE 1. Types of heteroaromatic cations.

Less well-known is the other possible class of heteroaromatic cations represented by the quinolizinium salts[8] (Figure 1). The main feature of these azonia cations is the presence of a

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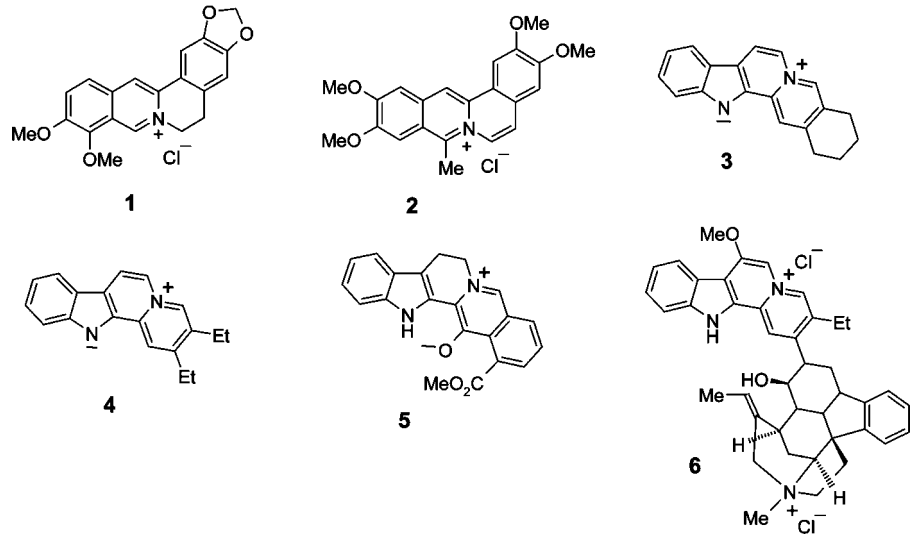

FIGURE 2. Quinolizinium system in natural alkaloids.

quaternary bridgehead nitrogen, which is responsible for the cationic nature of quinolizinium, the simplest cationic heterocyclic system belonging to this type and many other related cations.

Although the synthesis of quinolizinium-type cations is not as easy as the preparation of azinium- and azolium-type cations, the potential applications of the former systems appear to be very similar to those found for the latter class, and in some cases, new applications or improved behavior have been reported. As an example, results from our laboratory show that catiophores based on the quinolizinium system have much more interesting NLO properties than those based on azinium cations[9] (pyridinium, quinolinium, and isoquinolinium), and very promising antitumor activity has also been found in some DNA intercalator tetracyclic cationic compounds based on azaquinolizinium cations[10] targeting MET kinase and Bcl-X_L. Similarly, other groups have reported quinolizinium-based derivatives with interesting DNA-binding properties,[11] fluorophores for detecting biomolecules,[12] dyes for photovoltaic cells,[13] and new biological activities such as agents for the treatment of bipolar affective disorder in mammals,[14] selective inhibitors of human TRPM4,[15] and anti-inflammatory activity in cystic fibrosis bronchial cells.[16]

In addition, the quinolizinium system (and its dihydro form) is present in a variety of natural alkaloids known as berberines and protoberberines, with berberine itself (**1**) and coralyne (**2**) being the representative examples of this large family of alkaloids, which are widely spread over nine botanic families.[17] Moreover, quinolizinium ylides are well-known conjugated heterocyclic mesomeric betaines that are present in different families of alkaloids such as those based on the indolo[2,3-*a*]quinolizinium system represented by sempervirine (**3**), flavopereirine (**4**), neooxygambirtannine (**5**), and afrocurarine (**6**) inter alia[18] (Figure 2).

The lack of general methodologies to obtain derivatives of quinolizinium-type cations and our interest in this field led us to study two new approaches to these azonia cations. One of these approaches involved palladium-catalyzed cross-coupling methods,[19] and the other concerned metathesis strategies to build up the quinolizinium core. We report here our full results[20] from a comparative study of ring-closing metathesis (RCM) approaches to access the dihydro- and quinolizinium systems and discuss the scope of the best strategy to obtain quinolizinium derivatives.

Results and Discussion

Although the ring-closing metathesis reaction (RCM) has been extensively used in heterocyclic chemistry and has proven to be a powerful heterocyclization strategy,[21] the number of studies dealing with RCM on charged substrates is restricted to a few examples. These examples include two pioneering works on ammonium salts,[22] the synthesis of the macrocycle moiety of the (*R*)-(+)-muscopyridine alkaloid using a RCM on a pyridinium hydrochloride[23] and the total synthesis of manzamine, which involved as the key step a RCM reaction on an alkenyl pyridinium to build up the 13-membered ring of this alkaloid.[24]

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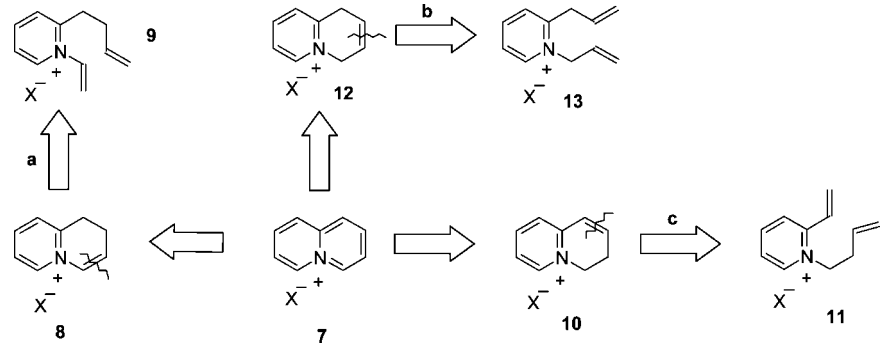
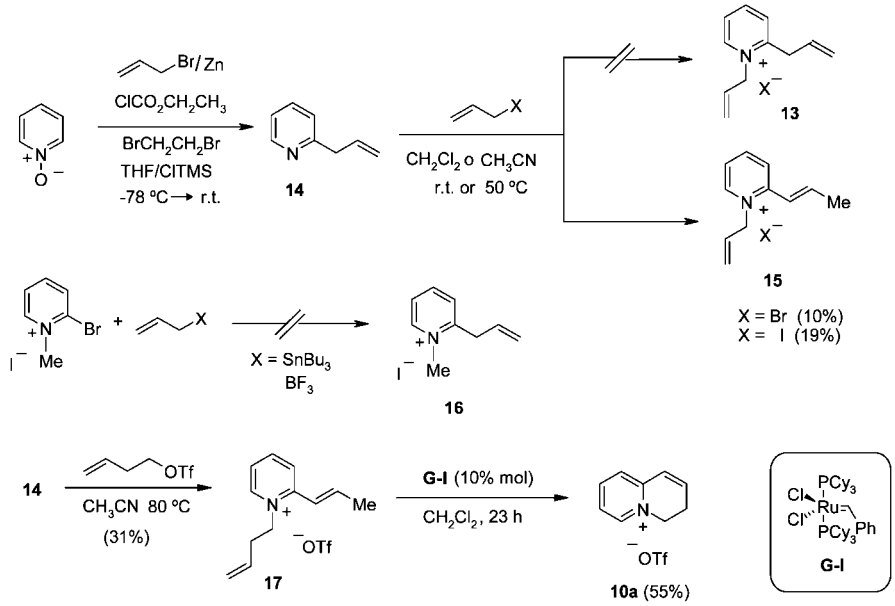
SCHEME 1. Retrosynthetic Strategies for the Quinolizinium System



SCHEME 2. Synthesis of 3,4-Dihydroquinolizinium Triflate 10a by a RCM Reaction



We envisaged that the quinolizinium system could be obtained from three different dihydro derivatives, which in turn could be obtained by three different disconnections (a, b, and c in Scheme 1) involving β, γ, and δ bonds with respect to the nitrogen atom of the pyridinium substrate.

Initially, strategy b seemed to be the most suitable because the other two approaches would involve the use of an electron-poor diene which, in principle, seemed less appropriate to participate in the metathesis reactions. Furthermore, the dienic precursor **13** appeared to be more easily available than the corresponding dienic substrates **9** and **11**. The synthesis of **13** was initially attempted from 2-propenylpyridine (**14**), the synthesis of which is described[25] from the reaction of pyridinium *N*-oxide under the conditions shown in Scheme 2. When **14** was subjected to alkylation with either allyl bromide or allyl iodide, the expected pyridinium diene **13** was not obtained under a variety of different conditions, with the isomeric diene **15** being isolated in low yields (10−19%). Several attempts to avoid the migration of the double bond proved fruitless, and we therefore explored the synthesis of **13** by an alternative route starting from a pyridinium salt functionalized at the C2 position with the propenyl substituent. Our choice was 2-bromo-1-methylpyridinium iodide as this is the simplest model to study the feasibility of the introduction of the allylic substituent at the C2 position. Unfortunately, all attempts to prepare derivative **16** were unsuccessful using either propenyltributyl stannane under Stille coupling conditions or allyl trifluoroborate under Suzuki coupling conditions. The most promising result of these initial studies was achieved when **14** was alkylated with butenyl triflate[26] to yield, as expected, the corresponding diene **17**. Furthermore, we were able to prove that this diene is a suitable substrate for a RCM reaction to afford the 3,4-dihydroquinolizinium triflate (**10a**) in moderate yield (55%). This result strongly supported our strategy based on disconnection c since it proved that a 1-(3′-butenyl)-2-vinylpyridinum salt can be an appropriate substrate for the desired RCM reaction.

Clearly, the next step was the preparation of the dienic substrate **11a** in order to test it in the RCM reaction. In this case, the commercially available 2-vinylpyridine was chosen as starting material, which was easily alkylated with 3-butenyl triflate to yield **11a** in 82% yield (Scheme 3). It was found that **11a** was a good substrate for the RCM reaction under different

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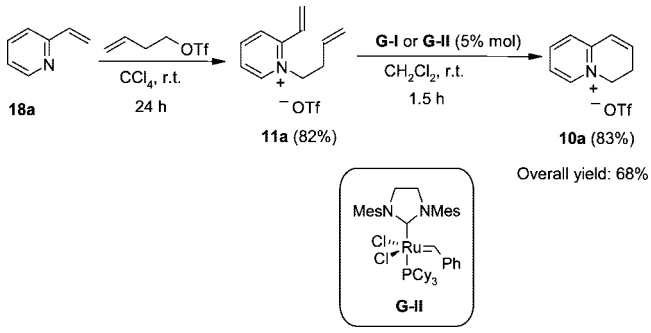
SCHEME 3. Improved Synthesis of 10a by a RCM Reaction



conditions using first generation Grubbs catalyst (**G-I**).[27] The best results (83% yield of isolated product) were achieved in dichloromethane, at room temperature, for 1.5 h and using 5 mol % of the catalyst. The metathesis reaction of **11a** in the presence of the second generation Grubbs catalyst (**G-II**) gave the same yield (83%). It is worth noting that this route to 3,4-dihydroquinolizinium triflate (**10a**), based on the RCM reaction as the key step, affords the desired product in 68% overall yield while the previously reported three-step synthesis of **10a** starting from 2-methylpyridine gave this dihydro derivative as the bromide in 32% overall yield.[28]

The conversion of **10a** into quinolizinium **7a** was first reported by Boekelheide and Gall in their pioneering synthesis of the quinolizinium heterocycle, and this oxidation was the main drawback of this synthesis since the yield was only 15% when using Pd/C as catalyst in refluxing ethanol.[28] An improved synthesis of **7a** was later reported by the same authors, with the oxidation step improved to give 34% yield using P/C in refluxing *n*-butanol.[29] Other oxidants such as NBS, chloranil, selenium dioxide, and oxygen in the presence of platinum either in acetic acid or nitrobenzene gave the fully oxidized cation in yields ranging from 3 to 26%.

In order to improve the reported yields of this oxidation, we also studied the transformation of **10a** into **7a** in the hope of finding synthetically more useful conditions for this conversion. A summary of the conditions and yields for the oxidation of **10a** to **7a** is given in Table 1. We tested the oxidation using DDQ in toluene (100 °C) and DMF (120 °C), but only the latter conditions afforded the oxidation product, albeit in only 35% yield after 21 h (Table 1, entries 8 and 9). The use of the reported conditions (Pd/C, HOAc) for the oxidation of some 1,4-dihydropyridines bearing electron-withdrawing substituents[30] led to a considerable improvement in the yield to 66%, although the reaction required 14 days to reach completion (Table 1, entry 11). We thought that this disadvantage could by circumvented by carrying out the reaction under microwave irradiation due to the well-known efficacy of this technique to reduce reaction times significantly.[31] Attempts to carry out the reaction in a microwave reactor in the absence of solvent, heating at 160−200 °C at 100 W, afforded variable mixtures of **10a**, **7a**, and the 1,2,3,4-tetrahydroquinolizinium **21a** or the two latter compounds

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(28) Boekelheide, V.; Gall, W. G. *J. Am. Chem. Soc.* **1954**, *76*, 1832.
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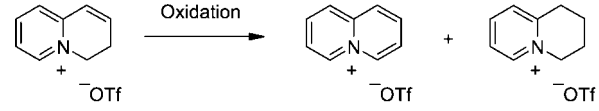
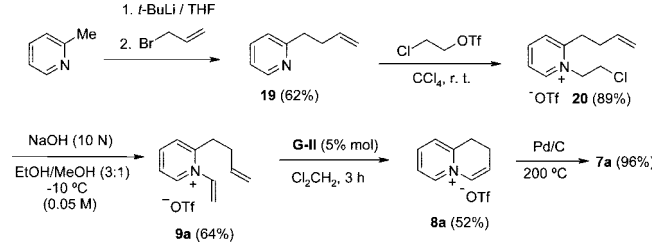
TABLE 1. Optimization of Reaction Conditions for the Oxidation of 10a (NR: No Reaction)



entry	conditions	results (yield %)[a]
1	Pd/C, EtOH reflux	15[b]
2	NBS, Et_3N	6[c]
3	SeO_2	3[c]
4	chloranil	10[c]
5	O_2/Pt, AcOH	23[c]
6	O_2/ Pt, $PhNO_2$	26[c]
7	Pd/C, *n*-BuOH reflux	34[c]
8	DDQ/toluene 24 h, 110 °C	NR
9	DDQ/DMF, 21 h, 120 °C	35
10	Pd/C, AcOH, 24 h, 80 °C	NR
11	Pd/C, AcOH, 14 days, 117 °C	66
12	10% Pd/C, 160 °C, MW, 100 w, 5 min	**11a**:**7a**:**21a** 0.04:0.8:0.8
13	10% Pd/C, 200 °C, MW, 100 w, 5 min	**11a**:**7a**:**21a** 0:1:1
14	30% Pd/C, 200 °C, MW, 100 w, 5 min	**11a**:**7a**:**21a** 0:1:1
15	30% Pd/C, 200 °C, 2 h	79

[a] Yields refer to **7a** as isolated products. [b] Yield reported in ref 29. [c] Yields reported in ref 30.

SCHEME 4. Synthesis of the 1,2-Dihydroquinolizinium Triflate 8a by a RCM Reaction

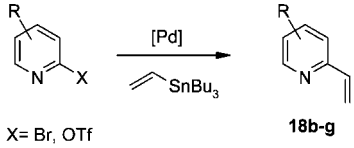


if the starting material was completely consumed (Table 1, entries 12−14). Several attempts to avoid the formation of **21a** in the presence of hydrogen acceptors proved unsuccessful either in the microwave reactor or in a domestic microwave oven with the reaction carried out in an open vessel. Finally, it was found that under conventional heating at 200 °C and increasing the amount of catalyst to 40% the quinolizinium triflate was obtained in 79% yield in only 2 h (Table 1, entry 15).

Although it seemed feasible to extend the synthetic procedure developed for **7a** to different quinolizinium derivatives, we decided to explore the approach involving the disconnection of the β bond (strategy a in Scheme 1) in order to compare the two approaches before proceeding to study the scope of these reactions. The desired diene **9a** was synthesized in three steps from 2-methylpyridine as shown in Scheme 4. The dehydrohalogenation reaction conditions employed to generate **9a** from **20** were those reported by Katritzky[32] for the formation of *N*-vinyl derivatives. Under these conditions, the diene **9a** was obtained in moderate yield (64%), and this could not be improved by changing the base ($NaHCO_3$, Na_2CO_3, and Cs_2CO_3) and/or the solvent (MeCN, EtOH/MeOH, CH_2Cl_2/H_2O, MeCN/*i*-PrOH). Under the same conditions as used for the RCM reaction of **11a**, diene **9a** afforded **8a** in moderate yield (52%). Attempts to improve this yield using the second generation Grubbs catalyst (**G-II**) and Hoveyda−Grubbs catalyst (**H-G**, see below in Table 6) were unsuccessful. It is noteworthy that

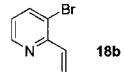
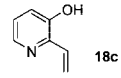
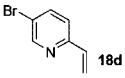
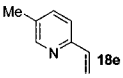
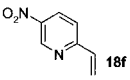
(32) Katritzky, A. R.; Rubio-Teresa, O. *J. Org. Chem.* **1983**, *48*, 4017.

TABLE 2. Synthesis of 2-Vinylpyridines 18



X= Br, OTf

18b-g

entry	R	conditions	vinylpyridine (**18**)	yield (%)[a]
1	3-Br	5% $Pd_2(dba)_3$/10% TFP/ 3 equiv. LiCl,THF, 65 °C	 **18b**	65[b]
2	3-OH	5% $Pd(PPh_3)_4$, DMF, 120 °C	 **18c**	86
3	5-Br	5% $Pd_2(dba)_3$/10% TFP, THF, 65 °C	 **18d**	76
4	5-Me	5% $Pd_2(dba)_3$/10% TFP, CH_3CN, 80 °C	 **18e**	70
5	5-NO_2	5% $Pd_2(dba)_3$/10% TFP, THF, 65 °C	 **18f**	50

[a] Yields refer to **18** as isolated products. [b] X = OTf; TFP = trifurylphosphine.

this is the first route that allows the synthesis of the parent 1,2-dihydroquinolizinium system in a synthetically useful overall yield (18%), and this enabled the first full characterization of this system as the previously reported synthesis of the 1,2-dihydroquinolizinium picrate gave a very poor yield (overall yield not given).[33] Finally, the oxidation of **8a** under the optimized conditions used for **10a** gave **7a** in almost quantitative yield.

A simple comparison between these two strategies for the synthesis of the quinolizinium system shows the advantage of the approach based on the disconnection of the δ bond (strategy c) (Scheme 1) since it affords the quinolizinium triflate **7a** in a 54% overall yield, while strategy a, based on the β bond disconnection, gave **7a** in only 18% overall yield.[34] Consequently, our next step was to study the scope of the RCM reaction based on strategy c to produce differently substituted 3,4-dihydroquinolizinium derivatives by using appropriate dienic pyridinium salts as substrates for the RCM reaction. The simplest approach to substituted 3,4-dihydroquinolizinium salts was to use a variety of substituted 2-vinylpyridines as starting materials to obtain the appropriate cationic dienes. As a result, our first goal was the synthesis of these intermediates since most of these pyridine derivatives are currently unknown. It was found that various vinylpyridines **18b**−**f** could be prepared in moderate or good yields by a Stille reaction between tributylvinyl stannane and the corresponding 2-bromo- or 2-trifluoromethanesulfonyloxypyridine under the optimized conditions for each substrate (see Table 2). In addition, two more substrates **18g**,**h** were obtained from **18c** and **18b**, respectively, under the conditions shown in Scheme 5. It is worth noting that neither **18g** nor **18h** could be obtained from the corresponding substituted 2-bromo- or 2-trifluoromethanesulfonyloxypyridine under the Stille coupling conditions employed for the preparation of **18b**−**f**.

SCHEME 5. Synthesis of 3-Substituted 2-Vinylpyridines 18g,h

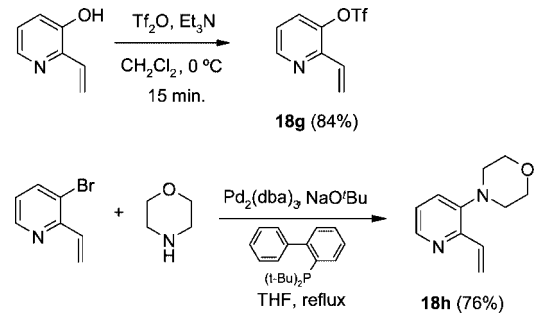
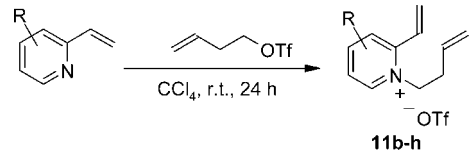
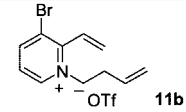
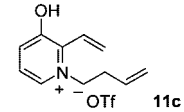
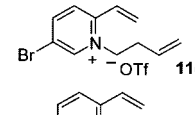
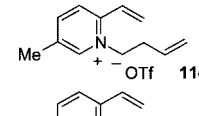
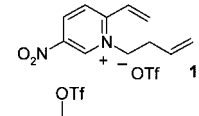
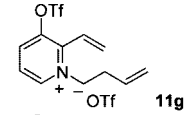
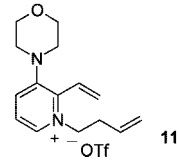


TABLE 3. Synthesis of Pyridinium Dienes 11b−h (NR: No Reaction)



11b-h

entry	vinylpyridine (**18**)	diene (**11**)	yield (%)[a]
1	**18b**	 **11b**	67
2	**18c**	 **11c**	–[b]
3	**18d**	 **11d**	41
4	**18e**	 **11e**	60
5	**18f**	 **11f**	NR
6	**18g**	 **11g**	NR
7	**18h**	 **11h**	55

[a] Yields refer to **11** as isolated products. [b] Inseparable mixture of **18c**, **11c**, and the O-alkylation product.

The *N*-alkylation of **18b**−**h** was carried out with 3-butenyltriflate under the same conditions used for the synthesis of the diene **11a**. The results are summarized in Table 3 and show that the reaction failed with **18f** and **18g** while the attempted *N*-alkylation of **18c** under different conditions gave, in all cases, inseparable mixtures of the desired diene along with the *O*-alkylation product (main component) and the starting material. For the rest of the vinylpyridines, the *N*-alkylation reaction afforded the expected dienes in moderate yields (41−67%). The failure of the reaction with **18f**,**g** could be due to the electron-withdrawing effect of the substituents on the pyridine ring. On

(33) Glover, E. E.; Jones, G. *J. Chem. Soc.* **1959**, 1686.
(34) The best synthesis of the quinolizinium bromide was reported in also 54% overall yield by Miyadera, T.; Iwai, I. *Chem. Pharm. Bull.* **1964**, *12*, 1338.

the other hand, the moderate yields obtained in all cases seem to be more related to the low stability of the alkylating agent. In fact, this species had to be generated and used in situ in order to minimize its decomposition, which takes place under moderate heating or even at room temperature with prolonged reaction times.

To investigate further the potential of the RCM reaction as a general method for the synthesis of substituted 3,4-dihydroquinolizinium salts and eventually the corresponding quinolizinium derivatives after oxidation, we undertook the synthesis of a series of dienic quinolizinium derivatives **11i**−**s** bearing substituents in the vinyl and/or butenyl moieties. The synthesis of some ethenyl pyridines is shown in Scheme 6. Two synthetic strategies are outlined for 2-(2′-propenyl)pyridine (**18k**). The upper route has been reported previously,[35] but we found that a better yield could be obtained by using the lower route, which involves a Wittig reaction on 2-acetylpyridine with the appropriate ylide. This pyridine derivative was also the starting compound for the synthesis of the silylenol ether derivative **18j**. The styryl pyridine derivative **18i** was obtained in moderate yield by a Suzuki coupling reaction between 2-bromopyridine and the 2-(phenylethynyl)boronic acid. On the other hand, two commercially available 3-substituted 3-butenoles (3-bromo- and 3-methyl-3-butenol) were used for the synthesis of the corresponding triflates. In addition, 3-bromo-3-butenol was also employed as the starting material for the preparation of some 3-aryl-3-butenoles by a Suzuki coupling reaction according to literature procedures.[36] A literature procedure was also followed for the preparation of 3-iodo-3-butenol from 3-butynol.[37]

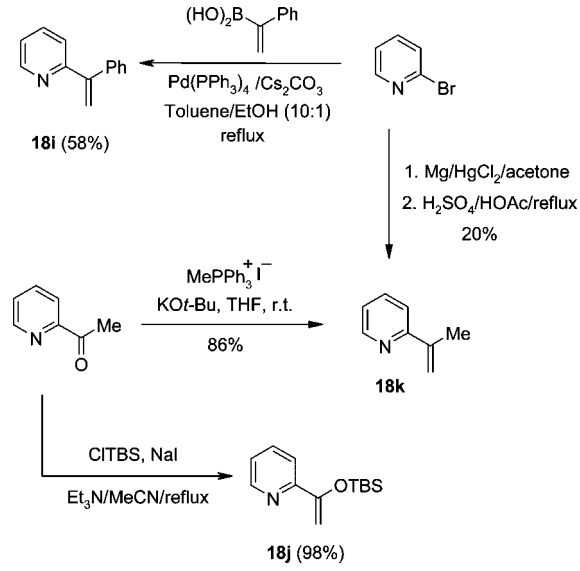
The synthesis of the series of dienic pyridinium derivatives with a variety of substitution patterns was carried out using the method described above for **11a**−**h**. The results of the *N*-alkylation reactions of the 2-propenylpyridines with the 3-substituted butenyl triflates are summarized in Table 4.

The yields obtained for dienes **11i**−**s** are similar to or lower than those obtained from vinylpyridines **18b**−**h** in their reactions with 3-butenyl triflate. The lower yields seem to be related to the reduced stability of these substituted dienes, which are prone to decompose at room temperature. It is noteworthy that the instability of diene **11p** precluded its isolation and characterization. On the other hand, the higher temperature needed to complete some N-alkylations, such as those detailed in entries 2 and 11, favored the decomposition and led to decreases in the isolated yields.

Before submitting the pyridinium dienes **11** to the ring-closing metathesis reaction, we further studied the process using the dienes **11b** and **11h** as model systems which bear an electron-donating and an electron-withdrawing group in the pyridine ring, respectively. In both cases, the second generation Grubbs catalyst (**G-II**) proved to be more efficient than **G-I** as it gave better yields of the corresponding 3,4-dihydroquinolizinium derivatives (**11b**, 80 vs 40%; **11h**, 85 vs 78%). Consequently, catalyst **G-II** was initially chosen to carry out the RCM reaction, and very good yields were obtained from dienes **11b**,**d**,**e**,**h**, as shown in Table 5.

The monosubstituted dienes on the ethenyl moieties **11i**−**k** were next subjected to the RCM reaction using the conditions detailed in Table 6. These conditions proved to be very efficient

SCHEME 6. Synthesis of Ethenylpyridines 18i−k



for the diene **11k** (bearing a methyl substituent), which afforded the corresponding 1-methyl-3,4-dihydroquinolizinium triflate (**10k**) in 91% yield. However, only a moderate yield was obtained in the RCM reaction of **11i** (61%), and in the case of **11j**, only partial conversion was observed along with the formation of polymerization products, which resulted in only 23% yield of the corresponding 3,4-dihydroquinolizinium derivative **10j**. On heating the reaction mixture under reflux under higher dilution conditions (0.01 M), the yield increased to 40%. In an attempt to improve this yield, the Hoveyda−Grubbs catalyst (**H-G**) was also tested due to its known potential in metathesis reactions with electron-deficient olefins[38] and its higher thermal stability.[39] The reaction performed in CH_2Cl_2 under refluxing conditions in the presence of 5 mol % of **H-G** gave 60% yield of the RCM product, and polymerization products were not formed, although some starting diene still remained in the reaction mixture. Next, using the best catalyst, **H-G**, the reaction temperature and catalyst loading were varied. It was found that, in 1,2-dichloroethane at 65 °C, full conversion of the diene **11j** was observed after 3 h and product **10j** could be isolated in 78% yield. The use of 2 mol % of **H-G** again led to incomplete conversion of the diene after the same reaction time.

It is noteworthy that these optimized conditions for the synthesis of **10j** did not lead to the expected improvement in the yield of the dihydroquinolizinium **10i**. For this reason, the RCM reaction on substituted dienes on the butenyl moiety and on disubstituted dienes was, in all cases, tested with both the **G-II** and **H-G** catalysts. The results are shown in Table 6, and these represent the optimal conditions for the metathesis reaction in each case.

The metathesis reaction involving substitution in the butenyl diene moiety (dienes **11l**−**o**) afforded the 2-methyl- and 2-phenyl-3,4-dihydroquinoliziniums **10l** and **10m** in good yields using the **G-II** catalyst under the conditions shown in entries 4 and 5. However, neither **H-G** nor **G-II** catalysts were able to

(35) (a) Bachman, G. B.; Micucci, D. *J. Am. Chem. Soc.* **1948**, *70*, 2381. (b) Adamson, D. W.; Billinghurst, J. W. *J. Chem. Soc.* **1950**, 1039.

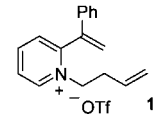
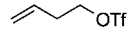
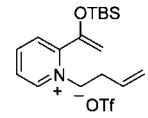
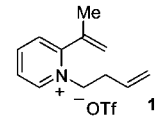
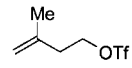
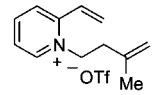
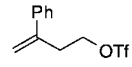
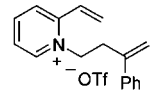
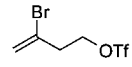
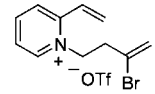
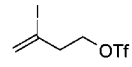
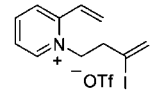
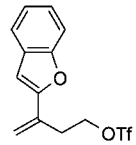
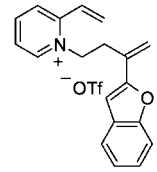
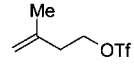
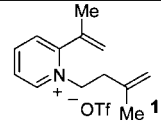
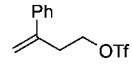
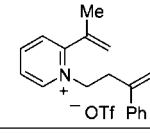
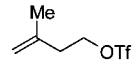
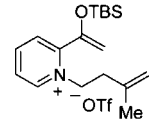
(36) Huang, Q.; Fazio, A.; Dai, G.; Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 7460.

(37) Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, 675.

(38) (a) Randl, S.; Gessler, S.; Wakamatsu, H.; Blechert, S. *Synlett* **2001**, *3*, 430. (b) Randl, S.; Connon, S. J.; Blechert, S. *Chem. Commun.* **2001**, 1692. (c) Randl, S.; Connon, S. J.; Blechert, S. *Chem. Commun.* **2001**, 1796.

(39) (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168. (b) Kingsbury, J. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 4510.

TABLE 4. Synthesis of Substituted Pyridinium Dienes 11i−s

entry	ethenyl-pyridine (**18**)	butenyl triflate	T (°C)	diene (**11**)	yield[a] (%)
1	**18i**		r.t.	 **11i**	51
2	**18j**		40°C	 **11j**	40
3	**18k**		r.t.	 **11k**	36
4	**18a**		r.t.	 **11l**	46
5			r.t.	 **11m**	60
6			r.t.	 **11n**	74
7			r.t.	 **11o**	46
8			r.t.	 **11p**	-[b]
9	**18k**		r.t.	 **11q**	28
10			r.t.	 **11r**	21
11	**18j**		40 °C	 **11s**	23

[a] Yields refer to **11** as isolated products. [b] Decomposition.

produce the cyclization reaction of substrates **11n**,**o**, both of which bear a halogen as a substituent in the butenyl moiety.

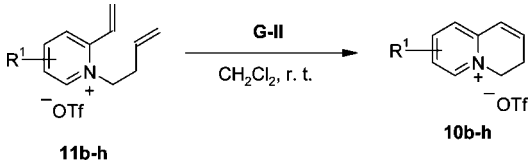
This result seems to be consistent with previous reports on the failure of cross-metathesis reactions using vinyl halides[40] or those describing the feasibility of the RCM reaction with vinyl chlorides but not with vinyl bromides.[41] Apparently, the higher reactivity of the catalyst toward the halogen when compared to the terminal alkene leads to the formation of an unreactive Fisher carbene, thus precluding the RCM reaction.

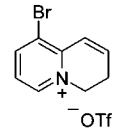
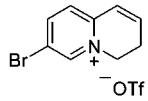
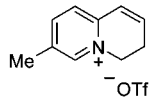
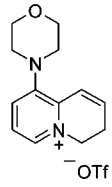
Substitution in both the ethenyl and butenyl moieties required the use of the **H-G** catalyst, higher temperatures, and longer

(40) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783.

(41) Chao, W.; Weinreb, S. M. *Org. Lett.* **2003**, *5*, 2505.

TABLE 5. Synthesis of 3,4-Dihydroquinolizinium Salts 10b−h by RCM Reaction of 11



entry	diene (**11**)	RCM product (**10**)	yield (%)[a]
1	**11b**	 **10b**	80[b]
2	**11d**	 **10d**	80[c]
3	**11e**	 **10e**	82[b]
4	**11h**	 **10h**	85[c]

[a] Yields refer to **10** as isolated products. [b] Reaction time: 1 h. [c] Reaction time: 2 h.

reaction times to afford the desired 1,2-disubstituted 3,4-dihydroquinolizinium salts, as exemplified by the formation of **10q** (entry 8). However, even harsher conditions were not sufficient to achieve the cyclization of dienes **11r**,**s**, which were partially recovered from the reaction mixtures after 24 h at 120 °C in tetrachloroethane (Table 6, entries 9 and 10).

The failure of the RCM reaction on dienes **11r**,**s** along with the higher temperatures and/or longer reaction times needed to complete the reaction on dienes **11l** and **11m** when compared with dienes bearing the same substituents (Me and Ph) in the ethenyl moiety (**10k** and **10i**) strongly supports the mechanism of the reaction as being initiated with the insertion of the Ru alkylidene into the double bond of the butenyl alkene rather than into the double bond of the ethenyl moiety because of the electronic deficiency of the latter. If this is the case, the steric effect of the substituent on the butenyl moiety will have a crucial influence on the rate of the reaction (Scheme 7).

The final goal of our study was to transform the substituted 3,4-quinolizinium salts **10** into the corresponding quinolizinium derivatives **7** in order to demonstrate both the scope of the oxidation conditions used for the formation of the quinolizinium **7a** from **10a** and the power of the RCM reaction to access the quinolizinium derivatives or to improve their synthesis in cases where they are known. Thus, the synthesized 3,4-dihydroquinolizinium derivatives were subjected to the oxidation conditions explored for the transformation of **10a** into **7a**. The results obtained in a comparative study under two different sets of conditions [reflux in acetic acid or heating at 200 °C in the presence of a high ratio of Pd/C (10%)] are summarized in Table

SCHEME 7. Mechanism for the Formation of 3,4-Dihydroquinolizinium Salts 10 by the RCM Reaction of Pyridinium Dienes 11

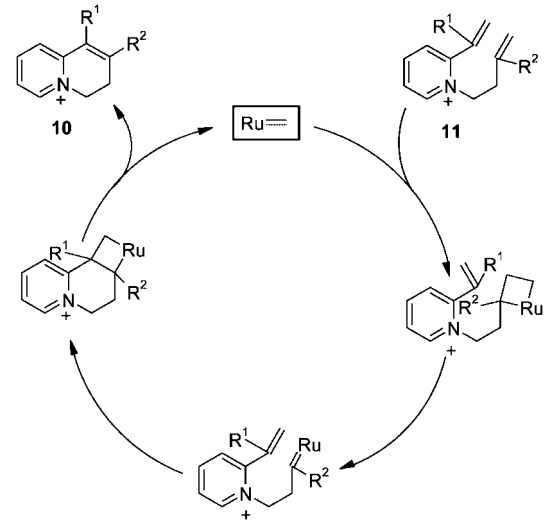
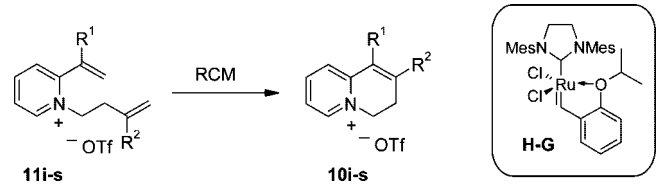
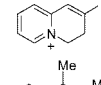


TABLE 6. Synthesis of Salts 10 by RCM Reaction of 11

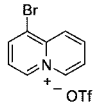
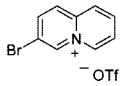
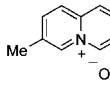
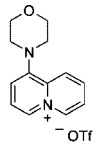
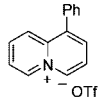
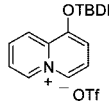
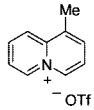
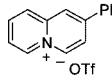
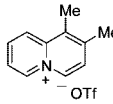


entry	diene (**11**)	conditions	RCM product (**10**)	yield (%)[a]
1	**11i**	**G-II**/CH_2Cl_2/r.t. 1.5 h	 **10i**	61
2	**11j**	**H-G**/$ClCH_2CH_2Cl$/ 65ºC, 3 h	 **10j**	78
3	**11k**	**G-II**/CH_2Cl_2/r.t. 2 h	 **10k**	91
4	**11l**	**G-II**/CH_2Cl_2/r.t. 2.5 h	 **10l**	68
5	**11m**	**G-II**/CH_2Cl_2/40 ºC 3 h	 **10m**	69
6	**11n**	**H-G**/$ClCH_2CH_2Cl$/ 83 ºC 24 h	 **10n**	--
7	**11o**	**G-II**/CH_2Cl_2/40 ºC 24 h	 **10o**	--
8	**11q**	**H-G**/$ClCH_2CH_2Cl$/ 83 ºC, 17 h	 **10q**	61
9	**11r**	**H-G**/$Cl_2CHCHCl_2$/ 120 ºC, 24 h	 **10r**	--
10	**11s**	**H-G**/$Cl_2CHCHCl_2$/ 120 ºC, 24 h	 **10s**	--

[a] Yields refer to **10** as isolated product.

7. The oxidation of the 3,4-dihydroquinolizinium derivatives with substituents in the pyridinium ring (**10b**, **10d**, **10e**, and **10h**) were successful except for derivative **10h**, which under both sets of conditions tested could not be completely trans-

TABLE 7. Synthesis of Quinolizinium Salts 7 by Oxidation of 3,4-Dihydroquinolizinium Salts 10

entry	DHQ (**10**)	quinolizinium (**7**)	yield (%)[a,b] time	yield (%)[a,c] time
1	**10a**	 **7a**	66 14 days	79 2 h
2	**10b**	 **7b**	79 12 h	83 0.5 h
3	**10d**	 **7d**	--[d] 14 days	67 5 h
4	**10e**	 **7e**	89 14 days	81 3 h
5	**10h**	 **7h**	-[d] 17 days	-[c] 5 h
6	**10i**	 **7i**		84 3h
7	**10j**	 **7j**		--[e]
8	**10k**	 **7k**	98 21 days	94 2 h
9	**10l**	 **7l**		67 5 h
10	**10m**	 **7m**		75 5 h
11	**10q**	 **7q**		57 24 h

[a] Yields refer to **7** as isolated products. [b] Conditions: 40% Pd/C (10%)/HOAc. [c] Conditions: 40% Pd/C (10%)/200 °C. [d] Incomplete reaction. [e] Decomposition.

formed into the desired oxidation product and gave inseparable mixtures from which the corresponding quinolizinium derivative could not be isolated (some charged decomposition products were also formed).

A similar result was obtained for **10d** under acidic conditions, although in this case, the thermal oxidation allowed the completion of the reaction and the isolation of the 2-bromoquinolizinium derivative **7d** in 67% yield (Table 7, entry 3). The quinolizinium derivatives **7b** and **7e** were both obtained in good yields under both sets of conditions, although for **7e**, very long times were required to complete the reaction under acidic conditions (entry 4) whereas a more acceptable time was needed for the oxidation of the 1-bromo-substituted derivative **10b** (12 h vs 14 days, entries 2 and 4).

The oxidation of derivatives with a substituent in the dihydroquinolizinium ring seemed to be even harder in acetic acid. For instance, the oxidation of **10k** proceeded cleanly to afford **7k** in quantitative yield, but 21 days were required for completion of the reaction. A slightly lower yield (94%) was obtained under thermal conditions, but complete oxidation took only 2 h. For these reasons, derivatives **10i**, **10j**, **10l**, **10m**, and **10q** were only tested under thermal conditions, and the yields are shown in Table 7 (entries 6, 7, and 9−11). These conditions were found to be unsuitable for the oxidation of **10j**, which decomposed under these conditions. On the other hand, **7q** required the longest reaction time to afford the lowest yield of the corresponding quinolizinium derivative (entry 11). Methyl (**7k**,**l**) and phenyl (**7i** and **7m**) derivatives were obtained in good yields when the substituent is in the C1 position (entries 6 and 8) and in moderate yields if either the phenyl or the methyl substituent are in the C2 position (entries 9 and 10).

While most of the 3,4-dihydroquinolizinium derivatives **10** synthesized here are unknown, most of the corresponding quinolizinium salts obtained from their oxidation have been reported previously. It is worth noting the preparation for the first time of the 1,2-dimethylquinolizinium salt **7q** with an overall yield of 10% (entry 11) and the significant improvement achieved for 1-bromo-, 3-bromo-, and 1-phenylquinolizinium salts **7b**[42] (29 vs 2%), **7d**[42] (17 vs 9%), and **7i**[33] (15 vs 0.04%) (entries 2, 3, and 6, respectively). By contrast, 3-methyl-, 2-methyl-, and 2-phenylquinolizinium triflates **7e**,[34] **7l**,[43] and **7m**[43] were obtained in lower yields than those previously reported (entries 4, 9, and 10, respectively). The parent quinolizinium **7a** was obtained with the same yield (54%) as that previously reported[38] (entry 1), and 1-methylquinolizinium **7k** was achieved in a very similar yield[34] (27 vs 26%, entry 8).

In conclusion, the results described above show that RCM is a viable reaction on *N*-alkenyl-α-vinylpyridinium systems to give a variety of 3,4-dihydroquinolizinium derivatives in good overall yields from readily available starting materials. Moreover, our studies also allowed a significant improvement in the oxidation of these 3,4-dihydroquinolizinium derivatives to the corresponding quinolizinium salts under thermal conditions in the presence of Pd/C. This approach, which is based on a RCM reaction as the key step for the construction of the fused six-membered ring on quinolizinium-type systems, can provide access to biologically relevant cations based on this cationic heteroaromatic system.

Experimental Section

General Procedure for the Preparation of Dienes 11. A solution of the corresponding 3-butenol (2.6 mmol) and dry pyridine (0.205 g, 2.6 mmol) in dry CCl_4 (2 mL) was stirred at room temperature for 5−10 min under argon. The mixture was added dropwise (5−10 min) to a cooled (−10 °C) solution of triflic anhydride (0.733 g, 6 mmol) in dry CCl_4 (3 mL). The resulting white solid was filtered off through sodium sulfate; the solution was added by cannula to a solution of the vinyl derivative **18** (2 mmol) in dry CCl_4 (2 mL), and the reaction mixture was stirred for 24 h at room temperature or 40 °C. The solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent: CH_2Cl_2/MeOH 9.5:0.5) or by washing with Et_2O.

1-(But-3-enyl)-2-vinylpyridinium triflate (11a). Following the general procedure, the reaction of 2-vinylpyridine (0.21 g, 2 mmol)

(42) Sanders, G. M.; van Dijk, M.; van der Plas, H. *Heterocycles* **1981**, *15*, 213.
(43) Glover, E. E.; Jones, G. *J. Chem. Soc.* **1958**, 3021.

and 3-butenyl triflate (0.53 g, 2.6 mmol) afforded 0.507 g (82%) of **11a** as a pale-yellow oil: IR (NaCl) ν_{max} (cm^{-1}) 3087, 1621, 1257, 1512, 1161, 1030, 785; ^1H NMR (300 MHz, $CDCl_3$) δ 8.92 (d, 1H, $J = 6.2$ Hz), 8.39 (t, 1H, $J = 7.9$ Hz), 8.02 (d, 1H, $J = 8.2$ Hz), 7.90 (t, 1H, $J = 6.4$ Hz), 7.13 (dd, 1H, $J = 11.3$, 17.0 Hz), 6.28 (dd, 1H, $J = 1.3$, 17.0 Hz), 6.13 (dd, 1H, $J = 1.1$, 11.2 Hz), 5.84−5.71 (m, 1H), 5.06 (d, 1H, $J = 10.2$ Hz), 4.94 (dd, 1H, $J = 1.3$, 17.0 Hz), 4.79 (t, 2H, $J = 6.9$ Hz), 2.65 (dd, 2H, $J = 6.9$, 14.1 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 153.2, 146.6, 133.2, 130.5, 128.3, 127.6, 127.3, 119.7, 58.2, 34.7; MS (ESI^+) *m/z* (relative intensity) 160 (M^+). Anal. Calcd for $C_{12}H_{14}NSO_3F_3$: C, 46.60; H, 4.56; N, 4.53; S, 10.37. Found: C, 46.52; H, 4.79; N, 4.44; S, 10.41.

Ring-Closing Metathesis of Dienes 11. General Procedure for 3,4-Dihydroquinolizinium 10. The ruthenium catalyst **G-II** (5 mol %, 0.01 mmol, 8.5 mg) or **H-G** (5 mol %, 0.01 mmol, 6.2 mg) in CH_2Cl_2 or $ClCH_2CH_2Cl$ (1 mL) was added to a solution of the corresponding diene **11** (0.2 mmol) in dry CH_2Cl_2 or $ClCH_2CH_2Cl$ (1.5 mL) under an argon atmosphere. The reaction mixture was stirred at room temperature or under heating for the appropriate time. The solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography (eluent: CH_2Cl_2/MeOH 9.3:0.7).

3,4-Dihydroquinolizinium Triflate (10a). Following the general procedure, after stirring for 1.5 h, 46.8 mg (83%) of **10a** was obtained as a gray powder: mp 124−125 °C (acetone/Et_2O); IR (NaCl) ν_{max} (cm^{-1}) 3086, 1646, 1507, 1263, 1150, 1031, 808; ^1H NMR (300 MHz, $CDCl_3$) δ 8.92 (d, 1H, $J = 6.2$ Hz), 8.33 (t, 1H, $J = 7.8$ Hz), 7.80 (t, 1H, $J = 7.1$ Hz), 7.65 (d, 1H, $J = 7.9$ Hz), 6.89−6.83 (m, 1H), 6.72 (d, 1H, $J = 9.7$ Hz), 4.81 (t, 2H, $J = 7.7$ Hz), 2.85 (dd, 2H, $J = 7.7$, 12.3 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 146.7, 146.1, 140.6, 126.6, 126.0, 122.1, 53.7, 22.9; MS (ESI^+) *m/z* (relative intensity) 132 (M^+). Anal. Calcd for $C_{10}H_{10}NSO_3F_3$: C, 42.71; H, 3.58; N, 4.98; S, 11.40. Found: C, 42.40; H, 3.76; N, 4.85; S, 11.34.

9-Bromo-3,4-dihydroquinolizinium Triflate (10b). Following the general procedure, after stirring for 1 h, 57.6 mg (80%) of **10b** was obtained as a pale-brown solid: mp 145−147 °C (CH_2Cl_2/Et_2O); IR (NaCl) ν_{max} (cm^{-1}) 3084, 1632, 1477, 1262, 1149, 1029, 784; ^1H NMR (300 MHz, $CDCl_3$) δ 9.03 (d, 1H, $J = 5.8$ Hz), 8.86 (d, 1H, $J = 8.2$ Hz), 7.94 (t, 1H, $J = 8.1$ Hz), 7.27−7.17 (m, 2H), 4.97 (t, 2H, $J = 7.5$ Hz), 3.02−2.85 (m, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 150.1, 147.2, 146.2, 143.8, 126.3, 121.7, 121.2, 55.4, 22.8; MS (ESI^+) *m/z* (relative intensity) 211 (M^+), 213 (M + 2). Anal. Calcd for $C_{10}H_9NBrSO_3F_3$: C, 33.35; H, 2.52; N, 3.89. Found: C, 33.12; H, 2.74; N, 3.51.

1-Methyl-3,4-dihydroquinolizinium Triflate (10k). Following the general procedure, after stirring for 2 h and purified by precipitation, 53.9 mg (91%) of **10k** was obtained as a white solid: mp 130−132 °C (CH_2Cl_2/Et_2O); IR (NaCl) ν_{max} (cm^{-1}) 3076, 1620, 1510, 1442, 1262, 1149, 1031, 736; ^1H NMR (300 MHz, acetone-d_6) δ 8.99 (d, 1H, $J = 6.2$ Hz), 8.64 (t, 1H, $J = 7.9$ Hz), 8.13 (d, 1H, $J = 8.2$ Hz), 8.02 (t, 1H, $J = 7.1$ Hz), 6.77 (t, 1H, $J = 4.6$ Hz), 4.88 (t, 2H, $J = 7.5$ Hz), 2.85 (dd, 2H, $J = 4.6$, 7.6 Hz), 2.27 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 147.0, 146.4, 136.4, 128.3, 126.2, 124.2, 54.7, 22.8, 18.1; MS (ESI^+) *m/z* (relative intensity) 146 (M^+, 100), 147 (M + 1, 25), 441 (2M + OTf, 14). Anal. Calcd for $C_{11}H_{12}NSO_3F_3$: C, 44.74; H, 4.10; N, 4.74; S, 10.86. Found: C, 44.56; H, 4.32; N, 4.65; S, 10.58.

2-Phenyl-3,4-dihydroquinolizinium Triflate (10m). Following the general procedure, after heating for 3 h and purified by chromatography, 49.3 mg (69%) of **10m** was obtained as a green solid: mp 122−123 °C; IR (NaCl) ν_{max} (cm^{-1}) 2924, 1504, 1257, 1225, 1161, 1029, 774; ^1H NMR (300 MHz, acetone-d_6) δ 8.97 (d, 1H, $J = 6.2$ Hz), 8.57 (td, 1H, $J = 1.1$, 7.9 Hz), 8.09 (d, 1H, $J = 8.0$ Hz), 7.96 (td, 1H, $J = 1.1$, 7.5 Hz), 7.88−7.85 (m, 2H), 7.55−7.51 (m, 4H), 5.08 (t, 1H, $J = 7.7$ Hz), 3.45 (td, 1H, $J = 0.9$, 8.0 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 150.5, 146.4, 145.5, 136.9, 131.5, 129.8, 127.2, 127.0, 125.5, 116.8, 113.1, 54.2, 25.4; MS (ESI^+) *m/z* (relative intensity) 208 (M^+, 100), 209 (M + 1, 87). Anal. Calcd for $C_{16}H_{14}NSO_3F_3$: C, 53.78; H, 3.95; N, 3.92; S, 8.97. Found: C, 53.97; H, 3.66; N, 4.01; S, 9.18.

1,2-Dimethyl-3,4-dihydroquinolizinium Triflate (10q). Following the general procedure, after heating for 19 h and purified by chromatography, 37.3 mg (61%) of **10q** was obtained as a gray needles: mp 124−125 °C; IR (KBr) ν_{max} (cm^{-1}) 3081, 1570, 1512, 1258, 1148, 1032, 793; ^1H NMR (300 MHz, acetone-d_6) δ 8.89 (d, 1H, $J = 6.3$ Hz), 8.57 (td, 1H, $J = 1.0$, 8.3 Hz), 8.09 (d, 1H, $J = 8.2$ Hz), 7.92 (t, 1H, $J = 6.5$ Hz), 4.83 (t, 2H, $J = 7.5$ Hz), 2.88 (t, 2H, $J = 7.7$ Hz), 2.22 (t, 3H, $J = 0.8$ Hz), 2.18 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 150.3, 146.6, 145.9, 145.1, 124.2, 123.3, 121.7 (c, $J = 320.5$ Hz), 121.5, 53.5, 20.0, 13.3; MS (ESI^+) *m/z* (relative intensity) 160 (M^+, 100). Anal. Calcd for $C_{12}H_{14}NSO_3F_3$: C, 46.60; H, 4.56; N, 4.53; S, 10.37. Found: C, 46.49; H, 4.51; N, 4.48; S, 10.22.

2-(But-3-enyl)pyridine (19). To a solution of 2-picoline (0.186 g, 2 mmol) in dry THF (2 mL), under argon atmosphere at −78 °C, was added *tert*-butyllithium (1.235 mL, 2.1 mmol), and the reaction mixture was stirred for 1 h. Then, allyl bromide was added dropwise over the cooled solution, and the reaction mixture was stirred at −78 °C for 30 min and left to stand overnight at room temperature. Then, the mixture was extracted with water (5 mL) and EtOAc (2 × 5 mL), the organic phase dried over $MgSO_4$, and the solvent evaporated under reduced pressure. Compound **19** was isolated as a yellow oil by flash chromatography on silica gel using hexane/EtOAc (8:2) as eluent (0.215 g, 81%): IR (NaCl) ν_{max} (cm^{-1}) 2925, 1591, 1474, 1435; ^1H NMR (300 MHz, acetone-d_6) δ 8.47 (d, 1H, $J = 4.8$ Hz), 7.64 (td, 1H, $J = 1.8$, 7.5 Hz), 7.21 (d, 1H, $J = 7.7$ Hz), 7.14 (t, 1H, $J = 4.9$ Hz), 5.93−5.80 (m, 1H), 5.06−4.98 (m, 2H), 2.83 (t, 2H, $J = 7.3$ Hz), 2.50−2.42 (m, 2H); ^{13}C NMR (200 MHz, acetone-d_6) δ 162.0, 149.9, 138.9, 136.8, 123.4, 121.7, 115.0, 38.1, 34.2; HRMS (DIP/QI) *m/z* calcd for $C_9H_{12}N$: 134.0968. Found: 134.0970.

2-(But-3-enyl)-1-(2-chloroethyl)pyridinium Triflate (20). To a solution of 2-chloroethanol (0.105 g, 1.3 mmol) in dry CCl_4 (1 mL), under argon atmosphere, was added dry pyridine (0.103 g, 1.3 mmol), and the reaction mixture was stirred at room temperature for 5−10 min. Then, this solution was added dropwise (5−10 min) over a cooled solution (−10 °C) of triflic anhydride (0.327 g, 0.219 mL, 1,3 mmol) in dry CCl_4 (1.5 mL). The resulting white solid formed was filtered off through sodium sulfate, and the solution was added via cannula to a solution of 2-(but-3-enyl)-pyridine **19** (1 mmol) in dry CCl_4 (1.5 mL). The reaction mixture was stirred at room temperature for 24 h. Removal of the solvent under reduced pressure and purification by flash chromatography on silica gel using CH_2Cl_2/MeOH (9.5:0.5) gave **20** (0.307 g, 89%) as a yellow oil: IR (NaCl) ν_{max} (cm^{-1}) 3087, 1632, 1512, 1454, 1261, 1158, 1030, 779; ^1H NMR (200 MHz, acetone-d_6) δ 9.14 (d, 1H, $J = 6.4$ Hz), 8.68 (td, 1H, $J = 1.3$, 9.1 Hz), 8.24 (d, 1H, $J = 8.0$ Hz), 8.14 (t, 1H, $J = 6.4$ Hz), 6.03−5.89 (m, 1H), 5.30 (t, 2H, $J = 5.7$ Hz), 5.17−5.04 (m, 2H), 4.35 (t, 2H, $J = 5.8$ Hz), 3.51 (t, 2H, $J = 7.5$ Hz), 2.72−2.64 (m, 2H); ^{13}C NMR (300 MHz, acetone-d_6) δ 159.6, 147.4, 147.1, 136.4, 130.3, 126.6, 117.4, 58.8, 43.6, 32.5, 32.4; MS (ESI^+) *m/z* 196 (M^+), 198 (M + 2). Anal. Calcd for $C_{12}H_{15}NClSO_3F_3$: C, 41.68; H, 4.37; N, 4.05; S, 9.27. Found: C, 41.37; H, 4.59; N, 4.31; S, 9.15.

2-(But-3-enyl)-1-vinylpyridinium Triflate (9a). To a solution of **20** (0.086 g, 0.25 mmol) in EtOH/MeOH (3:1) (5 mL) was added dropwise at −10 °C for 10 min a solution of aqueous NaOH (10 N, 0.275 mmol, 1.1 equiv). The reaction mixture was stirred for 15 min, neutralized with acetic acid, and the solvent removed under reduced pressure at 20 °C. The residue was filtered off, and the solution was concentrated under reduced pressure at 20 °C and purified by flash chromatography on silica gel using CH_2Cl_2/MeOH (9.5:0.5) as eluent. Compound **9a** (49.0 mg, 64%) was obtained as a brown oil: IR (NaCl) ν_{max} (cm^{-1}) 3493, 1627, 1497, 1276, 1158, 1031, 787; ^1H NMR (300 MHz, acetone-d_6) δ 9.07 (d, 1H, $J = 6.2$ Hz), 8.69 (td, 1H, $J = 1.5$, 8.0 Hz), 8.19 (d, 1H, $J = 8.0$ Hz), 8.13 (t, 1H, $J = 7.5$ Hz), 7.89 (c, 1H, $J = 8.2$ Hz), 6.22 (dd, 1H, $J = 2.2$, 14.8 Hz), 6.07 (dd, 1H, $J = 2.0$, 8.2 Hz), 5.99−5.85 (m, 1H),

5.15−5.02 (m, 2H), 3.37 (t, 2H, J = 7.5 Hz), 2.66−2.58 (m, 2H); ^{13}C NMR (200 MHz, acetone-d_6) δ 147.6, 145.5, 137.2, 136.4, 129.3, 126.8, 121.0, 117.2, 32.8, 31.7; HRMS (ESI$^+$) m/z calcd for $C_{11}H_{14}N$: 160.1126. Found: 160.1122.

1,2-Dihydroquinolizinium Triflate (8a). To solution of the diene **9a** (0.2 mmol) in dry CH_2Cl_2 (1.5 mL) was added ruthenium catalyst **G-II** (5 mol %) in CH_2Cl_2 (1 mL) under argon atmosphere. The reaction mixture was stirred for 3 h at room temperature. Then, the solvent was evaporate under reduced pressure and the residue purified by flash chromatography (eluent: CH_2Cl_2/MeOH 9.5:0.5) to give 29.0 mg (52%) of **8a** as a brown solid: mp 153−155 °C; IR (KBr) ν_{max} (cm^{-1}) 2434, 1628, 1502, 1264, 1144, 1030, 791; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.96 (d, 1H, J = 6.2 Hz), 8.57 (td, 1H, J = 1.3, 7.9 Hz), 8.13−8.05 (m, 2H), 7.58 (d, 1H, J = 7.7 Hz), 6.60−6.58 (m, 1H), 3.52 (t, 2H, J = 8.2 Hz), 2.69−2.61 (m, 2H); ^{13}C NMR (200 MHz, acetone-d_6) δ 146.7, 142.8, 130.6, 129.1, 128.1, 126.9, 26.9, 18.1; HRMS (ESI$^+$) m/z calcd for $C_9H_{10}N$: 132.0813. Found: 132.0806.

Synthesis of Quinolizinium Triflates 7. General Procedure A: A solution of the corresponding 3,4-dihydroquinolizinium salt **10** (25 mg) in acetic acid (2 mL) and Pd/C 10% (40%, 10 mg) was heated under reflux for the appropriate time. The reaction mixture was concentrated in vacuo; acetone was added to the residue, and the mixture was filtered through Celite. The solvent was removed under reduced pressure, and the quinolizinium salt was purified by recrystallization.

General Procedure B: A mixture of **10** (25 mg) and Pd/C 10% (40%, 10 mg) was heated at 200 °C for 0.5−5 h. The quinolizinium salt was isolated as in procedure A and purified by recrystallization or by flash column chromatography.

Quinolizinium triflate (7a). From 8a: A mixture of 1,2-dihydroquinolizinium triflate **8a** (25 mg) and Pd/C 10% (40%, 10 mg) was heated at 200 °C for 2 h (monitored by NMR). Then, acetone was added to the reaction mixture and the resulting suspension was filtered through Celite. Removal of the solvent under reduced pressure afforded **7a** as a pale-yellow solid that was purified by flash chromatography on silica gel [CH_2Cl_2/MeOH (9:1)] or by recrystallization (23.8 mg, 96%).

From 10a: A mixture of **10** (25 mg) and Pd/C 10% (40%, 10 mg) was heated at 200 °C for 2 h (monitored by NMR). The reaction mixture was worked up as above to give 19.6 mg (79%) of **7a** as yellow crystals: mp 148−150 °C (CH_2Cl_2/Et_2O); IR (NaCl) ν_{max} (cm^{-1}) 3091, 1651, 1264, 1143, 1031, 801; ^{1}H NMR (300 MHz, acetone-d_6) δ 9.47 (d, 2H, J = 6.8 Hz), 8.68 (d, 2H, J = 8.6 Hz), 8.50 (td, 2H, J = 0.9, 7.1 Hz), 8.20 (t, 2H, J = 6.9 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 143.5, 137.4, 137.3, 126.6, 124.3, 121.5 (c, J = 319.6 Hz); MS (ESI$^+$) m/z (relative intensity) 130 (M$^+$, 100). Anal. Calcd for $C_{10}H_8NSO_3F_3$: C, 43.01; H, 2.89; N, 5.02; S, 11.48. Found: C, 43.29; H, 2.54; N, 5.08; S, 11.37.

1,2-Dimethylquinolizinium Triflate (7q). Following the general procedure, after heating for 24 h, **7q** (14.0 mg, 57%) was obtained as a brown oil: IR (NaCl) ν_{max} (cm^{-1}) 2918, 1639, 1407, 1278, 1159, 1031, 638; ^{1}H NMR (300 MHz, acetone-d_6) δ 9.34 (d, 1H, J = 6.8 Hz), 9.23 (d, 1H, J = 7.2 Hz), 8.72 (d, 1H, J = 8.9 Hz), 8.43 (t, 1H, J = 7.2 Hz), 8.11−8.02 (m, 2H), 2.82 (s, 3H), 2.76 (s, 3H); ^{13}C NMR (300 MHz, acetone-d_6) δ 148.6, 137.9, 137.3, 135.1, 133.7, 127.1, 124.5, 123.4, 55.4, 20.9, 14.8; MS (ESI$^+$) m/z 158 (M$^+$). Anal. Calcd for $C_{12}H_{12}NSO_3F_3$: C, 46.75; H, 4.25; N, 4.54; S, 10.40. Found: C, 46.66; H, 4.30; N, 4.70; S, 10.12.

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Note Added after ASAP Publication. Due to a production error Scheme 1 was incorrect, the correct Scheme 1 was published ASAP on May 6, 2009.

Supporting Information Available: Experimental procedures and full spectroscopic data and NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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