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PAPER

Synthesis of a family of 3-alkyl- or 3-aryl-substituted 1,2-dihydroquinazolinium salts and their isomerization to 4-iminium-1,2,3,4-tetrahydroquinolines†‡§

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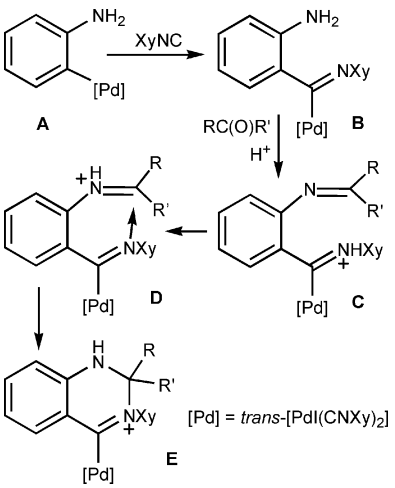
A straightforward synthesis of substituted 1,2-dihydroquinazolinium triflates (**3**) is reported by reaction of 2-imino-substituted anilines with a range of carbonyl compounds in the presence of triflic acid *via* intermediate iminium salts. Similar reactions with di- or trialdehydes and triflic acid give bis- or tris-(1,2-dihydroquinazolinium) salts. Some 4-methyl substituted 1,2-dihydroquinazolinium salts rearrange, under various conditions, to their corresponding 4-iminium-1,2,3,4-tetrahydroquinolinium isomers (**7**). Most of salts **3** derived from ketones are rather unstable, which prevents their isolation or full characterization. The crystal structures of various **3** and **7** salts have been determined.

Introduction

We have reported the synthesis of iminoacyl palladium complexes resulting from the insertion of isocyanides into the Pd–C bond of *ortho*-functionalized aryl palladium complexes.[1,2] In particular, the orthopalladated aniline **A** (Scheme 1) reacted with XyNC to afford the iminoacyl complex **B**. While studying the protonation of **B** in acetone we obtained, through the unprecedented intramolecular hydroiminiumation[3] of an imine (**C**), a 1,2-dihydro-3-xylylbenzoquinazolinium-4-yl palladium complex **E** (R = R′ = Me); the same occurred with aldehydes and other ketones.[4]

We have studied this process by DFT (B3LYP/LANL2DZ)[5] showing (1) that the hydroiminiumation process (**C** → **E**) occurs through an asynchronous concerted mechanism involving proton transfer to the imine N atom to give **D** followed by nitrogen attack at the imine carbon to give **E** and (2) that while different substituents on the carbonyl compound make a significant difference to the activation barrier, the metal exerts only a minor effect. This suggested to us that a similar cyclization process could also occur if [Pd] is replaced by H or an organic group, providing the first general synthesis of 1,2-dihydroquinazolinium salts. In this paper we report our results in the development of this idea.



Scheme 1

Compounds based on the quinazoline structure, including variously substituted dihydro-, tetrahydro or N-oxo derivatives, quinazolinones, *etc.*, are present in many natural and synthetic compounds with remarkable biological activity.[6–8] The methods described for the synthesis of 1,2-dihydroquinazolines usually require relatively high input of experimental manipulation and lack general application.[7–15] In addition, as some of them easily

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† Dedicated to Prof. Carmen Nájera on occasion of her 60th birthday.

‡ The patent of some of the results here reported has been applied for (P201031273).

§ Electronic supplementary information (ESI) available: Detailed syntheses of compounds **1**–**7**. ^{1}H and ^{13}C NMR spectra of the new compounds. Listing of all refined and calculated atomic coordinates, anisotropic thermal parameters, bond lengths and angles, CIF files and thermal ellipsoid representation plots for compounds **3a2**, **3b3**, **3d4**, **6d** and **7d2**. Experimental details of the X-ray crystallographic and voltammetric studies. CCDC reference numbers 800053–800057. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob00982b

undergo isomerization or dehydrogenation,[10,11] they have been less studied although some display interesting reactivity[14,16] or biological effects.[8,11,13,17] The few reported 3-alkyl- or 3-aryl-1,2-dihydroquinazolinium salts (Chart 1, **F**) have been prepared by using methods lacking general applicability.[18,19,12] In addition, some 1,2-dihydroquinazolinium internal salts,[15,20] and various dicationic tetrahydrodibenzodiazocinodiquinazolinium salts [21,22] have also been reported. Some of these salts have been structurally characterized by X-ray crystallography.[15,20–22]

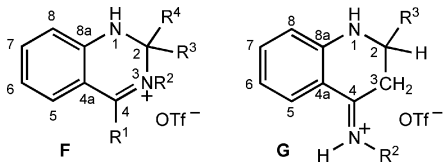


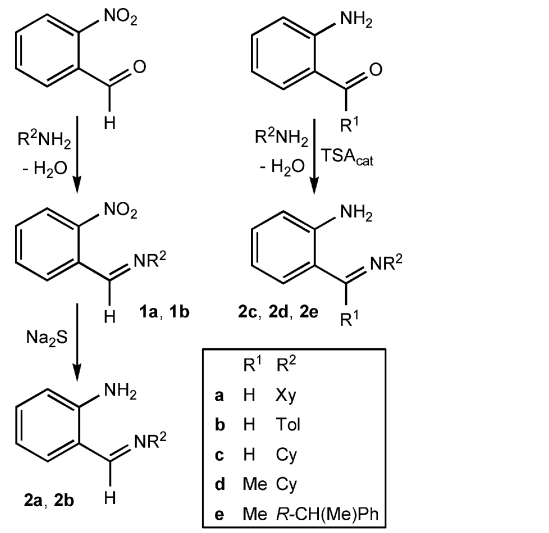
Chart 1

We describe here the synthesis of the first family of 1,2-dihydroquinazolinium salts of the type **F** (Chart 1) obtained by a way similar to that used for their palladium derivatives (**E**, Scheme 1). We also report on the conversion of some 1,2-dihydroquinazolinium salts with R^1 = Me into their 4-iminium-1,2,3,4-tetrahydroquinoline isomers **G**. As far as we are aware, neither is there a precedent for this transformation nor has a single compound of type **G** been described for any of the possible combinations of R^1 to R^4 being H or a C-bonded substituent.[23] (1-Amidomethyl-1*H*-quinolin-4-ylidene)arylamines containing the 1-*H*-quinolin-4-ylideneamine core related to our **G** compounds constitute a novel type of antimalarial compound showing excellent activity against a multi-drug-resistant *Plasmodium falciparum* strain.[24]

Results and discussion

Synthesis of 2-(alkyl)- or 2-aryl-(iminoalkyl)benzenamines

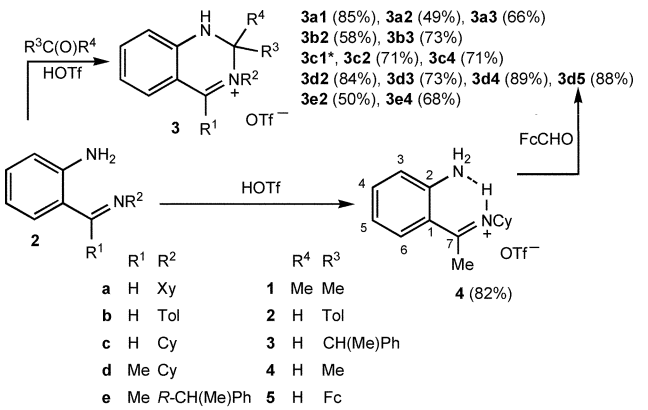
The precursors $H_2NC_6H_4C(R^1)$═NR^2-2 (**2**, Scheme 2) were prepared in two ways: (1) by condensation of the appropriate arylamine with 2-nitrobenzaldehyde to afford *N*-(2-nitrobenzylidene)arylamines (**1a**, **1b**)[25] followed by their reduction with $Na_2S{\cdot}9H_2O$ in refluxing EtOH,[26,27] to give the corresponding amino derivatives (R^1 = H, R^2 = Xy (**2a**), Tol (**2b**)), and (2) by direct condensation of the appropriate *o*-amino-substituted aldehyde or ketone $H_2NC_6H_4C(O)R^1$-2 with a large excess of the amine (R^2NH_2) in the presence of a catalytic amount of *p*-toluensulfonic acid (TSA)[27,28] (R^1 = H, R^2 = Cy (**2c**); R^1 = Me, R^2 = Cy (**2d**), *R*-CH(Me)Ph (*R*-**2e**)), as described in ESI§.



Scheme 2

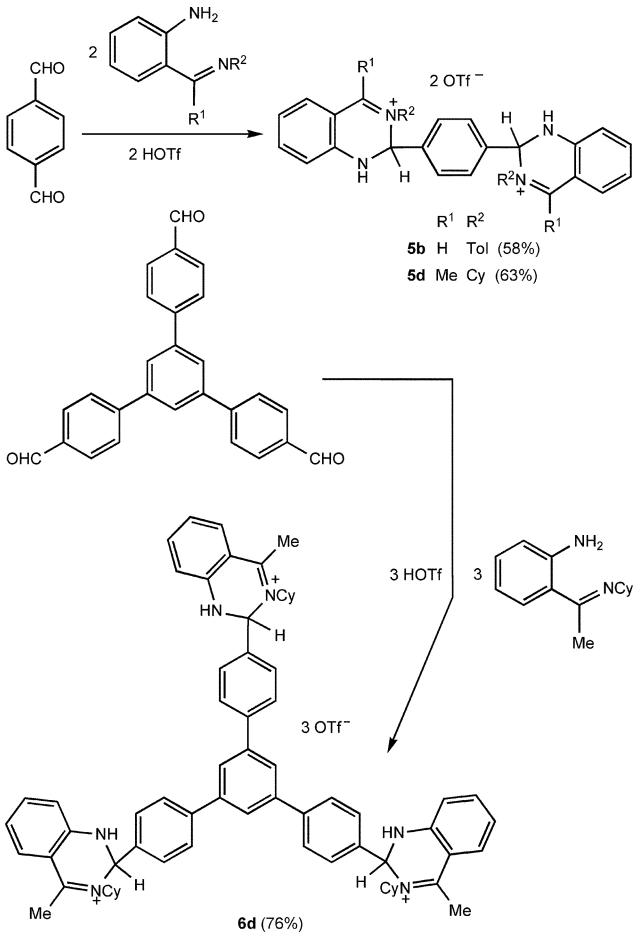
Synthesis of 1,2-dihydroquinazolinium salts

From 2, Aldehydes and triflic acid. Room-temperature reactions of compounds $H_2NC_6H_4C(R^1)$═NR^2-2 (**2**, Scheme 2) with moderate or large excess of aldehydes R^3CHO (R^3 = Tol, *rac*-CH(Me)Ph, Me) and a slight excess of HOTf, in CH_2Cl_2 or MeCN, afforded various 1,2-dihydroquinazolinium triflates (**3**, Scheme 3). Compounds **3d2** and **3e2** isomerize to the corresponding 4-iminium-1,2,3,4-tetrahydroquinolines (see below) at moderate (**3d2**) or room temperature (**3e2**). When the reaction between equimolar amounts of **2d**, [Fe(η^5-C_5H_5)(η^5-C_5H_4CHO)] (FcCHO) and HOTf in CH_2Cl_2 was carried out, decomposition took place to give an oily black insoluble material similar to that obtained when FcCHO was treated with HOTf. This moved us to perform the reaction in two steps, first isolating the protonated species $H_2NC_6H_4C(Me)$═$NHCy$-2 (**4**; Scheme 3) and then reacting it with FcCHO. The best results were obtained when the last step was carried out at 0 °C in the presence of an excess of FcCHO. Low temperatures and short reaction times were required to minimize the rearrangement of **3d5** into its 4-iminium-quinoline isomer **7d5** (see below). The excess of aldehyde, which can be easily removed, prevents the presence of **4**, which is difficult to separate from **3d5** (see below). This two-step process suggests that 1,2-dihydroquinazolinium salts form through the reaction pathway proposed for the synthesis of their palladium derivatives, shown in Scheme 1. DFT studies[5] and the ^{13}C NMR spectrum of **4** (see below) lead us to propose protonation at the iminic nitrogen, although, as depicted in Scheme 3, a N_{imine}–H···NH_2 hydrogen bond could be present, as in other related systems.[29]



Scheme 3

When terephthalaldehyde or $C_6H_3(C_6H_4CHO\text{-}4)_3$-1,3,5 were reacted with **2b** or **2d** and triflic acid, di- or tricationic 1,2-dihydroquinazolinium compounds formed, resulting from a double (**5b**, **5d**) or triple (**6d**) cyclization process (Scheme 4).



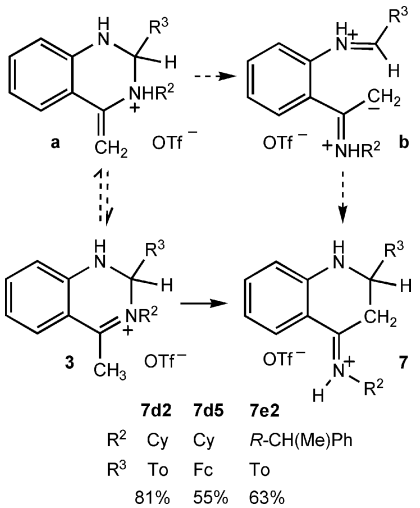
Scheme 4

The synthesis of **5b** was carried out in refluxing MeCN, using a large excess of **2b** with respect to terephthalaldehyde (4 : 1 instead of 2 : 1) because otherwise **5b** was contaminated with the starting reagents and, probably, with the mono-dihydroquinazolinium salt.[30] A slight excess of **2d** (6%) was also used in the synthesis of **6d** in order to avoid the formation of by-products, probably mono- or di-quinazolinium salts.

From 2, Ketones and triflic acid. The room temperature reactions of **2a** with a stoichiometric amount of HOTf in acetone led to the 1,2-dihydroquinazolinium salt **3a1**, which was isolated in good yield (Scheme 3). The reaction of equimolar amounts of **2c** and HOTf in acetone produced good yields of pure **3c1**, as shown by its ^{1}H NMR spectrum (measured on a freshly prepared sample) and its elemental analyses, although its $^{13}C\{^1H\}$ NMR showed some impurities formed during the acquisition time, indicating its limited stability in solution. Equimolar amounts of **2b** and HOTf in acetone at room temperature gave after 30 min of stirring a mixture containing minor amounts of the corresponding dihydroquinazolinium salt **3b1**,[31] which disappeared completely from the mixture if the reaction time was extended or the temperature was raised. The largest ratio of **3b1** (30%) in the mixture was detected by ^{1}H NMR when the reaction was carried out in a 1/20 v/v mixture of acetone–Et_2O over 5 min. Similarly, when **2d** was reacted in $CDCl_3$ with acetone (10% excess) and HOTf (1 : 1) at −30 °C, **3d1** was identified[32] but it disappeared quickly from the reaction mixture upon raising the temperature. The reaction of **2b** with HOTf (1 : 1) in MeC(O)Et produced a mixture containing the desired dihydroquinazolinium salt.[33] Upon extending the reaction time it transformed completely into a mixture of unidentified compounds. Various attempts to use *p*-nitroacetophenone as the carbonyl compound failed to give the desired compound **3**. We are currently studying these reactions with ketones in order to establish the identity of the decomposition products and to understand their different behaviour from that of aldehydes. The instability of these compounds contrasts with the great stability of their Pd(II) homologues (**E** in Scheme 1).[1,4]

Isomerization of 4-methyl-1,2-dihydroquinazolinium salts

As mentioned above, among compounds **3** with R^1 = Me only those containing R^3 = alkyl (**3d3**, **3d4**, **3e4**) and R^4 = H are indefinitely stable in solution, while those bearing an aryl or ferrocenyl substituent R^3 = Tol (**3d2**, **3e2**), Fc (**3d5**) convert easily into their 4-iminium-quinoline isomers **7d2**, **7e2** and **7d5** (Scheme 5), respectively. For this reason, they must be stored below 4 °C in the solid state. In contrast, compounds **7** are indefinitely stable both in the solid state and in solution. Scheme 5 shows a reasonable reaction pathway to account for this isomerization process. The electron-withdrawing ability of the aryl or ferrocenyl substituent R^3 group will facilitate the tautomerization step (**3** → **a**), the fragmentation of the carbon–nitrogen bond by conjugative effect (**a** → **b**), and be crucial in the cyclization process (**b** → **7**). Although 4-methylene-1,2,3,4-tetrahydroquinazolinium compounds (**a**, enamonium tautomers of **7**) have not been yet reported, their intermediacy in various racemization,[34] stereoselective hydrogenation or reductive amination processes,[35] or in the oxidation of yohimbine by sodium peroxodisulfate,[36] has been claimed; iminium–enamonium tautomeric equilibria have been studied in various types of compounds.[34,37]



Scheme 5

X-Ray crystal structures

The crystal structures of the quinazolinium salts **3a2**·$CHCl_3$, **3b3**, **3d4** and **6d**·$2CHCl_3$·CH_2Cl_2 and that of the 4-iminium-quinoline derivative **7d2** have been determined (see ESI§), supporting the structures shown in Schemes 3–5. The structural data of the first group are similar to those found in the few crystal structures of 1,2-dihydroquinazolinium salts previously reported.[1,15,20–22] In all cases the heterocycle ring has an envelope conformation with the C^2 (see Chart 1) atom out of the mean plane of the other atoms of the ring. Intermolecular hydrogen bonds of the types NH···O, CH···O or CH···F are observed in most salts (see ESI§).

As **7d2** is the first 4-iminium substituted 1,2,3,4-tetrahydroquinoline, there are no data with which to compare its structural parameters. The bond distances in the carbocycle C^{4a}–C^{8a} and that of the C^{8a}–N^1 bond (fragment 1) are significantly shorter than those between the remaining atoms in the heterocycle C^{4a}–C^2 and C^2–N^1 (fragment 2), respectively, but longer than C=C bond distances in olefins and C^4=N, respectively, which suggests an extended electron delocalization in **7d2** along fragment 1. Intermolecular NH···O and CH···O hydrogen bonds connect the cations and the anions giving dimers.

NMR Spectra

When the ^{1}H NMR spectrum of **2d** is compared with that of its protonated homologue **4** (Scheme 3) no significant differences are found. However, the ^{13}C NMR spectra show an important deshielding of 16.2 ppm in the C^7 (see Chart 1) resonance in **4** compared to **2d**, implying that protonation occurred on the imino nitrogen.

The 1,2-dihydroquinazolinium salts **3** show the NH resonance as a broad singlet or a broad doublet caused by coupling to R^4 = H. The position of this resonance is mainly influenced by the substituents on C^2 ($R^3 = R^4 = Me$; $R^4 = H$, R^3 = Tol, Fc: δ, 8.31–8.76 ppm; R^4 = H, R^3 = CH(Me)Ph, Me: δ, 7.30–8.28 ppm), whereas R^1 and R^2 do not affect it significantly. In compounds with R^1 = H, the singlet attributed to this proton appears in the range 8.24–8.97 ppm while the aromatic protons appear at 6.42–6.91 (H^6), 6.77–7.32 (H^8) and 6.74–7.72 (H^5) and 7.20–7.60 (H^7) ppm with the expected multiplicities. Regarding the ^{13}C NMR spectra, the aromatic carbons are scarcely affected by the R^1–R^4 substituents and resonate in the intervals: 111.0–116.7 (C^{4a}), 128.3–133.1 (C^5), 119.7–121.8 (C^6), 138.3–142.5 (C^7), 116.2–117.6 (C^8) and 144.4–148.7 (C^{8a}) ppm. The resonance of C^2 is more affected by R^2 than by its own substituents (R^3, R^4) since it is more shielded in compounds bearing R^2 = alkyl (Cy, CH(Me)Ph: 62.7–69.9 ppm), than in those with R^2 = aryl (Xy, Tol: 72.7–76.5 ppm), although **3c1** is an exception (R^2 = Cy, δ_{C2} = 76.5 ppm).

The rotation of the Xy group around the Xy–N bond in **3a2** is fast enough at 55 °C as to make its two halves equivalent (^{1}H and ^{13}C NMR spectra). However, the Me protons coalesce at room temperature and their carbons are observed as a very broad singlet, while a single resonance appears for each the *o*-Xy and *m*-Xy carbons. Upon cooling to −35 °C, two sets of sharp singlets are observed for the Me protons and carbons as well as the *m*-Xy and *o*-Xy carbons. This behaviour can be attributed to the restricted rotation of the Xy group at low temperatures caused by the close vicinity of the Tol group.

All compounds **3**, with the exception of those with $R^3 = R^4$ = Me (**3a1**, **3c1**) have at least one chiral center (C^2). In addition, some of them bear the chiral substituent R^2 = *R*-CH(Me)Ph (**3e2**, **3e4**) or R^3 = *R*- or *S*-CH(Me)Ph (**3a3**, **3b3**, **3d3**) and, as expected, the ^{1}H NMR spectra of the crude reaction products show two sets or resonances for the *RR* + *RS* or (*RR* + *SS*) + (*RS* + *SR*) diastereoisomeric pairs of enantiomers, respectively. In all cases they form in an approximate 2–3 : 1 molar ratio (33–50% diastereoisomeric excess, *de*) indicating that the chirality of R^2 or R^3 influences that of C^2.

In most cases, the 2–3 : 1 isomer ratios found in the crude **3e2**, **3e4**, **3a3** and **3b3** is maintained after the manipulations necessary for their isolation but it is nearly inverted in the case of **3d3**. A 50% *de* was found in the synthesis of a 1,2-dihydroquinazolinium-4-yl palladium complex using *rac*-Ph(Me)CHCHO.[4]

The isomerization of **3e2**→**7e2** maintains the same two chiral centres although in this case the *de* is greater (67%). NOESY experiments show cross peaks between the N^+H resonances (*ca* 10 ppm) and those corresponding to H^5 in **7** proving the configuration of the C=N bond to be *E* in solution, as observed for **7d2** in the solid state (see ESI§).

In compounds **5** and **6** the first generated chiral centre does not influence the chirality of C^2 in the second or third cyclization processes because of their mutual remoteness. The dicationic compounds **5b** and **5d** are obtained as equimolar mixtures of the *RR* + *SS* and *RS* diastereoisomers, as shown by the duplication of some of the resonances in both the ^{1}H and ^{13}C NMR spectra measured in 400 and 600 MHz spectrometers at 25 and −10 (**5b**) °C, respectively. Similarly, **6d** is also obtained as an equimolar mixture of the diastereoisomeric pairs of enantiomers *RRR* + *SSS* and *RRS* + *SSR* resulting in two sets of resonances in the NMR spectra. As the latter pair of enantiomers must give, for each nucleus, two resonances in 2 : 1 intensity ratio, three very close resonances are expected for each nucleus in a : b : c = 3 : 2 : 1 intensity ratios, which are in fact observed for the NH protons, while some others are observed as two or a unique resonance. Thus, a deconvolution analysis (iNMR) shows two Me resonances at 2.93 and 2.94 ppm in 2 : 1 [(a + c) : b] intensity ratio.

Some of the compounds crystallized as solvates; the solvent was quantified by NMR and confirmed by the elemental analyses. The elemental analyses of **3d3** showed that it crystallized with $0.5H_2O$; however, it was impossible to assign the corresponding NMR resonance because of the presence of various multiplets of the Cy group in the 1–2 ppm region.

Electrochemical studies

The voltammograms of **3d5** and **7d5** show both redox processes to be reversible. Their oxidation potentials are, respectively, 160 and 85 mV higher than that of ferrocene. The value found for **3d5** shows the electron-withdrawing ability of the 1,2-dihydroquinazolinium substituent on the ferrocene moiety and an efficient communication between the iminoacyl nitrogen, in which the positive charge of the substituent is mainly localized, and the iron centre in close vicinity. The lower oxidation potential found for **7d5** must be attributed to the fact that the iminium nitrogen supporting the positive charge is exocyclic and far more distant from the ferrocenyl fragment.

Experimental section

Synthesis of *N*-(2-nitrobenzylidene)arylamines (1) and of alkyl- or aryl-(iminoalkyl)bencenamines (2)

See Scheme 2 and ESI§.

Representative procedure for the syntheses of 1,2-dihydroquinazolinium triflates (3)

Experimental details for each particular compound **3** are in ESI§.

Synthesis of 3a1. To a solution of, **2a** (260 mg, 1.16 mmol) in Me_2CO (10 ml) was added HOTf (105 μL, 1.20 mmol). After 30 min of stirring, the resulting solution was concentrated under vacuum (1 mL) and cold Et_2O was added (25 mL, 0 °C), the suspension was stirred at 0 °C for 15 min and filtered. The solid collected was washed with cold Et_2O (3 × 5 mL, 0 °C) and dried under vacuum to give the title compound as an orange solid, which was stored below 4 °C. Yield: 408.5 mg, 0.99 mmol, 85%. Mp 100 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ 1.67 (s, 6 H), 2.29 (s, 6 H), 6.91 ("dt", 1 H, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 0.4 Hz), 7.21 (d, 2 H, $^3J_{HH}$ = 7.6 Hz), 7.32 (m, 2 H) 7.59 (ddd, 1 H, $^3J_{HH}$ = 8.0 Hz, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 1.6 Hz), 7.64 (d, 1 H, $^3J_{HH}$ = 8.0 Hz), 8.28 (s, 1 H), 8.45 (br s, 1 H). ^{13}C{^{1}H} NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ 18.6, 24.3, 75.9, 114.9, 117.0, 120.3 (q, $^1J_{CF}$ = 320 Hz), 121.8, 129.6, 130.3, 132.7, 134.9, 138.6, 141.3, 147.9, 160.5. IR (Nujol, cm^{-1}): 3231, 1630, 1595, 1584, 1563. HRMS (ESI) *m/z* calc. for $C_{18}H_{21}N_2$ [M]$^+$, 265.1699; found 265.1698. Anal. calc. for $C_{19}H_{21}F_3N_2O_3S$: C, 55.06; H, 5.11; N, 6.76; S, 7.74. Found: C, 55.06; H, 5.04; N, 6.70; S, 7.94%.

Synthesis of 3d5. To a solution of **4** (see below, 70 mg, 0.19 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added ferrocene carbaldehyde (80 mg, 0.33 mmol) and the reaction mixture was stirred for 1.5 h at 0 °C. The resulting red solution was concentrated under vacuum (1 mL) and cold Et_2O (30 mL, 0 °C) was added. The suspension was stirred at 0 °C for 15 min and filtered. The solid collected was washed with cold Et_2O (3 × 5 mL, 0 °C) and dried first by suction and then under vacuum (6 h) to give **3d5** as a red solid, which must be stored below 4 °C. Yield: 94.7 mg, 0.17 mmol, 88%. Mp 135 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 0 °C, TMS): δ 1.24–1.40 (m, 3 H), 1.71–2.02 (various m, 7 H), 2.63 (s, 3 H), 3.50 (s br, 1 H), 3.98 (s br, 1 H), 4.09 (m, 1 H), 4.16 (s br, 1 H), 4.28 (s, 5 H), 4.34 (s br, 1 H), 6.42 (d, 1 H, $^3J_{HH}$ = 4.4 Hz), 6.93 (t, 1 H, $^3J_{HH}$ = 7.4 Hz), 7.22 (d, 1 H, $^3J_{HH}$ = 8.0 Hz), 7.55–7.60 (m, 2 H), 8.25 (d br, 1 H, $^3J_{HH}$ = 3.6 Hz). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$, 0 °C, TMS): δ 17.9, 24.3, 25.3, 25.4, 31.7, 32.0, 63.9, 64.1, 66.5, 68.1, 68.7, 68.9, 69.5, 85.9, 115.7, 116.7, 118.9, 120.5 (q, $^1J_{CF}$ = 320 Hz), 128.9, 138.8, 145.5, 165.3. IR (Nujol, cm^{-1}): 3226, 1621, 1583, 1557. HRMS (ESI) *m/z* calc. for $C_{25}H_{29}N_2Fe$ [M]$^+$, 413.1675; found 413.1677. Anal. calc. for $C_{26}H_{29}F_3FeN_2O_3S$: C, 55.52; H, 5.20; N, 4.98; S, 5.70. Found: C, 55.54; H, 4.94; N, 5.06; S, 5.43%.

Synthesis of 4

To a solution of **2d** (309 mg, 1.43 mmol) in CH_2Cl_2 (5 mL) was added HOTf (125 μL, 1.43 mmol). The solution was stirred for 0.5 h, concentrated under vacuum (1 mL) and cold Et_2O was added (20 mL, 0 °C). The suspension was stirred for 15 min at 0 °C and filtered. The solid collected was washed with cold Et_2O (3 × 5 mL, 0 °C) and dried to give **4** as a pale yellow solid. Yield: 428.4 mg, 1.17 mmol, 82%. Mp 99 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ 1.13–1.42 (m, 3 H), 1.53–1.67 (m, 3 H), 1.77 (m, 2 H), 2.03 (m, 2 H), 2.78 (s, 3 H), 3.93 (m, 1 H), 6.05 (s br, 3 H), 6.83 (d, 1 H, $^3J_{HH}$ = 8.1 Hz), 6.90 (t, 1 H, $^3J_{HH}$ = 7.7 Hz), 7.33–7.38 (m, 2 H). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$, 25 °C, TMS): δ 18.8, 24.2, 24.4, 30.5, 58.0, 119.1, 119.7), 119.8, 130.4, 135.5, 147.1, 182.9. IR (Nujol, cm^{-1}): 3350, 3286, 3178, 1652, 1613, 1579. HRMS (ESI) *m/z* calc. for $C_{14}H_{21}N_2$ [M]$^+$, 217.1699; found 217.1700. Anal. calc. for $C_{15}H_{21}F_3N_2O_3S$: C, 49.17; H, 5.78; N, 7.65; S, 8.75. Found: C, 48.83; H, 5.77; N, 7.65; S, 8.69%.

Representative procedure for the syntheses of bis- and tris-(1,2-dihydroquinazolinium) triflates (5b, 5d and 6d)

Experimental details for each particular compound **5** are in ESI§.

Synthesis of 6d

To a solution of **2d** (350 mg, 1.62 mmol) in CH_2Cl_2 (20 mL) were successively added $C_6H_3(C_6H_4CHO\text{-}4)_3$-1,3,5[38] (200 mg, 0.51 mmol) and HOTf (150 μL, 1.72 mmol) with a 30 min interval. After 5 h of stirring, the resulting yellow solution was filtered through a short pad of anhydrous $MgSO_4$ and concentrated under vacuum (1 mL); Et_2O (30 mL) was added and the suspension was filtered. The yellow solid collected was recrystallized from CH_2Cl_2–Et_2O (2 mL/30 mL), washed with Et_2O (3 × 3 mL) and dried under vacuum (8 h) to give **6d**·2H_2O as a mixture of two diastereoisomeric pairs of enantiomers (*RRR* + *SSS* and *RRS* + *SSR*) in 1 : 1 molar ratio. **6d** must be stored below 4 °C. Yield: 570.2 mg, 0.3875 mmol, 76%. Mp 210 °C. ^{1}H NMR (600 MHz, CD_2Cl_2, −10 °C): δ 1.14 (m, 6 H), 1.43 (m, 18 H), 1.63–1.69 (various m, 12 H), 1.90–2.00 (various m, 24 H), 2.22–2.71 (br s, 4 H), 2.93 (s br, 12 H), 2.94 (s br, 6 H), 4.49 (m, 6 H), 6.59 (m, 6 H), 6.79–6.85 (various m, 18 H), 6.70 (m, 12 H), 7.16 (m, 6 H), 7.41 (m, 12 H), 7.55 (m, 12 H), 8.17 (s br, 1 H), 8.24 (s br, 5 H). ^{13}C{^{1}H} NMR (150.9 MHz, CD_2Cl_2, −10 °C): δ 18.29, 18.32, 24.4, 24.6, 24.8, 25.3, 29.37, 29.4, 30.5, 32.02, 32.07, 64.00, 64.04, 64.9, 116.66, 116.74, 120.1, 120.7 (q, $^1J_{CF}$ = 320 Hz), 124.8, 126.9, 127.39, 127.51, 129.8, 135.3, 138.8, 140.64, 140.70, 141.12, 141.15, 144.87, 144.94, 169.7. IR (Nujol, cm^{-1}): 3603, 3495, 3262, 1621, 1593, 1556. HRMS (ESI) *m/z* calc. for $C_{69}H_{75}N_6$ [M]$^{3+}$, 329.2012; found 329.2017. Anal. calc. for $C_{72}H_{75}F_9N_6O_9S_3$·2H_2O: C, 58.76; H, 5.41; N, 5.71; S, 6.54. Found: C, 58.99; H, 5.45; N, 5.66; S, 6.45%. Crystals of **6d**·2$CHCl_3$·CH_2Cl_2 suitable for an X-ray diffraction study were obtained by diffusion of *n*-pentane into a solution of the product in a 1 : 1 mixture of $CHCl_3$ and CH_2Cl_2.

Syntheses of *E*-4-iminium-1,2,3,4-tetrahydroquinoline triflates (7)

Synthesis of 7d2. A solution of **3d2** (114 mg, 0.23 mmol) in $CHCl_3$ (2 mL) was heated with stirring in a Carius tube to 45 °C for 48 h. The resulting solution was filtered through a short pad of anhydrous $MgSO_4$ and concentrated under vacuum (0.5 mL). A cold mixture of Et_2O and *n*-pentane was added (10 : 20 mL, 0 °C) to give a yellow suspension, which was stirred at 0 °C for 15 min and then filtered. The solid collected was washed with cold *n*-pentane (3 × 5 mL, 0 °C) and dried first by suction and then under vacuum (6 h) to give *E*-**7d2** as a bright yellow solid. Yield: 89.2 mg,

0.19 mmol, 81%. Mp 88 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ 1.25 (m, 2 H), 1.63–2.01 (various m, 8.4 H), 2.38 (s, 3 H), 3.02, 3.20 (AB part of an ABX system, 2 H, $^2J_{AB}$ = 16.7 Hz, $^3J_{BX}$ = 13.8 Hz, $^3J_{BX}$ = 4.2 Hz), 3.72 (m, 1 H), 4.69 (dd, X part of an ABX system, 1 H, $^3J_{HH}$ = 13.2 Hz, $^3J_{HH}$ = 4.0 Hz), 5.43 (v br s), 6.78–6.83 (m, 2 H), 7.24 (d, 2 H, $^3J_{HH}$ = 7.6 Hz), 7.38 (m, 3 H), 8.19 (d, 1 H, $^3J_{HH}$ = 8.4 Hz), 10.70 (s br, 1 H). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$, 25 °C, TMS): δ 21.2, 24.2, 24.6, 24.7, 30.8, 31.0, 35.4, 55.5, 57.8, 110.0, 117.3, 119.8, 126.6, 127.5, 130.0, 135.5, 138.9, 139.3, 152.4, 171.0. IR (Nujol, cm^{-1}): 3300, 3255, 3166, 1621, 1612, 1569, 1525, 1515, 1489. Anal. calc. for $C_{23}H_{27}F_3N_2O_3S{\cdot}0.2H_2O$: C, 58.51; H, 5.85; N, 5.93; S, 6.79. Found: C, 58.29; H, 5.97; N, 5.90; S, 6.65%. Crystals of **7d2** suitable for an X-ray diffraction study were obtained by slow diffusion of *n*-pentane into a solution of the product in $CHCl_3$.

Synthesis of 7d5. A solution containing **4** (200 mg, 0.56 mmol) and ferrocene carbaldehyde (234 mg, 1.09 mmol) in $CHCl_3$ (20 mL) was stirred and heated in a Carius tube to 45 °C for 3 h. The resulting red solution was filtered through a short pad of anhydrous $MgSO_4$ and concentrated to dryness. The oily residue was washed with a cold mixture of $CHCl_3$ and Et_2O (1 : 20, 3 × 21 mL, 0 °C), dissolved in $CHCl_3$ (1 mL), and cold *n*-pentane was added (20 mL, 0 °C) with stirring to give a red suspension, which was stirred at 0 °C for 15 min and then filtered. The solid collected was dissolved in $CHCl_3$ (1 mL), filtered through a short pad of anhydrous $MgSO_4$ and slowly added dropwise to a cold mixture of Et_2O and *n*-pentane (10 : 30 mL, 0 °C). The resulting suspension was stirred at 0 °C for 30 min and then filtered. The solid collected was washed with cold *n*-pentane (3 × 5 mL, 0 °C) and dried first by suction and then under vacuum (6 h) to give *E*-**7d5**·0.5H_2O as a red solid. Yield: 168.3 mg, 0.30 mmol, 55%. Mp 93 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ 1.30 (m, 3 H), 1.63–1.99 (various m, 8.5 H), 3.26, 2.95 (AB part of an ABX system, 1 H, $^2J_{AB}$ = 14.2 Hz, $^3J_{BX}$ = 13.8 Hz, $^3J_{BX}$ = 2.2 Hz), 3.77 (m, 1 H), 4.22–4.30 (m, 9 H), 4.42 (d br, X part of an ABX system, 1 H, $^3J_{HH}$ = 7.6 Hz), 5.83 (s, 1 H), 6.73 (t, 1 H, $^3J_{HH}$ = 7.6 Hz), 6.84 (d, 1 H, $^3J_{HH}$ = 8.4 Hz), 7.35 (t, 1 H, $^3J_{HH}$ = 7.6 Hz), 8.12 (d, 1 H, $^3J_{HH}$ = 8.4 Hz), 10.50 (s br, 1 H). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$, 25 °C, TMS): δ 24.2, 24.7, 24.8, 30.9, 31.1, 34.8, 50.2, 57.5, 66.4, 67.0, 68.9, 109.6, 117.2, 119.2, 127.1, 138.8, 151.9, 171.0. IR (Nujol, cm^{-1}): 3314, 3243, 3158, 1621, 1567, 1524. HRMS (ESI) *m*/*z* calc. for $C_{25}H_{29}N_2Fe$ [M]$^+$, 413.1675; found 413.1676. Anal. calc. for $C_{26}H_{29}FeF_3N_2O_3S{\cdot}0.5H_2O$: C, 54.65; H, 5.29; N, 4.90; S, 5.61. Found: C, 54.43; H, 5.36; N, 4.92; S, 5.39%.

Synthesis of 7e2. A mixture of *R*-**2e** (300 mg, 1.33 mmol), *p*-tolyl aldehyde (160 μL, 1.35 mmol) and HOTf (120 μL, 1.38 mmol) in CH_2Cl_2 (10 mL) was stirred in a Carius tube at room temperature for 1 h and then at 45 °C overnight. The resulting solution was concentrated under vacuum to dryness and the residue was washed with a 1 : 30 mixture of CH_2Cl_2–Et_2O (3 × 31 mL) and dried under vacuum for 6 h to give *E*-**7e2**·0.5H_2O as a mixture of the *RR* and *RS* isomers, A and B, in a 5 : 1 molar ratio. Yield: 422.2 mg, 0.84 mmol, 63%. Mp 86 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ: major isomer: 1.69–1.82 (very broad s, 1 H, major + minor), 1.76 (d, 3 H, $^3J_{HH}$ = 6.8 Hz), 2.28 (s, 3 H), 2.94, 3.14 (AB part of an ABX system, 2 H, $^2J_{AB}$ = 16.7 Hz, $^3J_{BX}$ = 12.6 Hz, $^3J_{AX}$ = 4.2 Hz), 4.34 (dd, X part of an ABX system, 1 H, $^3J_{HH}$ = 12.6 Hz, $^3J_{HH}$ = 4.6 Hz), 4.98 ("quint", 1 H, $^3J_{HH}$ = 6.8 Hz), 5.94 (s v br, 2 H, major + minor), 6.67 (m, 2 H, major + minor), 6.81 (d, 1H, $^3J_{HH}$ = 8.4 Hz), 7.04–7.42 (several m, 18 H, major + minor), 8.17 (d overlapped d, 2 H, major + minor, $^3J_{HH}$ = 8.0 Hz), 10.86 (v br d, 1 H, $^3J_{HH}$ = 6.4 Hz); minor isomer: δ 1.80 (d, 3 H, $^3J_{HH}$ = 6.4 Hz), 2.25 (s, 3 H), 2.68, 3,32 (AB part of an ABX system, 2 H, $^2J_{AB}$ = 16.8 Hz, $^3J_{BX}$ = 12.2 Hz, $^3J_{AX}$ = 5.4 Hz), 4.61 (dd, X part of an ABX system, 1 H, $^3J_{HH}$ = 12.0 Hz, $^3J_{HH}$ = 4.8 Hz), 5.14 (m, 1 H, $^3J_{HH}$ = 7.0 Hz), 6.77 (d, 1H, $^3J_{HH}$ = 8.8 Hz), 6.98 (d, 2 H), 10.71 (vbr d, 1 H, $^3J_{HH}$ = 6.8 Hz). ^{13}C{^{1}H} NMR (100.8 MHz, $CDCl_3$, 25 °C, TMS): major isomer: δ 21.04, 21.8, 35.5, 54.6, 57.9, 109.5, 117.6, 119.3, 120.4 (q, $^1J_{CF}$ = 320 Hz), 126.1 (major + minor), 126.2 (major + minor), 127.3, 128.7, 129.5, 129.8, 135.1 (major + minor), 138.8, 139.3, 139.7, 153.0, 173.1; minor isomer: 21.02, 21.9, 34.9, 53.9, 57.7, 109.4, 117.5, 119.1, 127.1, 128.3, 129.3, 129.6, 138.4, 139.1, 139.9, 152.9, 172.8. IR (Nujol, cm^{-1}): 3304, 3248, 1622, 1615, 1603, 1567, 1525 and 1516. HRMS (ESI) *m*/*z* calc. for $C_{24}H_{25}N_2$ [M]$^+$, 341.2012; found 341.2010. Anal. calc. for $C_{25}H_{25}F_3N_2O_3S{\cdot}0.5H_2O$: C, 60.11; H, 5.25; N, 5.61; S, 6.42. Found: C, 59.79; H, 5.37; N, 5.60; S, 6.46%.

Conclusion

The designed extension of the hydroiminiumation of an imine, previously reported in palladium chemistry, has been successfully applied to the synthesis of 1,2-dihydroquinazolinium salts. The method is of a wide applicability. Although most studied ketones gave the expected compounds, their instability prevented the isolation of most of the corresponding 1,2-dihydroquinazolinium salts. The study of the isomerization of some 4-methyl derivatives led to the preparation of the first 4-iminium-1,2,3,4-tetrahydroquinolines.

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30 ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C), δ 9.97 (s, CHO), 9.04 (s, H^4), 8.07 (s, H^2).

31 ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ 1.75 (s, 6 H, Me_2C), 2.46 (s, 3 H, Me^{Tol}), 6.85 ("dt", 1 H, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HH}$ = 0.8 Hz), 7.14 (m, 2 H), 7.23–7.44 (m obscured by the resonances of other components, 4 H, $Tol^{ortho + meta}$), 7.58 (ddd, 1 H, $^{3}J_{HH}$ = 8.4 Hz, $^{3}J_{HH}$ = 7.2 Hz, $^{4}J_{HH}$ = 1.6 Hz), 8.07 (s, 1 H, H4), 8.34 (s br, 1 H, NH).

32 ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ 1,75 (s, CMe_2).

33 ^{1}H NMR (200 MHz, CD_3CN, 25 °C): δ 0.91 (t, 3 H, $MeCH_2$, $^{3}J_{HH}$ = 7.4 Hz), 1.93 (s, 3 H, Me^{Tol}), 2.41 (q, 2 H, $MeCH_2$, $^{3}J_{HH}$ = 7.2 Hz).

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