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Easy α-alkylation of ketones with alcohols through a hydrogen autotransfer process catalyzed by $RuCl_2(DMSO)_4$

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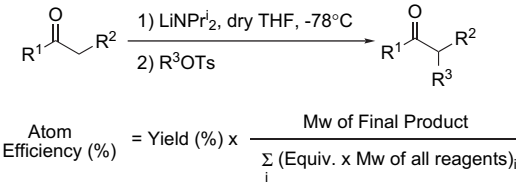
Abstract—The electrophilic α-alkylation of ketones with alcohols is accomplished by a hydrogen autotransfer process catalyzed by $RuCl_2(DMSO)_4$. The reaction can produce either simple alkylated ketones or α,β-unsaturated ketones just by choosing the appropriate starting ketones (methyl ketones or bicyclic methylenic ketones, respectively), as well as quinolines (by using 2-aminobenzyl alcohol derivatives) or the corresponding alcohol derivatives by the addition of an extra equivalent of the initial alcohol. In the last case, after the above alkylation process reduction of the carbonyl compound takes place. A mechanistic study seems to indicate that the process goes through the oxidation of the alcohols with ruthenium (after a previous deprotonation) to yield the corresponding aldehyde and a ruthenium hydride intermediate. In turn, the aldehyde suffers a classical aldol reaction with the starting ketone to form the corresponding α,β-unsaturated ketone, which finally is reduced through a Michael-type addition by the aforementioned ruthenium hydride intermediate.

1. Introduction

One of the challenges that chemists should face in this new century is to develop transformations that are not only efficient, selective and high yielding, but also environmentally benign, which could be integrated in sustainable processes.[1] There are two main strategies in order to minimize the environmental impact of a reaction: one of them involves the use of 'greener' solvents,[2] and another implies the use of less prejudicial or recyclable catalysts and reagents.[3] Some pivotal methods in organic synthesis like carbon–carbon bond formation reactions,[4] especially the electrophilic α-alkylation of carbonyl compounds,[5] are against these principles. For instance, the classical protocols for this reaction create some problems (e.g., LDA, dry THF, alkyl tosylates, etc., Scheme 1), not only from a synthetic but also from an economic and environmental point of view. The waste problems, such as the unavoidable inorganic salts derived from the leaving group and bases, make sometimes these classical alkylation methods not very practical for industrial use.[6] Another important aspect (many times forgotten) is the atom economy or efficiency,[7] which is in these cases very low (≈20%) due to the high molecular weight of strong bases as well as the leaving group of the alkylating electrophiles used.



Scheme 1. Example of classical α-alkylation of ketones.

Some of the aforementioned problems, such as the low atom efficiency or the enormous wastage of inorganic salts, have been overcome by the α-alkylation of methyl ketone derivatives with alcohols with the use of a hydrogen autotransfer process, which can be considered as a new type of domino reaction.[8] This type of process involves an initial removal of hydrogen from one of the initial reagents (R^1–H) by a catalyst (C), followed by reaction of the new reagents (R^1 and R^2) to form a new compound (P), which is in turn the hydrogen acceptor of the previously formed hydrogenated catalyst(C–H), renewing the catalyst (Scheme 2). The first catalyst used was a mixture of oxides supported in alumina ($CuO/ZnO/Al_2O_3$ 1/1/8), which gave the expected alkylated ketones with very low yields (25%).[9] Similar results were obtained with only alumina slightly doped with sodium.[10] The introduction of ruthenium complexes such as $Ru(MeCOCHCOMe)_3$[11] and $RuCl_2(PPh_3)_3$[12] improved yields up to the range of 50% and 90%, respectively, although in the last case, the addition of large amounts of 1-dodecene decreased the atom efficiency. Other different transition metal complexes such as $[IrCl(COD)]_2$[13] and palladium supported

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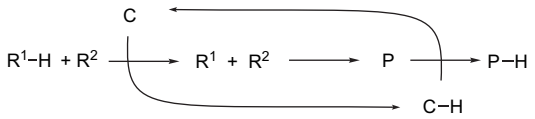
either on carbon charcoal[14] or on aluminum hydroxide[15] have been introduced as alternatives.



Scheme 2. General scheme for a hydrogen autotransfer process.

Alcohols are generally not considered as electrophiles[16] due to the high energy of the C–O bond (≈90 kcal/mol), the poor leaving group character of the OH being even increased after its deprotonation under the classical basic conditions for the alkylation reactions. However, their hypothetical use as electrophiles would have an extraordinary advantage, since the lost molecule will be water, a very small weight and environmentally friendly molecule. The reason of this contradictory behavior (being usually nucleophile but under some conditions electrophile) is based on the in situ transformation of alcohols into highly electrophilic aldehydes, which can react now with other usual nucleophiles such as phosphorous ylides[17] or α-deprotonated nitriles,[18] and even with methyl ketone derivatives, in situ formed through a Oppenauer oxidation of the corresponding secondary alcohol.[19] Not only metal complexes are the catalysts for these hydrogen autotransfer processes, but also enzymes worked nicely.[20]

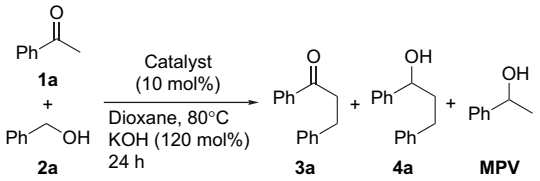
2. Results and discussion

We have recently introduced the alternative use of $RuCl_2(DMSO)_4$[21] as a cheap and easily handled complex for the regioselective α-alkylation of methyl ketone derivatives with primary alcohols.[22] This ruthenium complex possesses a Lewis acid character similar to other late transition metal chloride complexes,[23] as it was proven in the multicomponent[24] Strecker reaction.[25] Here, we report the systematic study of different parameters of the reaction and additives, which could have some impact on the reaction, as well as its application to the synthesis of the corresponding alcohols, quinolines, and α,β-unsaturated ketones of commercial interest. The reaction process has been extended for the first time to methylenic ketone derivatives. A labeling reagent–product study permitted to determine the possible reaction pathway.

2.1. α-Alkylation of methyl ketone derivatives with alcohols

The alkylation of acetophenone (**1a**) with benzyl alcohol (**2a**) to give the corresponding ketone **3a** was chosen as the reaction model in order to optimize all different parameters, studying first the nature of the catalyst (Table 1). The reaction using a typical Meerwein–Ponndorf–Verley catalyst such as aluminum triisopropoxide gave a mixture nearly equimolecular of the expected ketone **3a**, as well as the related alcohol **4a**, which came from the reduction of the above ketone, and 1-phenyl-1-ethanol (**MPV** product), which is the expected product from a classical Meerwein–Ponndorf–Verley reduction.[26] The use of transition metallic salts such as those derived from vanadium or chromium did not produce any important change in the above results (Table 1, entries 2 and 3). Iron trichloride showed more promising results with a 60% yield and 40% atom efficiency (see Scheme 1) for ketone **3a**. However, the change of the anionic ion or the oxidation state of cationic iron atom decreased the yield (Table 1, entries 4–6). Moving along the periodic table did not have any reasonable improvement (entries 7–12). To our delight, the reaction with $RuCl_2(DMSO)_4$ gave a satisfactory 80% yield and 49% atom efficiency, with only trace of 1-phenyl-1-ethanol (**MPV**). In our hands, the reaction with $RuCl_2(PPh_3)_3$ gave lower results (compare entries 13 and 14). Moving again along the periodic table did not have any reasonable improvement (entries 15 and 16). Finally, it should be pointed out that the reaction with the dimeric complex $[IrCl(COD)]_2$ gave similar yield to that obtained with $RuCl_2(DMSO)_4$ (compare entries 13 and 17) and slightly lower atom efficiency (47%, see Scheme 1).

Table 1. Catalyst optimization

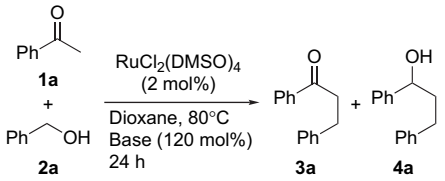


Entry	Catalyst	Yields (%)[a]		
		3a	**4a**	**MPV**
1	$Al(O^iPr)_3$	15	25	25
2	VCl_2	21	16	41
3	$CrCl_2$	26	19	32
4	$FeCl_3$	60	12	15
5	$Fe(acac)_3$	0	18	59
6	$FeCl_2$	25	21	33
7	$CoCl_2$	24	34	7
8	$NiCl_2$	16	28	22
9	$NiCl_2$[b]	0	0	16
10	$CuCl_2$	25	30	11
11	$Cu(OTf)_2$	38	23	16
12	$ZnCl_2$	16	35	10
13	$RuCl_2(DMSO)_4$	80	8	<1
14	$RuCl_2(PPh_3)_3$	61	15	7
15	$RhCl(PPh_3)_3$	49	20	10
16	$PdCl_2$	52	11	21
17	$[IrCl(COD)]_2$	82	5	<1

[a] Yields determined by ^1H NMR using *N,N*-diphenyl formamide as internal standard.
[b] A 40 mol % of $P(OEt)_3$ was added.

Once the best catalyst was found (Table 1, entry 13), other parameters of the reaction were tested (Table 2). The reaction using stoichiometric amounts of all starting reagents and only 2 mol % of catalyst in 1,4-dioxane gave the expected ketone in 72% yield after 24 h at 80 °C (entry 1). Changing the solvent by other less coordinating one, such as toluene, methylene chloride or THF, gave worse results, increasing the amount of the isolated alcohol **4a** (entries 2–4). The nature and the amount of the base were also tested, finding that the reaction failed when neither a base nor triethylamine were used. Even using substoichiometric amount of KOH (10 mol %) or CsOH gave modest results (entries 6 and 8). When the reaction was performed using only 1 mol % of the ruthenium catalyst, the yield decreased deeply (entry 9), the reaction failed when only 0.2% was

Table 2. Conditions optimization



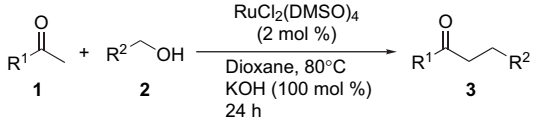
Entry	Solvent	Base	Yield **3a** (%)[a]	Yield **4a** (%)[a]
1	1,4-Dioxane	KOH	78 (72)[b]	6 (4)[b]
2	PhMe	KOH	61	18
3	CH_2Cl_2	KOH	13	10
4	THF	KOH	64	18
5	1,4-Dioxane	—	0	0
6	1,4-Dioxane	KOH[c]	12	0
7	1,4-Dioxane	Et_3N	0	0
8	1,4-Dioxane	CsOH	36	31
9[d]	1,4-Dioxane	KOH	35	3
10	1,4-Dioxane[e]	KOH	58	20
11[f]	1,4-Dioxane	KOH	77	10
12[g]	1,4-Dioxane	KOH	74	13
13[h]	1,4-Dioxane	KOH	32	54

[a] Yields determined by ^{1}H NMR using *N*,*N*-diphenyl formamide as internal standard.
[b] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).
[c] A 10 mol % of KOH was used.
[d] A 1 mol % of $RuCl_2(DMSO)_4$ was used.
[e] Reaction performed at reflux temperature.
[f] A 2 mol % of 2,6-pyridinedicarboxylic acid was added.
[g] A 4 mol % of 2,6-pyridinedicarboxylic acid was added.
[h] A 200 mol % of **2a** was used.

added. The reaction temperature had also an appreciable impact on the ratio of products, increasing the amount of alcohol **4a** when the temperature was increased (entry 10). In the last case, the GC–MS analysis of the reaction mixture at different reaction times showed the presence of benzaldehyde and chalcone as by-products, which can indicate the possible reaction pathway (vide infra). The presence of different amounts of 2,6-pyridinedicarboxylic acid, as stabilizing ruthenium ligand,[27] decreased the ratio of products. However, the increase of amount of alcohol **2a** (200 mol %, entry 13) changed the main isolated product, in this case being alcohol **4a** (vide infra).

Once the best conditions were found (Table 2, entry 1), this protocol was employed with other ketones and alcohols (Table 3). The reaction gave excellent results using methyl aryl ketones and aromatic alcohols independently of the electron character of the substituted alcohol (entries 1–3 and 12–15). In the case of using heteroaromatic alcohol derivatives, the yield decreased (entries 4 and 5), the reaction failing for aliphatic or propargyl alcohols[28] (entries 6 and 8). An especial case occurred when cinnamyl alcohol was used (entry 7), since instead of the expected δ,ε-unsaturated ketone the related saturated ketone **3g** was isolated in 48% yield, this ketone arising from the reduction of the double bond of the expected product. In order to improve the chemical yield, the reaction was repeated using a double amount of cinnamyl alcohol to ensure the total reduction of all carbon–carbon double bonds, obtaining in this case a 78% yield. Concerning the ketone scope, it should be pointed out that the alkylation process unfortunately failed for aliphatic methyl ketones (entry 6). However, the results

Table 3. α-Alkylation of methyl ketone derivatives with alcohols catalyzed by $RuCl_2(DMSO)_4$



Entry	R^1	R^2	No.	Yield (%)[a]
1	Ph	Ph	**a**	72
2	Ph	3-$PhCH_2OC_6H_4$	**b**	86
3	Ph	2-BrC_6H_4	**c**	93
4	Ph	2-Furyl	**d**	25
5	Ph	3-Indenyl	**e**	20
6	Ph	^{i}Pr	**f**	<5
7	Ph	(*E*)-PhCH=CH	**g**	48[b] (78)[b,c]
8	Ph	HC≡C	**h**	0[d]
9	*n*-C_5H_{11}	Ph	**i**	<5
10	4-MeC_6H_4	Ph	**j**	96
11[e]	4-MeC_6H_4	Ph	**j**	68
12	4-MeC_6H_4	4-$MeOC_6H_4$	**k**	92
13	4-MeC_6H_4	4-ClC_6H_4	**l**	85
14	4-MeC_6H_4	2-ClC_6H_4	**m**	92
15	4-MeC_6H_4	3,4-$(MeO)_2C_6H_3$	**n**	69
16	4-$F_3CC_6H_4$	Ph	**o**	0[f]
17	2-H_2N-4,5-$(OCH_2)C_6H_2$	Ph	**p**	55
18	2-Naphthyl	Ph	**q**	87
19	2-Thienyl	Ph	**r**	45
20	2-Thienyl	2-BrC_6H_4	**s**	41
21	*N*-Methylpyrrol-2-yl	Ph	**t**	80
22	Ferrocenyl	Ph	**u**	17[g]
23	3-Indenyl	Ph	**v**	0[h]

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate); yields obtained using 2 equiv of alcohols in parenthesis.
[b] The corresponding full hydrogenated ketone was the only isolated product.
[c] Cinnamyl alcohols (2 equiv) were used.
[d] The starting acetophenone (**1a**) was recovered in practically quantitative yield.
[e] KO^{t}Bu was used as base instead of KOH.
[f] The corresponding alcohol **4o** was isolated in 48–89% yield (see text).
[g] The related α,β-unsaturated ketone **6u** was isolated in 60% yield.
[h] The related α,β-unsaturated ketone **6v** was isolated in 79% yield.

obtained using different methyl aryl ketones were good independently of the electronic character of the substituent on the aromatic ring (compare entries 1, 10, and 16–18, and footnote e). The atomic efficiency reached up to 70% in the case of ketone **1j** (entry 10). It should be pointed out that changing the KOH base for a slightly stronger KO^{t}Bu as base in the reaction, the yield decreased significantly and consequently the atomic efficiency (entry 11). In the case of using *p*-trifluoromethylacetophenone, instead of the expected ketone **3o**, the only product isolated was the related alcohol **4o** (48%), which comes from the expected alkylation process followed by a reduction of the ketone **3o**. When the reaction was repeated with 2 equiv of alcohol (the source of alkylating as well as the reducing agent) the yield of **4o** increased up to 89% (entry 16).

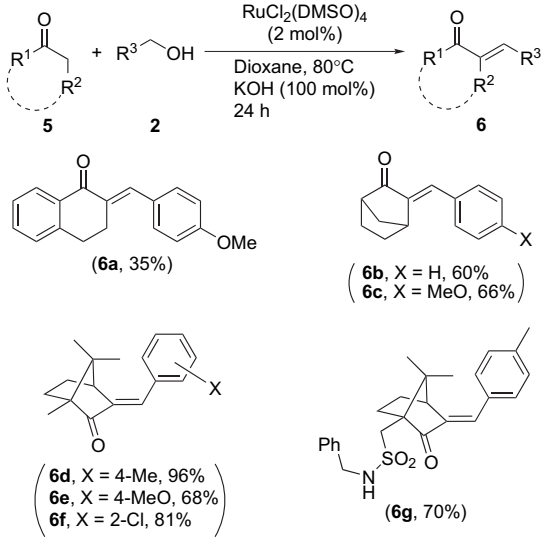
The reaction was also expanded to heteroaromatic methyl ketones (Table 3, entries 19–23), giving in these cases different results depending on the nature of the heteroaromatic system. Thus, the reaction with thiophene derivative gave the expected ketones **3r**,**s** with moderated yield, the only by-product detected being the related Meerwein–Ponndorf–Verley alcohol coming from the reduction of starting ketone. In the case of the pyrrol ketone, the result was similar to

other aryl ketones. Finally, when the reaction was performed with either ferrocenyl or indenyl ketone derivatives, the main isolated product was not the corresponding expected ketone **3u** or **3v**, but the related α,β-unsaturated ketone of type **6** (see infra). In these two cases, the final hydrogenation of the double bond failed, at least partially, but not the catalytic cycle. At this moment, we do not have any clear explanation for this behavior, but it is known that in the aerobic oxidation of amines by ruthenium complexes, oxygen[29] is the final scavenger for hydrogen, and here it could occur something similar, the direct generation of hydrogen being not excluded.[30]

The reaction of propiophenone with benzyl alcohol merits a separated comment, since this reaction gave a mixture of different products being the starting ketone the major one, followed by the Meerwein–Ponndorf–Verley alcohol derived from its reduction, the expected ketone of type **3**, and the related α,β-unsaturated ketone of type **6** being minor components of the crude mixture (estimated yields by ^{1}H NMR lower than 5% in any case). However, when the reaction was performed in the presence of equal amounts of propiophenone, acetophenone, and benzyl alcohol, the process showed a high selectivity giving ketone **3a** in a 78% yield and recovering the starting propiophenone in a higher 90% yield, the estimated yield of secondary alcohol **4a** and the Meerwein–Ponndorf–Verley alcohol (1-phenylpropanol) being less than 7% for both. This result shows the high selectivity of the alkylation process for methyl aryl ketones.

2.2. α-Alkenylation of bicyclic ketone derivatives with alcohols

As noticed in the above paragraph, the reaction with ketones different from methyl derivatives failed. In the literature, the hydrogen autotransfer strategy had been only applied with moderated success to benzofused α-tetralone (**5a**) and related systems.[12–15] The only isolated product was surprisingly ketone **6a** when the above reaction was performed using ketone **5a** and 4-methoxybenzyl alcohol, albeit with moderated yield (35%). The reaction with other bicyclic ketones **5** (not only benzofused but also aliphatic ones) gave the corresponding α,β-unsaturated ketone **6** as the only product with good to excellent yields (Scheme 3). In order to understand the catalytic turnover of ruthenium species, we hypothesize the reoxidation of the ruthenium hydride intermediate by reaction with oxygen or by direct generation of hydrogen as it was previously pointed out. The presence of functional groups on the aromatic ring of the aldehyde did not have any influence on the results, in all cases the chemical yield being good. However, the structure of the starting ketone has a higher impact on the results. It is worthy to note that synthesized chiral benzylidenecamphor derivatives **6d–f** have different applications, such as in the synthesis of second-order non-linear optical materials,[31] as chiral dopants for nematic liquid crystals which induce ordering into a helix in the nematic phase[32] or as sunscreens (**6e**).[33] The previous preparation of all this type of compounds involved the condensation between camphor and the corresponding aromatic aldehyde using anhydrous solvents and strong and expensive bases, such as $NaNH_2$ or potassium *tert*-butoxide, with the yield never being higher than 75%.[34] With this new protocol, the yields are significantly higher, avoiding the necessity of using dry solvents, special handle reagents, and aromatic aldehydes, which have stability problems with their storage (usually they are oxidized by the atmospheric oxygen).



Scheme 3. α-Alkenylation of bicyclic ketones.

The *Z*-configuration of the double bond was unambiguously determined by the X-ray of compound **6e** (Fig. 1) and by NOESY experiments of compounds **6c**, **e**, and **f**. It should be pointed out that the reaction of *N*-benzyl camphorsulfonamide[35] with 4-methylbenzyl alcohol failed under standard conditions (Scheme 3), recovering the starting ketone unchanged. We attributed this failure to the presence of an acidic proton in the ketone structure, which competed with the alcohol to be deprotonated. However, the expected ketone **6g** was obtained with a fair chemical yield when the same reaction was performed under similar conditions but using 300 mol % of KOH, this type of camphorsulfonamide derivatives having been tested as alternative sunscreen.[36]

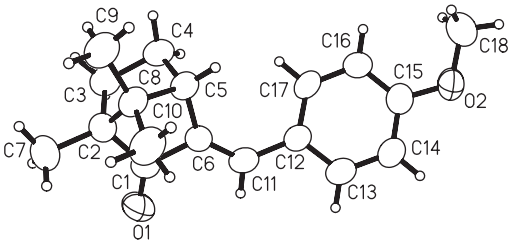
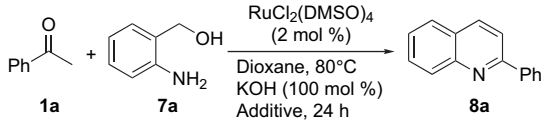


Figure 1. ORTEP drawing of compound **6e**.

2.3. Synthesis of quinolines by α-alkylation of ketones with 2-aminobenzyl alcohol derivatives

Another interesting application of this reaction appeared when it was performed using 2-aminobenzyl alcohol (**7a**) as alkylating agent and acetophenone (**1a**). In this case, quinoline **8a** was the only product isolated (Table 4), instead of the corresponding ketone of type **3**. The isolation of pure quinoline was very easy just by an acidic–basic extraction. This product arises formally from the internal condensation of the

Table 4. Optimization of the cyclization process



1a **7a** **8a**

Entry	Additive	Amount (%)	Yield (%)[a]
1	—	—	70
2	1-Hexene	200	86
3	1-Hexene	1200	75
4	Acetone	200	89
5	PhCOMe (**2a**)	200	81
6	PhCOPh	200	94

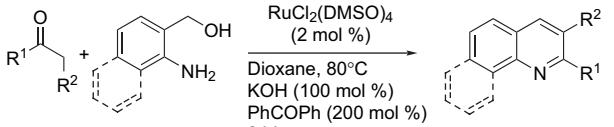
[a] Isolated yield after acidic/basic aqueous extraction.

amine moiety with the corresponding α,β-unsaturated ketone of type **6**.[37] The presence of a quinoline scaffold in the framework of various pharmacologically active compounds possessing anti-malarial, anti-inflammatory, anti-asthmatic, anti-bacterial, and anti-hypersensitive activities,[38] spurred on the optimization of this process, as well as on the study of its scope.[39] In order to improve the results, other hydrogen scavengers for the ruthenium hydride intermediate different from atmospheric oxygen such as olefins or ketones were tested, finding that all these scavengers gave better results than oxygen. It should be pointed out that it was also possible to use acetone as hydrogen scavenger, since its condensation with the corresponding in situ formed 2-aminobenzaldehyde seems to be slower than with acetophenone, so not interfering in the desired reaction. Despite all, the best result was found when benzophenone was used as hydrogen scavenger. Although the presence of these additives could be seen as an inconvenience for the isolation of quinoline, this is not true since the simple acidic–basic aqueous extraction yielded the pure compound **8a**.

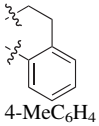
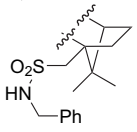
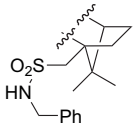
Once the best conditions were found (Table 4, entry 6), this protocol was employed with other ketones and alcohols (Table 5). The reaction gave excellent results using alcohol **7a**, not only with methyl aryl ketones but also with ketones bearing larger substituents than methyl or cyclic systems such as α-tetralone (entries 1–4). All these results, compared with those obtained previously with simple benzylic alcohols, could be an evidence that the condensation between the carbonyl group of the ketone with the amine to form the corresponding imine, takes place prior to the aldol condensation and therefore favoring it. High yields are also obtained for a broad set of different aryl methyl ketones, including heteroaromatic compounds (entries 7–10) and a ferrocenyl derivative (entry 11). In the last case, the crystallographic analysis of compound **8k** showed the co-planarity between both aromatic systems (Fig. 2) of great importance for a possible non-linear optical behavior.[40]

When the reaction was performed using camphor, together with the expected camphor-based chiral quinoline **8o**,[41] the related (*E*)-3-(2-aminophenyl)methylene-camphor (**6o**) was isolated in 20% yield. This α,β-unsaturated ketone **6o** could be easily transformed into the corresponding quinoline **8o** in quantitative yield by treatment with a catalytic amount of *para*-toluenesulfonic acid and azeotropic removal of water with benzene. Whereas the reaction using the related

Table 5. Synthesis of quinolines **8**



1 or **5** **7a**: benzyl **7b**: naphthyl **8**

Entry	Alcohol	No.	R^1	R^2	Yield (%)[a]
1	**7a**	**8a**	Ph	H	94[b]
2	**7a**	**8b**	Ph	Me	81[b]
3	**7a**	**8c**	Ph	Et	67[b]
4	**7a**	**8d**			98[b]
5	**7a**	**8e**	4-MeC_6H_4	H	96[b]
6	**7b**	**8f**	4-MeC_6H_4	H	93
7	**7a**	**8g**	2-Pyridyl	H	93
8	**7a**	**8h**	2-Furyl	H	93
9	**7a**	**8i**	2-Thienyl	H	96
10	**7a**	**8j**	*N*-Methylpyrrol-2-yl	H	76
11[d]	**7a**	**8k**	Ferrocenyl	H	88
12	**7a**	**8l**	Et	Me	96
13	**7a**	**8m**	$-(CH_2)_4-$		88
14	**7a**	**8n**			75
15	**7a**	**8o**			30[c]
16	**7a**	**8p**			65[d]
17	**7b**	**8q**			66[d]

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).
[b] Isolated yields after acidic/basic aqueous extraction.
[c] A 20% yield of (*E*)-3-(2-aminophenyl)methylene-camphor (**6o**) was isolated.
[d] Yield obtained using 300 mol % of KOH.

camphorsulfonamide and 1 equiv of base failed, when the amount of base was increased up to 3 equiv, the expected quinoline **8p** was isolated in similar yield compared to other compounds **8**. The change of alcohol **7a** by the naphthyl derivative **7b** gave similar results (compare entries 5, 6, 16, and 17 in Table 5).

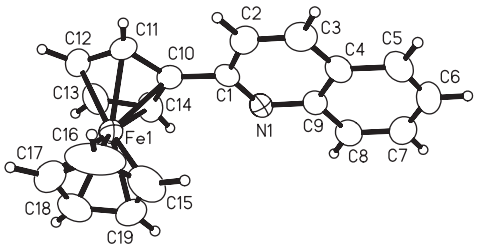


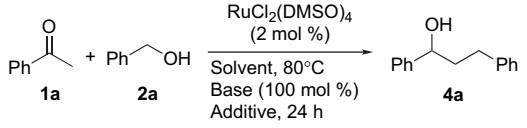
Figure 2. ORTEP drawing of compound **8k**.

2.4. Synthesis of secondary alcohols by a tandem α-alkylation of methyl ketone derivatives with alcohols and reduction

The reaction conditions shown in Table 3 could be changed to produce alcohols **4** as the main products,[42] instead of the related ketones **3**. Thus, when the reaction was performed using a double amount of alcohol **2a**, referred to ketone **1a**, under an argon atmosphere and in a pressure tube, the main isolated product was alcohol **4a** (Table 6, entry 1). This compound came formally from a α-alkylation process followed by a Meerwein–Ponndorf–Verley reduction.[26] As in previous cases of simple alkylations, lowering the amount of either catalyst or base gave poorer yield. However, the result did not improve increasing the amount of alcohol **2a** up to 6 equiv (entry 5). The nature of the initial ruthenium complex seems to be very important, since the reaction using $[RuHCl(CO)(PPh_3)_3]$ as catalyst gave very poor results (entry 2).[43] The effect of the solvent and base was also tested, the best results being obtained using dioxane and KOH (entries 1 and 6–13). Finally, we studied the influence of different additives. Thus, the reaction using a mixture of ruthenium complex and triphenyl phosphine in 1/1 molar ratio gave a slight better result. However, the increase of the phosphine/ruthenium ratio or the use of a diphosphine or nitrogenated ligands, as well as a phase transfer catalyst did not improve the previous results (entries 15–17).

The aforementioned protocol (Table 6, entry 14) was then used with other ketones and alcohols (Table 7). Unfortunately, the reaction only worked nicely when both reagents, the ketone and the alcohol, were aromatic. The reaction using isobutanol gave only 45% yield (entry 2), the same range of yield was found for the combination of aliphatic ketones with benzyl alcohol. It should be pointed out that the reaction using 2-heptanone only gave one product (entry 4), which arises from the alkylation of the methyl substituent, and not from the methylenic alkylation.

Table 6. Optimization of tandem process of α-alkylation and reduction

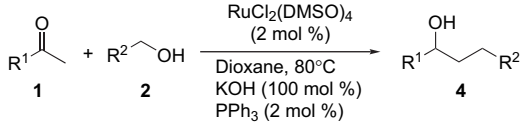


1a 2a 4a

Entry	Solvent	Base	Additive[a]	Yield (%)[b]
1	1,4-Dioxane	KOH	—	78
2[c]	1,4-Dioxane	KOH	—	7
3	1,4-Dioxane	KOH[d]	—	0
4[e]	1,4-Dioxane	KOH	—	0
5	1,4-Dioxane	KOH	**2a** (600)	69
6	PhMe	KOH	—	61
7	CH_2Cl_2	KOH	—	10[f]
8	THF	KOH	—	72
9	DMF	KOH	—	<5
10	MeCN	KOH	—	0
11	1,4-Dioxane	CsOH	—	53
12	1,4-Dioxane	K_2CO_3	—	0
13	1,4-Dioxane	Et_3N	—	0
14	1,4-Dioxane	KOH	PPh_3 (2)	82
15	1,4-Dioxane	KOH	$Ph_2P(CH_2)_2PPh_2$ (2)	61
16	1,4-Dioxane	KOH	$Me_2N(CH_2)_2NMe_2$ (2)	72
17	1,4-Dioxane	KOH	*n*-Bu_4NBr (100)	28

[a] In parenthesis mol % of additive used.
[b] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).
[c] $RuClH(CO)(PPh_3)_3$ was used instead of $RuCl_2(DMSO)_4$.
[d] A 10 mol % of KOH was used.
[e] A 0.2 mol % of $RuCl_2(DMSO)_4$ was used.
[f] Ketone **3a** was obtained in 13% yield.

Table 7. Synthesis of alcohols **4** by a tandem process of α-alkylation and reduction



1 2 4

Entry	No.	R^1	R^2	Yield (%)[a]
1	**4a**	Ph	Ph	82
2	**4b**	Ph	^{i}Pr	45
3	**4c**	^{t}Bu	Ph	25
4	**4d**	*n*-C_5H_{11}	Ph	35

[a] Isolated yields after column chromatography (silica gel: hexane/ethyl acetate).

2.5. Mechanistic considerations

Although similar processes using different catalysts have been described, the possible mechanistic pathway is totally unknown, only speculative catalytic cycles having been proposed based only on by-products detected, such as aldehyde and α,β-unsaturated ketone. The last part of this study was focused on the possible catalytic pathway of the reaction, for the standard reaction between 4-methylacetophenone and benzyl alcohol. The same reaction was performed with different combinations of labeled reagents finding in all cases the product **3j** labeled in different ratio and/or positions (Table 8). Thus, the reaction using only deuterated alcohol gave the expected ketone **3j** with a poor incorporation of deuterio only at the α-position with respect to the carbonyl group (entry 1). When the same reaction was repeated using KOD, the same labeled product was obtained, only increasing the deuterium incorporation (entry 2). The reaction using d_3-4-methylacetophenone[44] as the only labeled reagent gave again the same α-deuterated ketone **3j** (entry 3) with a similar deuterium incorporation to the previous case, what could indicate the presence of several enolate equilibriums, even during the aqueous work-up. The reaction using the three previous labeled reagents gave the expected ketone **3j** with a double incorporation of deuterium at the α-position (entry 4). Finally, instead of labeling the acidic hydrogens of different reagents, we labeled the benzylic position of the

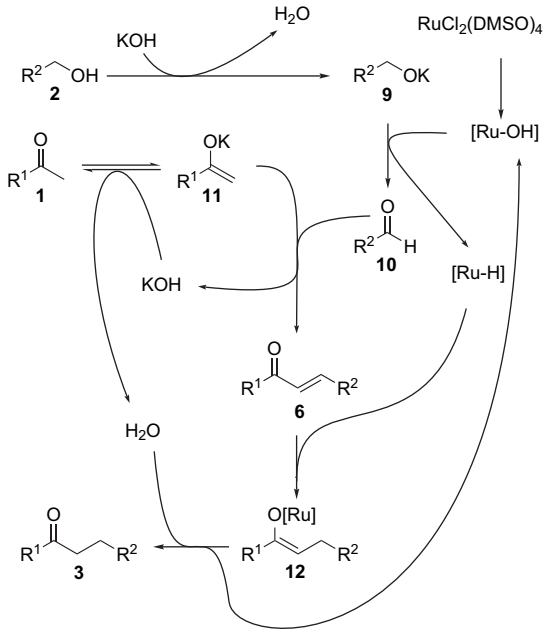
Table 8. Preparation of deuterated ketone **3j** by the use of labeled reagents

Entry	Labeled reagents	Deuterated ketone **3j**	Deuterium incorporation (%)[a]
1	$PhCH_2OD$	4-$MeC_6H_4COCDHCH_2Ph$	10
2	$PhCH_2OD$, KOD	4-$MeC_6H_4COCDHCH_2Ph$	50
3	4-$MeC_6H_4COCD_3$	4-$MeC_6H_4COCDHCH_2Ph$	50
4	4-$MeC_6H_4COCD_3$, $PhCH_2OD$, KOD	4-$MeC_6H_4COCD_2CH_2Ph$	75
5	$PhCD_2OH$	4-$MeC_6H_4COCH_2CD_2Ph$	94

[a] Isolated compound in yields higher than 85% after column chromatography (silica gel: hexane/ethyl acetate); the deuterium incorporation was estimated on the basis of ^{1}H NMR spectrum.

benzyl alcohol (prepared by reduction of methyl benzoate with $LiAlD_4$).[45] In this case, the reaction gave the product **3j** with a double deuterium incorporation in the β-position (entry 5).

All the above results, together with the observation of different by-products of the reaction, drove us to propose the mechanism pathway depicted in Scheme 4. Probably, in the reaction medium, the initial ruthenium complex evolves to form the real catalyst, which could be a polymetallic species, even bearing hydroxy groups,[46] although the permanence of chlorine ligands cannot be ruled out.[47] In turn, this species reacts with the primary alkoxide derivative to form the corresponding mono- or dihydride ruthenium catalytic active species.[47] The necessary use of stoichiometric amounts of base can indicate that its role is not only the deprotonation of the starting ketone **1** but also the deprotonation of alcohol **2** to yield water and the corresponding alkoxide **9**, which is the real substrate for the oxidation step giving the corresponding aldehyde **10** (detected in some cases by GC–MS) and a new ruthenium hydride species. The condensation of enolate **11** with the in situ formed aldehyde **10** leads to the α,β-unsaturated ketone **6**. This ketone suffers a Michael-type hydride addition by the ruthenium hydride to form the corresponding ruthenium enolate **12**, which is hydrolyzed by water to form the final ketone **3**, renewing the starting catalytic ruthenium species.[48] Water comes either from the deprotonation of alcohol **2** (α-labeling of ketone **3j** when $PhCH_2OD$ was used) or from the deprotonation of the starting ketone **1** (α-labeling of ketone **3j** when d_3-4-methylacetophenone was used), this hypothesis being confirmed by the increase of the deuterium incorporation when all these reagents were labeled. Finally, it should be pointed out that the reduction of the double bond of compound **6** seems to be a Michael-type process since only the β-position in the final ketone **3** was doubly labeled when $PhCD_2OH$ was used, no cross-over labeling occurring.



Scheme 4. Proposed catalytic cycle for the α-alkylation of ketones using alcohols as electrophiles and catalyzed by $RuCl_2(DMSO)_4$.

3. Conclusions

In summary, we have described here the use of $RuCl_2(DMSO)_4$ for a simple and direct α-alkylation of ketones with not only high yields, but also good atom efficiency, using alcohols as the electrophilic partner. The final product depends strongly on the ketone nature, obtaining either the simple alkylation for methyl ketones or α,β-unsaturated ketones (firstly described) when methylenic bicyclic ketones were used as starting materials. In this way, different quinolines could be prepared with excellent yields just by using a 2-aminoaryl alcohol derivative as alkylating agent. A labeled reagent/product study showed that the process goes through an oxidation of the alcohol, classical condensation, ruthenium hydride Michael addition, and final hydrolysis to give the final ketone, renewing the catalytic ruthenium species. It is worthy to note that this procedure constitutes an excellent example of very high atom efficiency reaction. Moreover, the waste material of the reactions is water, being a very interesting process from an environmental and industrial point of view. The catalyst used is very cheap, stable, easy to handle and to be prepared.[49] All these facts make the $RuCl_2(DMSO)_4$-catalyzed alkylation process very interesting comparing to the classical alkylation protocols, using strong bases, dry solvents, and hazardous alkylating agents, as well as other alternative expensive and difficult handle catalysts.

4. Experimental

4.1. Chemicals and instrumentation

Full general statements were described elsewhere.[50] 1-Aminonaphth-1-ylmethanol (**7b**) was prepared by standard $NaBH_4$ reduction of the corresponding aldehyde in 93% yield. In turn, the above starting aldehyde was obtained in 5% overall yield from 2-methylnaphthalene, after four synthetic steps, following the reported procedure.[51] The $RuCl_2(DMSO)_4$ complex was prepared in excellent yields (85–99%) by short time refluxing of $RuCl_3 \cdot 3H_2O$ in DMSO.[49] All other reagents were commercially available (Acros, Aldrich, Strem) and were used as received. Solvents were dried by standard procedures.[52]

4.2. General procedure for reaction of ketones with alcohols

To a solution of $RuCl_2(DMSO)_4$ (0.048 g, 0.1 mmol) and KOH (0.330 g, 5 mmol) in 1,4-dioxane (5 mL) was added the corresponding ketone **1** or **5** (5 mmol) followed by the corresponding alcohol **2** or **7** (5 mmol). In the case of using amino alcohols **7**, benzophenone (1.822 g, 10 mmol) was also added. The mixture was stirred and heated at 80 °C for a period of 24 h. Then, the mixture was quenched by the addition of a saturated NH_4Cl solution (20 mL) and extracted with ethyl acetate (3×15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvents removed under reduced pressure. The resulting residue was purified by flash chromatography on silica gel using suitable mixtures of hexane/ethyl acetate to afford the corresponding product **3**, **4**, **6** or **8**. Yields are included

in Tables 1–8 and Scheme 3. Physical and spectroscopic data as well as literature references follow.

4.2.1. 1,3-Diphenyl-1-propanone (3a).[12] t_R 15.0; R_f 0.65 (hexane/ethyl acetate: 4/1); ν (film) 3058, 3021, 1597 (C=CH), 1678 cm^{-1} (C=O); δ_H 3.00–3.05 (2H, m, PhCH_2), 3.20–3.25 (2H, m, CH_2CO), 7.15–7.50 and 7.90–7.95 (8 and 2H, respectively, 2m, 2×Ph); δ_C 29.9, 40.2, 125.95, 127.85 (2C), 128.25 (2C), 128.35 (2C), 128.4 (2C), 132.85, 136.6, 141.1, 198.9; *m/z* 210 (M^+, 59%), 105 (100), 91 (10), 77 (36).

4.2.2. 3-(3-Benzyloxyphenyl)-1-phenyl-1-propanone (3b). t_R 23.4; R_f 0.64 (hexane/ethyl acetate: 4/1); ν (film) 3065, 1602, 1492 (C=CH), 1689 (C=O), 1252, 1028 cm^{-1} (C–O); δ_H 2.95–3.05 (2H, m, CH_2CH_2CO), 3.20–3.30 (2H, m, CH_2CO), 5.00 (2H, s, CH_2O), 6.80–6.90, 7.15–7.50, and 7.90–7.95 (3, 9, and 2H, respectively, 3m, ArH); δ_C 29.95, 40.1, 69.7, 112.1, 115.0, 120.9, 127.35, 127.8, 127.9, 128.4 (2C), 128.45 (2C), 129.4, 132.9, 136.6, 136.9, 142.8, 158.8, 198.9; *m/z* 316 (M^+, 19%), 196 (11), 105 (11), 91 (100), 77 (10); HRMS: M^+ found 316.1467. $C_{22}H_{20}O_2$ requires 316.1463.

4.2.3. 3-(2-Bromophenyl)-1-phenyl-1-propanone (3c).[53] t_R 16.9; R_f 0.63 (hexane/ethyl acetate: 4/1); ν (film) 3067, 1592 (C=CH), 1692 cm^{-1} (C=O); δ_H 3.10–3.20 (2H, m, PhCH_2), 3.25–3.30 (2H, m, CH_2CO), 7.00–7.55 and 7.90–7.95 (7 and 2H, respectively, 2m, ArH); δ_C 30.6, 38.4, 124.2, 127.5, 127.85, 127.9 (2C), 128.45 (2C), 130.65, 132.7, 132.95, 136.55, 140.4, 198.65; *m/z* 288 (M^+, <0.1%), 210 (16), 209 (100), 105 (56), 77 (32).

4.2.4. 3-(2-Furyl)-1-phenyl-1-propanone (3d).[54] t_R 13.4, R_f 0.40 (hexane/ethyl acetate: 4/1); ν (film) 3060, 1603, 1506 (C=CH), 1682 cm^{-1} (C=O); δ_H 3.50–3.55 (2H, m, PhCH_2), 3.75–3.80 (2H, m, CH_2CO), 6.45–6.50, 6.70–6.75, 7.74, 7.85–8.00, and 8.35–8.45 (1, 1, 1, 3, and 2H, respectively, 2m, s, and 2m, respectively, ArH); δ_C 22.4, 36.85, 105.25, 110.2, 127.95 (2C), 128.55 (2C), 133.05, 136.65, 141.0, 154.7, 198.55; *m/z* 201 (M^++1, 11%), 200 (M^+, 76), 105 (100), 95 (32), 94 (10), 81 (37), 77 (51), 51 (12).

4.2.5. 3-(1*H*-3-Indenyl)-1-phenyl-1-propanone (3e).[55] Mp 123–125 °C; t_R 14.6; R_f 0.37 (hexane/ethyl acetate=4/1); ν (KBr) 3418 (N–H), 3058, 1597 (C=CH), 1680 cm^{-1} (C=O); δ_H 3.20–3.25 (2H, m, PhCH_2), 3.35–3.45 (2H, m, CH_2CO), 7.05–7.65 and 7.95–8.00 (9 and 2H, respectively, 2m, ArH); δ_C 19.7, 39.3, 111.15, 115.5, 118.7, 119.3, 121.55, 122.05, 127.25, 128.0 (2C), 128.55 (2C), 132.95, 136.3, 136.95, 199.9; *m/z* 250 (M^++1, 11%), 249 (M^+, 57), 144 (55), 131 (10), 130 (100), 117 (12), 105 (12), 77 (20).

4.2.6. 1,5-Diphenyl-1-pentanone (3g).[56] t_R 16.6; R_f 0.62 (hexane/ethyl acetate=4/1); ν (film) 3062, 1605 (C=CH), 1690 cm^{-1} (C=O); δ_H 1.65–1.80 (4H, m, C$H_2CH_2CH_2CO$), 2.60–2.70 and 2.95–3.05 (2 and 2H, respectively, 2m, C$H_2CH_2CH_2CH_2CO$), 7.10–7.55 and 7.90–7.95 (8 and 2H, respectively, 2m, 2×Ph); δ_C 23.9, 31.05, 35.75, 38.35, 125.7, 128.0 (2C), 128.25 (2C), 128.35 (2C), 128.5 (2C), 132.85, 137.0, 142.2, 200.2; *m/z* 238 (M^+, 15%), 147 (10), 133 (36), 129 (11), 121 (11), 120 (96), 117 (10), 105 (100), 91 (29), 77 (50).

4.2.7. 1-(4-Methylphenyl)-3-phenyl-1-propanone (3j).[12] Mp 60–62 °C; t_R 15.9; R_f 0.59 (hexane/ethyl acetate=4/1); ν (KBr) 3067, 1605 (C=CH), 1677 cm^{-1} (C=O); δ_H 2.34 (3H, s, CH_3), 3.00–3.05 (2H, m, PhCH_2), 3.20–3.25 (2H, m, CH_2CO), 7.15–7.30 and 7.81 (7 and 2H, respectively, m and d, respectively, J=8.3 Hz, ArH); δ_C 21.4, 30.0, 40.1, 125.9, 128.0 (2C), 128.25 (2C), 128.35 (2C), 129.0 (2C), 134.2, 141.25, 143.6, 198.6; *m/z* 224 (M^+, 33%), 209 (22), 119 (100), 91 (32).

4.2.8. 3-(4-Methoxyphenyl)-1-(4-methylphenyl)-1-propanone (3k).[57] Mp 57–58 °C; t_R 18.2; R_f 0.53 (hexane/ethyl acetate: 4/1); ν (KBr) 3030, 1614 (C=CH), 2837 (OCH_3), 1675 cm^{-1} (C=O); δ_H 2.39 (3H, s, C$H_3C_6H_4$), 2.95–3.00 (2H, m, CH_2CH_2CO), 3.20–3.25 (2H, m, CH_2CO), 3.77 (3H, s, CH_3O), 6.82, 7.16, 7.23, and 7.85 (2H each one, 4d, J=8.7, 8.7, 7.9, and 7.9 Hz, respectively, ArH); δ_C 21.6, 29.3, 40.55, 55.2, 113.85 (2C), 128.1 (2C), 129.2 (2C), 129.3 (2C), 133.35, 134.4, 143.75, 157.9, 199.0; *m/z* 255 (M^++1, 16%), 254 (M^+, 27), 239 (11), 135 (15), 121 (100), 120 (10), 119 (90), 108 (15), 91 (42), 65 (12).

4.2.9. 3-(4-Chlorophenyl)-1-(4-methylphenyl)-1-propanone (3l).[58] Mp 83–84 °C; t_R 17.6; R_f 0.74 (hexane/ethyl acetate: 4/1); ν (KBr) 3021, 1606 (C=CH), 1669 cm^{-1} (C=O); δ_H 2.40 (3H, s, CH_3), 3.00–3.05 (2H, m, CH_2CH_2CO), 3.20–3.25 (2H, m, CH_2CO), 7.15–7.25 and 7.84 (6 and 2H, respectively, m and d, respectively, J=8.1 Hz, ArH); δ_C 21.6, 29.4, 40.0, 128.1 (2C), 128.55 (2C), 129.3 (2C), 129.8 (2C), 131.9, 134.25, 139.8, 43.95, 198.5; *m/z* 300 (M^++2, 9%), 258 (M^+, 27), 243 (18), 119 (100), 91 (24).

4.2.10. 3-(2-Chlorophenyl)-1-(4-methylphenyl)-1-propanone (3m). t_R 17.5; R_f 0.72 (hexane/ethyl acetate: 4/1); ν (film) 3066, 2921, 1606 (C=CH), 1683 cm^{-1} (C=O); δ_H 2.40 (3H, s, CH_3), 3.10–3.20 (2H, m, CH_2CH_2CO), 3.25–3.30 (2H, m, CH_2CO), 7.10–7.35 and 7.86 (6 and 2H, respectively, m and d, respectively, J=8.3 Hz, ArH); δ_C 21.6, 28.4, 38.3, 126.9 (2C), 127.65, 128.15 (2C), 129.25, 129.5, 130.75, 133.9, 134.25, 138.9, 143.85, 198.65; *m/z* 258 (M^+, <1%), 224 (17), 223 (100), 119 (90), 91 (26); HRMS: M^+ found 258.0820. $C_{16}H_{15}OCl$ requires 258.0811.

4.2.11. 3-(3,4-Dimethoxyphenyl)-1-(4-methylphenyl)-1-propanone (3n).[59] t_R 19.7; R_f 0.28 (hexane/ethyl acetate: 4/1); ν (film) 3061, 1607 (C=CH), 2834 (CH_3O), 1678 cm^{-1} (C=O); δ_H 2.40 (3H, s, C$H_3C_6H_4$), 2.95–3.00 (2H, m, CH_2CH_2CO), 3.2–3.3 (2H, m, CH_2CO), 3.85 and 3.86 (3H each one, 2s, 2×CH_3O), 6.75–6.80, 7.24, and 7.86 (3, 2, and 2H, respectively, m and 2d, respectively, J=7.9 Hz, ArH); δ_C 21.55, 29.8, 40.5, 55.7, 55.85, 111.2, 111.7, 120.1, 128.1 (2C), 129.2 (2C), 133.9, 134.35, 143.75, 147.25, 148.8, 198.95; *m/z* 285 (M^++1, 19%), 284 (M^+, 100), 165 (50), 151 (90), 119 (49), 91 (31).

4.2.12. 1-(6-Amino-1,3-benzodioxol-5-yl)-3-phenyl-1-propanone (3p). Mp 116–118 °C; t_R 20.4; R_f 0.26 (hexane/ethyl acetate: 4/1); ν (KBr) 3481, 3345 (NH_2), 3063, 1606 (C=CH), 1647 cm^{-1} (C=O); δ_H 3.00–3.15 (4H, m, CH_2CH_2), 5.86 (2H, s, OCH_2O), 6.11 and 7.08 (1 and 1H, respectively, 2s, $NO_2C_6H_2$), 6.45 (2H, s, NH_2), 7.10–7.30 (5H, m, Ph); δ_C 30.7, 40.9, 96.8, 101.2, 107.9, 110.2,

125.95, 128.35 (2C), 128.42 (2C), 138.7, 141.5, 149.45, 152.85, 198.85; *m/z* 270 (M^++1, 17%), 269 (M^+, 100), 165 (12), 164 (10), 137 (32), 136 (20); $C_{16}H_{15}NO_3$: requires C 71.36, H 5.61, N 5.20; found C 71.39, H 5.69, N 5.17.

4.2.13. 1-(2-Naphthyl)-3-phenyl-1-propanone (3q).[60] Mp 85 °C; t_R 19.6; R_f 0.64 (hexane/ethyl acetate: 4/1); ν (KBr) 3056, 3025, 1621 (C=CH), 1678 cm^{-1} (C=O); δ_H 3.05–3.15 (2H, m, PhCH_2), 3.35–3.40 (2H, m, CH_2CO), 7.15–7.30, 7.45–7.55, 7.80–8.00, and 8.40 (5, 2, 4, and 1H, respectively, 3m and s, respectively, ArH); δ_C 30.1, 40.4, 123.7, 126.05, 126.65, 127.65, 128.3 (2C), 128.35 (2C), 128.45 (2C), 129.4, 129.55, 132.35, 134.0, 135.4, 141.25, 198.95; *m/z* 261 (M^++1, 11%), 260 (M^+, 55), 156 (15), 155 (100), 127 (48).

4.2.14. 3-Phenyl-1-(2-thienyl)-1-propanone (3r).[60] t_R 15.2; R_f 0.68 (hexane/ethyl acetate: 4/1); ν (film) 3078, 1521 (C=CH), 1666 cm^{-1} (C=O); δ_H 3.05–3.10 (2H, m, PhCH_2), 3.20–3.30 (2H, m, CH_2CO), 7.10–7.30 and 7.60–7.70 (6 and 2H, respectively, 2m, ArH); δ_C 30.35, 41.1, 126.2, 128.1 (2C), 128.4 (2C), 128.5, 131.8, 133.55, 141.0, 144.1, 192.15; *m/z* 216 (M^+, 56%), 111 (100), 105 (14), 104 (19), 91 (15).

4.2.15. 3-(2-Bromophenyl)-1-(2-thienyl)-1-propanone (3s). t_R 17.1; R_f 0.56 (hexane/ethyl acetate: 4/1); ν (film) 3093, 2913 (C=CH), 1661 cm^{-1} (C=O); δ_H 3.10–3.30 (4H, m, 2×CH_2), 7.05–7.25 (7H, m, ArH); δ_C 31.1, 39.2, 124.3, 127.65, 128.05, 128.1, 130.85, 131.95, 132.85, 133.7, 140.2, 144.05, 191.95; *m/z* 216 (15%), 215 (M^+−79, 100), 111 (49); HRMS: M^+ found 215.0522. $C_{13}H_{11}OS$ requires 215.0531.

4.2.16. 1-(*N*-Methyl-1*H*-2-pyrrolyl)-3-phenyl-1-propanone (3t). t_R 14.8; R_f 0.53 (hexane/ethyl acetate: 4/1); ν (film) 3024, 1532 (C=CH), 1652 cm^{-1} (C=O); δ_H 3.00–3.15 (4H, m, 2×CH_2), 3.95 (3H, s, CH_3), 6.79, 6.09–6.15, 6.93–6.95, 7.20–7.30 (1, 1, 1, and 5H, respectively, s and 3m, respectively, ArH); δ_C 30.85, 37.7, 40.7, 107.9, 119.0, 126.0, 128.4 (2C), 128.45 (2C), 130.55, 139.95, 141.5, 190.15; *m/z* 213 (M^+, 56%), 108 (100), 81 (61), 53 (13); HRMS: M^+ found 213.1141. $C_{14}H_{15}NO$ requires 213.1154.

4.2.17. 1-Ferrocenyl-3-phenylpropanone (3u).[61] Mp 83–85 °C; t_R 20.0; R_f 0.47 (hexane/ethyl acetate: 4/1); ν (KBr) 3092, 1600 (C=CH), 1664 cm^{-1} (C=O); δ_H 3.00–3.10 (4H, m, CH_2CH_2), 4.07 (5H, s, C_5H_5Fe), 4.45–4.50 and 4.75–4.80 (2H each one, 2m, C_5H_4Fe), 7.20–7.35 (5H, m, Ph); δ_C 30.1, 41.5, 69.25 (2C), 69.65 (5C), 72.2 (2C), 78.95, 126.15, 128.5 (2C), 128.6 (2C), 141.6, 203.1; *m/z* 319 (M^++1, 23%), 318 (M^+, 100), 253 (27), 185 (10), 129 (11), 121 (23).

4.2.18. 1,3-Diphenyl-1-propanol (4a).[12] t_R 15.18; R_f 0.5 (hexane/ethyl acetate: 4/1); ν (film) 3399 (O–H), 3100, 1616 (C=CH), 1065 cm^{-1} (C–O); δ_H 1.90 (1H, s, OH), 1.95–2.20 (2H, m, PhCH_2), 2.55–2.75 (2H, m, CH_2CO), 4.68 (1H, dd, *J*=7.6, 5.5 Hz, CHO), 7.15–7.35 (10H, m, 2×Ph); δ_C 32.0, 40.45, 73.85, 125.85, 125.9, 127.6 (2C), 128.35 (2C), 128.4 (2C), 128.5 (2C), 141.75, 144.5; *m/z* 212 (M^+, 10%), 210 (16), 207 (19), 195 (11), 194 (79), 193 (17), 179 (12), 178 (10), 170 (26), 115 (13), 108 (12), 107 (100), 106 (11), 105 (46), 104 (11), 103 (17), 92 (24), 91 (39), 79 (47), 78 (12), 77 (54), 65 (14), 51 (12).

4.2.19. 1-Phenyl-4-methyl-1-pentanol (4b).[62] t_R 10.11; R_f 0.34 (hexane/ethyl acetate: 4/1); ν (film) 3374 (O–H), 3065, 3034 cm^{-1} (C=CH); δ_H 0.86 and 0.88 [3H each one, d, *J*=1.7 Hz, CH(CH_3)$_2$], 1.15–1.20 [1H, m, CH(CH_3)$_2$], 1.25–1.35 and 1.45–1.55 (1H each one, 2m, CH_2CH), 1.65–1.80 (2H, m, CH_2CHO), 1.85 (1H, s, OH), 4.62 (1H, t, *J*=6.8 Hz, CHO), 7.20–7.40 (5H, m, Ph); δ_C 22.5, 22.6, 28.0, 34.9, 36.9, 75.0, 125.9 (2C), 127.5, 128.4 (2C), 144.9; *m/z* 178 (M^+, 2%), 117 (11), 107 (100), 79 (33), 77 (17).

4.2.20. 1-Phenyl-4,4-dimethyl-3-pentanol (4c).[63] t_R 10.57; R_f 0.24 (hexane/ethyl acetate: 10/1); ν (film) 3416 (O–H), 3062, 3027, 1604 cm^{-1} (C=CH); δ_H 0.89 (9H, s, 3×CH_3), 1.48 (1H, s, OH), 1.55–1.65, 1.80–1.90 (1H each one, 2m, PhCH_2), 2.55–2.70, 2.85–3.00 (1H each one, 2m, CH_2CHO), 3.23 (1H, d, *J*=10.4 Hz, CHO), 7.15–7.35 (5H, m, Ph); δ_C 25.6 (3C), 33.3, 33.4, 35.0, 79.4, 125.8, 128.4 (2C), 128.5 (2C), 142.4; *m/z* 192 (M^+, <1%), 118 (14), 117 (35), 104 (28), 92 (20), 91 (100), 57 (18).

4.2.21. 1-Phenyl-3-octanol (4d).[19c] t_R 12.13; R_f 0.27 (hexane/ethyl acetate: 4/1); ν (film) 3357 (O–H), 3062, 3026, 1603 cm^{-1} (C=CH); δ_H 0.85–0.95 (3H, m, CH_3), 1.20–1.55 [9H, m, $(CH_2)_4$ and OH], 1.65–1.85 and 2.65–2.80 [2H each one, 2m, Ph(CH_2)$_2$], 3.55–3.70 (1H, m, CHO), 7.15–7.35 (5H, m, Ph); δ_C 14.0, 22.6, 25.3, 31.9, 32.1, 37.6, 39.1, 71.4, 125.8, 128.35 (2C), 128.4 (2C), 142.2; *m/z* 206 (M^+, <1%), 188 (20), 117 (47), 105 (16), 104 (87), 92 (43), 91 (100), 78 (11), 55 (22).

4.2.22. 3-Phenyl-1-(4-trifluoromethylphenyl)-1-propanol (4o).[64] t_R 14.9; R_f 0.71 (hexane/ethyl acetate: 4/1); ν (film) 3370 (O–H), 3025, 1621 (C=CH), 1069 cm^{-1} (C–O); δ_H 1.90–2.10 (2H, m, CH_2CH$_2$CHO), 2.55–2.75 (2H, m, CH_2CHO), 2.79 (1H, s, OH), 4.60–4.65 (1H, m, CHO), 7.10–7.25, 7.35, and 7.53 (5, 2, and 2H, respectively, m and 2d, respectively, *J*=8.1 Hz, ArH); δ_C 31.7, 40.4, 73.0, 125.3, 124.1 (q, $J_{1,2}$=272.2 Hz, CF_3), 125.95 (2C), 126.1 (2C), 128.3 (2C), 128.4 (2C), 129.6 (q, $J_{1,3}$=31.8 Hz, CCF_3), 141.25, 148.45; *m/z* 280 (M^+, <10%), 263 (17), 262 (100), 261 (18), 193 (22), 175 (66), 127 (45), 105 (21), 92 (40), 91 (31), 78 (11), 77 (12).

4.2.23. 2-[(*E*)-1-(4-Methoxyphenyl)methylidene]-1,2,3,4-tetrahydro-1-naphthalenone (6a).[65] Mp 105–107 °C; t_R 21.2; R_f 0.74 (hexane/ethyl acetate: 1/1); ν (KBr) 3070, 1605 (C=CH), 2832 (OCH_3), 1669 cm^{-1} (C=O); δ_H 2.90–2.95 and 3.10–3.15 (2H each one, 2m, CH_2CH_2), 3.84 (3H, s, CH_3O), 6.95, 7.24, 7.30–7.50, and 8.12 (2, 1, 4, and 1H, respectively, 2d, m, and d, *J*=8.7, 8.1, and 8.1 Hz, respectively, ArH), 7.85 [1H, s, CH=C(CO)CH$_2$]; δ_C 27.15, 28.75, 55.3, 113.9 (2C), 126.9, 128.05, 128.1, 128.35, 131.7 (2C), 133.05, 133.45, 133.6, 136.65, 143.0, 159.9, 187.8; *m/z* 265 (M^++1, 12%), 264 (M^+, 67), 263 (100), 249 (22), 233 (25), 121 (12).

4.2.24. 3-[(*E*)-1-Phenylmethylidene]bicyclo[2.2.1]heptan-2-one (6b).[66] t_R 14.8; R_f 0.37 (hexane/ethyl acetate: 4/1); ν (film) 3060, 1645 (C=CH), 1727 cm^{-1} (C=O); δ_H

1.60–1.75 (4H, m, CH_2CH_2), 1.90–2.10 (2H, m, CHC*H*$_2$CH), 2.75–2.80 and 3.60–3.65 (1H each one, 2m, C*H*CH_2CH_2C*H*), 7.15 (1H, s, CH=CCO), 7.30–7.50 (5H, m, Ph); δ_C 24.25, 27.25, 37.75, 40.15, 48.5, 127.15, 128.6 (2C), 128.8, 129.65 (2C), 135.2, 141.6, 206.7; *m/z* 199 (M^++1, 15%), 198 (M^+, 100), 197 (18), 170 (14), 169 (33), 155 (31), 142 (26), 141 (38), 129 (23), 128 (32), 127 (10), 115 (25), 102 (11), 92 (14), 91 (20).

4.2.25. 3-[(*E*)-1-(4-Methoxyphenyl)methylidene]bicyclo[2.2.1]heptan-2-one (6c).[66] t_R 17.0; R_f 0.74 (hexane/ethyl acetate: 1/1); ν (film) 2871 (OCH_3), 1720 (C=O), 1643, 1605 cm^{-1} (C=CH); δ_H 1.60–1.75 (4H, m, CH_2CH_2), 1.90–2.05 (2H, m, CH_2), 2.75–2.80 and 3.60–3.65 (1H each one, 2m, C*H*CH_2CH_2C*H*), 3.83 (3H, s, CH_3), 6.92 and 7.45 (2H each one, 2d, J=8.7 Hz, ArH), 7.11 (1H, s, CH=CCO); δ_C 24.35, 27.2, 37.9, 40.1, 48.5, 55.2, 114.1 (2C), 127.1, 127.75, 131.35 (2C), 139.45, 160.15, 206.9; *m/z* 229 (M^++1, 17%), 228 (M^+, 100), 200 (32), 199 (20), 185 (35), 172 (29), 171 (15), 157 (15), 145 (12), 128 (14), 121 (16), 115 (16).

4.2.26. 1,7,7-Trimethyl-3-[(*E*)-1-(4-methylphenyl)methylidene]bicyclo[2.2.1]heptan-2-one (6d).[67] Mp 93–95 °C; t_R 16.5; R_f 0.57 (hexane/ethyl acetate: 3/2); $[\alpha]_D^{20}$ +373.8 (*c* 0.8, $CHCl_3$); ν (KBr) 3090, 1642, 1610 (C=CH), 1724 cm^{-1} (C=O); δ_H 0.79, 0.98, and 1.02 [3H each one, 3s, $(CH_3)_2CCCH_3$], 1.45–1.60, 1.70–1.80, 2.10–2.20 (2, 1, and 1H, respectively, 3m, CH_2CH_2), 2.36 (3H, s, C*H*$_3C_6H_4$), 3.05–3.10 (1H, m, C*H*CH_2), 7.15–7.20 and 7.35–7.40 (3 and 2H, respectively, 2m, C=C*H*C_6H_4); δ_C 9.2, 18.25, 20.4, 21.25, 25.8, 30.65, 46.55, 49.1, 56.95, 127.45, 129.3 (2C), 129.65 (2C), 132.7, 138.8, 141.15, 208.0; *m/z* 255 (M^++1, 20%), 254 (M^+, 100), 239 (30), 226 (12), 212 (11), 183 (28), 172 (27), 171 (36), 170 (29), 169 (28), 157 (16), 155 (26), 149 (12), 148 (10), 143 (24), 142 (12), 141 (20), 129 (16), 128 (38), 115 (22), 105 (24), 95 (11), 91 (12), 55 (10).

4.2.27. 3-[(*E*)-1-(4-Methoxyphenyl)methylidene]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (6e).[68] Mp 127–129 °C; t_R 17.9; R_f 0.46 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20}$ +404 (*c* 0.8, $CHCl_3$); ν (KBr) 3026, 1637, 1615 (C=CH), 2830 (OCH_3), 1724 cm^{-1} (C=O); δ_H 0.80, 0.99, and 1.02 [3H each one, 3s, $(CH_3)_2CCCH_3$], 1.45–1.60, 1.70–1.80, and 2.10–2.20 (2, 1, and 1H, respectively, 3m, CH_2CH_2), 3.05–3.10 (1H, m, $CHCH_2$), 3.82 (3H, s, CH_3O), 6.92 and 7.44 (2H each one, 2d, J=8.7 Hz, C_6H_4), 7.19 (1H, s, CH=CCO); δ_C 9.25, 18.3, 20.45, 25.8, 30.75, 46.7, 49.1, 55.2, 56.9, 114.1 (2C), 127.25, 128.15, 131.3 (2C), 139.9, 160.0, 208.15; *m/z* 271 (M^++1, 20%), 270 (M^+, 100), 242 (16), 227 (33), 199 (13), 188 (13), 187 (22), 186 (42), 185 (19), 171 (17), 159 (12), 128 (11), 121 (26), 115 (15). Crystal data: $C_{18}H_{22}O_2$, M=270.36; Orthorhombic, a=6.519 (2), b=12.2929 (13), c=18.989 (6) Å; V=1521.7 (7) $Å^3$; space group $P2_1$ 21 21; Z=4; D_c=1.180 mg/m^3; λ=0.71073 Å; μ=0.075 mm^{-1}; $F(000)$=584; T=23±1 °C. Data collection based on three ω-scan runs (starting ω=−34°) at values ϕ=0°, 120°, 240° with the detector at 2θ=−32°. An additional run of 100 frames, at 2θ=−32°, ω=−34° and ϕ=0°, was acquired to improve redundancy. For each of these runs, 606 frames were collected at 0.3° intervals and 30 s per frame. The diffraction frames were integrated using the program SAINT and the integrated intensities were corrected for Lorentz-polarization effects with SADABS. The structure was solved by direct methods and refined to all 1581 unique F_o^2 by full matrix least squares. All of the hydrogen atoms were placed at idealized positions and retained as rigid atoms. Final $wR2$=0.1216 for all data and 185 parameters; $R1$=0.1178 for 890 $F_o>4\sigma$ (F_o).

4.2.28. 3-[(*E*)-1-(2-Chlorophenyl)methylidene]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (6f).[69] Mp 85–87 °C; t_R 16.8; R_f 0.49 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20}$ +258 (*c* 0.8, $CHCl_3$); ν (KBr) 3067, 1660, 1615 (C=CH), 1728 cm^{-1} (C=O); δ_H 0.82, 0.98, and 1.04 [3H each one, 3s, $(CH_3)_2CCCH_3$], 1.45–1.65, 1.75–1.85, and 2.10–2.20 (2, 1, and 1H, respectively, 3m, CH_2CH_2), 2.90–2.95 (1H, m, C*H*CH_2), 7.20–7.30 and 7.35–7.45 (2H each one, 2m, C_6H_4), 7.50 (1H, s, CH=CCO); δ_C 9.15, 18.05, 20.45, 25.95, 30.35, 46.4, 48.7, 57.25, 123.8, 126.5, 129.45, 129.7, 129.75, 133.9, 135.1, 143.85, 207.35; *m/z* 276 (M^++2, 5%), 274 (M^+, 15), 240 (19), 239 (100), 157 (13), 128 (65), 127 (13).

4.2.29. *N*-Benzyl-7,7-dimethyl-3-[(*E*)-1-(4-methylphenyl)methylidene]-2-oxobicyclo[2.2.1]hept-1-ylmethanesulfonamide (6g). R_f 0.49 (hexane/ethyl acetate: 3/2); $[\alpha]_D^{20}$ +252.6 (*c* 17.4, $CHCl_3$); ν (film) 3296 (NH), 3032, 1634, 1609 (C=CH), 1728 cm^{-1} (C=O); δ_H 0.71 and 0.98 [3 and 3H, respectively, 2s, $C(CH_3)_2$], 1.58–1.64 and 2.00–2.25 (1 and 4H, respectively, 2m, $CHCH_2CH_2$), 2.38 (3H, s, C*H*$_3C_6H_4$), 2.94 and 3.27 (1 and 1H, respectively, 2d, J=15.1 Hz, CH_2SO_2), 3.07 (1H, d, J=2.8 Hz, C=CH), 4.39 (2H, d, J=6.4 Hz, CH_2N), 6.20 (1H, t, J=6.4 Hz, NH), 7.15–7.45 (9H, m, ArH); δ_C 18.4, 20.3, 21.25, 25.6, 27.75, 47.6, 48.4, 48.6, 50.5, 58.3, 127.55, 128.15 (2C), 128.5 (2C), 129.4 (2C), 129.7, 129.8 (2C), 131.85, 136.95, 139.2, 139.55, 205.4; *m/z* 255 (M^+−168, 18%), 254 (100), 253 (69), 252 (10), 239 (100), 237 (12), 225 (23), 211 (31), 209 (19), 197 (48), 183 (13), 171 (25), 169 (25), 155 (22), 143 (19), 141 (12), 129 (11), 128 (20), 119 (17), 115 (12), 107 (15), 106 (80), 105 (47), 91 (33), 79 (11), 77 (12); HRMS: M^+ found 423.1877. $C_{25}H_{29}SNO_3$ requires 423.1868.

4.2.30. 3-[(*E*)-1-(2-Aminophenyl)methylidene]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (6o).[41] R_f 0.12 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20}$ +336.5 (*c* 1.8, $CHCl_3$); ν (film) 3454, 3364 (NH_2), 3033, 1636 (C=CH), 1716 cm^{-1} (C=O); δ_H 0.81, 0.98, and 1.02 [3H each one, 3s, $(CH_3)_2CCCH_3$], 1.45–1.65, 1.75–1.80, and 2.10–2.20 (2H, 1, and 1H, respectively, 3m, CH_2CH_2), 2.95–3.00 (1H, m, CH_2CH), 6.65–6.80 and 7.10–7.25 (2 and 3H, respectively, 2m, ArH); δ_C 9.25, 18.2, 20.55, 26.25, 30.55, 46.5, 48.85, 57.4, 115.8, 118.15, 120.6, 122.25, 129.25, 129.85, 142.65, 145.85, 208.05; *m/z* 256 (M^++1, 16%), 255 (M^+, 87), 254 (25), 240 (19), 238 (35), 212 (25), 186 (32), 184 (11), 173 (18), 172 (100), 171 (48), 170 (18), 159 (16), 156 (16), 154 (14), 144 (44), 143 (41), 130 (20), 117 (26), 115 (11), 106 (17).

4.2.31. (*E*)-1-Ferrocenyl-3-phenyl-2-propenone (6u).[69] Mp 139–141 °C; t_R 21.9; R_f 0.36 (hexane/ethyl acetate: 4/1); ν (KBr) 3092, 1600 (C=CH), 1647 cm^{-1} (C=O); δ_H 4.22 (5H, s, C_5H_5Fe), 4.55–4.60 and 4.90–4.95 (2H each

one, 2m, C_5H_4Fe), 7.13 and 7.80 (1H each one, 2d, J=15.6 Hz, CH=CHCO), 7.40–7.45 and 7.65–7.70 (3 and 2H, respectively, 2m, Ph); δ_C 69.7 (2C), 70.1 (5C), 72.75 (2C), 80.6, 122.9, 128.25 (2C), 128.9 (2C), 130.1, 135.1, 140.8, 192.9; *m/z* 317 (M^++1, 23%), 316 (M^+, 100), 251 (17), 121 (12).

4.2.32. (*E*)-1-(1*H*-3-Indolyl)-3-phenyl-2-propen-1-one (6v).[70] Mp 225–230 °C; t_R 26.4; R_f 0.57 (hexane/ethyl acetate: 1/1); ν (KBr) 3126 (N–H), 1638 (C=O), 1569 cm^{-1} (C=CH); δ_H 7.20–7.90, 8.35–8.40, and 8.70–8.75 (10, 1, and 1H, respectively, 3m, C=CH), 12.11 (1H, s, NH); δ_C 113.2, 118.85, 122.85, 122.9, 24.1, 125.7, 127.0, 129.4 (2C), 129.8 (2C), 130.7, 135.7, 136.3, 137.95, 140.55, 184.7; *m/z* 248 (M^++1, 18%), 247 (M^+, 100), 246 (50), 219 (22), 218 (50), 217 (19), 144 (46), 117 (11), 116 (18), 89 (16).

4.2.33. 2-Phenylquinoline (8a).[37c] Mp 80–82 °C; t_R 16.3; R_f 0.61 (hexane/ethyl acetate: 4/1); ν (KBr) 3053, 1601, 1546 cm^{-1} (C=CH); δ_H 7.35–7.50, 7.60–7.80, and 8.00–8.20 (4, 3, and 4H, respectively, 3m, ArH); δ_C 118.8, 126.1, 127.0, 127.3, 127.4 (2C), 128.7 (2C), 129.15, 129.5, 129.55, 136.6, 139.45, 148.1, 157.1; *m/z* 206 (M^++1, 15%), 205 (M^+, 100), 204 (95), 203 (12), 102 (15).

4.2.34. 3-Methyl-2-phenylquinoline (8b).[37b] t_R 16.4 min; R_f 0.48 (hexane/ethyl acetate: 4/1); ν (film) 3058, 1605, 1558 cm^{-1} (C=CH); δ_H 2.36 (3H, s, CH_3), 7.35–7.70 (8H, m, Ph and H_{5-7}-quinoline), 7.87 (1H, s, H_4-quinoline), 8.14 (1H, d, J=8.4 Hz, H_8-quinoline); δ_C 20.3, 126.05, 126.4, 127.2, 127.85, 127.95 (2C), 128.4, 128.55 (2C), 128.8, 128.95, 136.4, 140.5, 146.25, 160.1; *m/z* 219 (M^+, 35%), 218 (100), 217 (28), 108 (12).

4.2.35. 3-Ethyl-2-phenylquinoline (8c).[71] t_R 16.8; R_f 0.53 (hexane/ethyl acetate: 4/1); ν (film) 3058, 1626, 1592 cm^{-1} (C=CH); δ_H 1.16 (3H, t, J=7.5 Hz, CH_3), 2.77 (2H, q, J=7.5 Hz, CH_2), 7.35–7.65 (7H, m, Ph and $H_{5,7}$-quinoline), 7.75–7.80 (1H, m, H_6-quinoline), 8.01 (1H, s, H_4-quinoline), 8.14 (1H, d, J=8.4 Hz, H_8-quinoline); δ_C 14.55, 25.85, 126.2, 126.75, 127.75, 127.95, 128.15 (2C), 128.55 (2C), 128.65, 129.05, 134.8, 135.10, 140.65, 146.1, 160.4; *m/z* 233 (M^+, 43%), 232 (100), 218 (11), 217 (39), 216 (11), 108 (13).

4.2.36. 1,2-Dihydrobenzo[*c*]acridine (8d).[37c] Mp 62–64 °C; t_R 18.7; R_f 0.78 (hexane/ethyl acetate: 4/1); ν (KBr) 3038, 1601 cm^{-1} (C=CH); δ_H 2.90–2.95 and 3.00–3.05 (2H each one, 2m, CH_2CH_2), 7.15–8.15 and 8.57 (7 and 1H, respectively, m and d, respectively, J=1.2 Hz, ArH); δ_C 28.25, 28.65 125.9, 125.95, 126.8, 127.2, 127.7, 127.85, 128.55, 129.25, 129.55, 130.45, 133.6, 134.55, 139.3, 147.45, 153.2; *m/z* 232 (M^++1, 16%), 183 (M^+, 99), 230 (100), 229 (13), 228 (17), 202 (10), 115 (14), 114 (12).

4.2.37. 2-(4-Methylphenyl)quinoline (8e).[37c] Mp 80–81 °C; t_R 17.2; R_f 0.75 (hexane/ethyl acetate: 4/1); ν (KBr) 3058, 1661, 1606 cm^{-1} (C=CH); δ_H 2.36 (3H, s, CH_3), 7.25 (2H, d, J=8.1 Hz, 2×CH_3CCH), 7.35–7.45 (1H, m, H_3-quinoline), 7.60–7.75 (3H, m, H_{5-7}-quinoline), 8.00–8.05 (3H, m, H_4-quinoline and 2×CH_3CCHCH), 8.15 (1H, d, J=4.1 Hz, H_8-quinoline); δ_C 21.15, 118.55, 125.8, 126.85, 127.2, 127.25 (2C), 128.05, 129.35 (2C), 129.4, 136.4, 136.6, 139.1, 148.05, 156.95; *m/z* 220 (M^++1, 17%), 219 (M^+, 100), 218 (51), 217 (20), 204 (21), 108 (13).

4.2.38. 2-(4-Methylphenyl)benzo[*h*]quinoline (8f). Mp 79–81 °C; t_R 23.6; R_f 0.74 (hexane/ethyl acetate: 4/1); ν (KBr) 3049, 2918, 1601, 1558 cm^{-1} (C=CH); δ_H 2.39 (3H, s, CH_3), 7.28 and 8.17 (2 and 2H, 2d, J=7.8 Hz, $CH_3C_6H_4$), 7.52 (1H, d, J=8.6 Hz, H_6), 7.60–7.70 (3H, m, H_9, H_7, and H_8), 7.81 (2H, d, J=8.6 Hz, H_5 and H_3), 7.98–8.01 (1H, m, H_4), 9.47 (1H, d, J=7.8 Hz, H_{10}); δ_C 21.25, 118.45, 124.6, 124.8, 125.0, 126.65, 127.0, 127.15 (2C), 127.6, 127.9, 129.4 (2C), 131.7, 133.75, 136.25, 136.8, 139.05, 146.0, 155.25; *m/z* 270 (M^++1, 22%), 269 (M^+, 100), 268 (27), 267 (13). $C_{20}H_{15}N$: requires C 89.19, H 5.61, N 5.20; found C 89.25, H 5.70, N 5.23.

4.2.39. 2-(2-Pyridyl)quinoline (8g).[37c] Mp 95–97 °C; t_R 16.1; R_f 0.5 (hexane/ethyl acetate: 4/1); ν (KBr) 3060, 1596 cm^{-1} (C=CH); δ_H 7.25–7.35 (1H, m, H_5-Py), 7.50–7.55 (1H, m, H_6-quinoline), 7.70–7.65 (1H, m, H_7-quinoline), 7.70–7.85 (2H, m, $H_{3,4}$-Py), 8.17 (1H, d, J=8.4 Hz, H_5-quinoline), 8.23 (1H, d, J=8.7 Hz, H_4-quinoline), 8.54 (1H, d, J=8.7 Hz, H_3-quinoline), 8.64 (1H, d, J=8.1 Hz, H_8-quinoline) 8.70–8.75 (1H, m, H_6-Py); δ_C 118.85, 121.75, 123.9, 126.65, 127.5, 128.1, 129.45, 129.65, 136.7, 136.8, 147.75, 149.0, 155.95, 156.1; *m/z* 207 (M^++1, 14%), 206 (M^+, 100), 205 (73), 178 (17).

4.2.40. 2-(2-Furyl)quinoline (8h).[37c] Mp 94 °C; t_R 14.7; R_f 0.45 (hexane/ethyl acetate: 4/1); ν (KBr) 3143, 1600 cm^{-1} (C=CH); δ_H 6.54 (1H, dd, J=1.9, 3.4 Hz, H_4-furyl), 7.19 (1H, dd, J=0.6, 3.4 Hz, H_3-furyl), 7.40–7.75 (5H, m, H_5-furyl and $H_{3,5-7}$-quinoline), 8.05 (1H, d, J=4.3 Hz, H_4-quinoline), 8.13 (1H, d, J=4.2 Hz, H_8-quinoline); δ_C 110.05, 112.05, 117.25, 126.0, 126.9, 127.4, 129.0, 129.7, 136.5, 143.9, 147.8, 148.75, 153.4; *m/z* 196 (M^++1, 14%), 195 (M^+, 100), 194 (26), 167 (30), 166 (23), 140 (12), 139 (14).

4.2.41. 2-(2-Thienyl)quinoline (8i).[37c] Mp 131–133 °C; t_R 16.6; R_f 0.62 (hexane/ethyl acetate: 4/1); ν (KBr) 3103, 3053, 1615, 1597 cm^{-1} (C=CH); δ_H 7.10–7.15 (1H, m, H_4-thienyl), 7.40–7.45 (2H, m, H_3-thienyl and H_3-quinoline), 7.60–7.75 (4H, m, H_5-thienyl, $H_{3,5-7}$-quinoline), 8.05 (1H, d, J=8.4 Hz, H_4-quinoline), 8.07 (1H, d, J=7.8 Hz, H_8-quinoline); δ_C 117.15, 125.75, 125.95, 127.05, 127.4, 128.0, 128.5, 129.0, 129.7, 136.5, 145.25, 147.95, 152.2; *m/z* 212 (M^++1, 16%), 211 (M^+, 100), 210 (29).

4.2.42. 2-(1-Methyl-1*H*-2-pyrrolyl)quinoline (8j).[72] Mp 61–63 °C; t_R 16.2; R_f 0.6 (hexane/ethyl acetate: 4/1); ν (KBr) 3104, 2948, 1609, 1558 cm^{-1} (C=CH); δ_H 4.15 (3H, s, CH_3), 6.20–6.25 and 6.70–6.75 (1 and 2H, respectively, 2m, CH_3NCH=CHCH), 7.35–7.40 (1H, m, H_3-quinoline), 7.55–7.70 (3H, m, H_{5-7}-quinoline), 7.97 (1H, d, J=8.6 Hz, H_4-quinoline), 8.00 (1H, d, J=8.6 Hz, H_8-quinoline); δ_C 37.6, 107.7, 112.25, 119.95, 125.35, 125.9, 127.35, 127.55, 128.9, 129.95, 132.0, 135.75, 147.5, 152.1; *m/z* 208 (M^+, 51%), 207 (100).

4.2.43. 2-Ferrocenylquinoline (8k).[73] t_R 21.3; R_f 0.52 (hexane/ethyl acetate: 4/1); ν (KBr) 3094, 1601 cm^{-1} (C=CH); δ_H 4.05 (5H, s, C_5H_5Fe), 4.40–4.45 and 5.00–5.05 (2H each

one, 2m, C_5H_4Fe), 7.40–7.75 and 8.00–8.10 (4 and 2H, respectively, 2m, quinoline); δ_C 67.9 (2C), 69.6 (5C), 70.4 (2C), 83.75, 119.45, 125.3, 126.6, 127.45, 128.85, 129.35, 135.4, 148.1, 159.45; *m/z* 314 (M^++1, 22%), 313 (M^+, 100), 248 (35). Crystal data: $C_{19}H_{15}FeN$, M=546.77; Monoclinic, a=6.1612 (4), b=12.1309 (9), c=19.1000 (14) Å; V=1420.28 (17) Å^3; space group P 21/n; Z=4; D_c=1.465 mg/m^3; λ=0.71073 Å; μ=1.053 mm^{-1}; $F(000)$=2368; T=21±1 °C. Data collection based on three ω-scan runs (starting ω=−34°) at values ϕ=0°, 120°, 240° with the detector at 2θ=−32°. An additional run of 100 frames, at 2θ=−32°, ω=−34° and ϕ=0°, was acquired to improve redundancy. For each of these runs, 606 frames were collected at 0.3° intervals and 30 s per frame. The diffraction frames were integrated using the program SAINT and the integrated intensities were corrected for Lorentz-polarization effects with SADABS. The structure was solved by direct methods and refined to all 2518 unique F_o^2 by full matrix least squares. All of the hydrogen atoms were placed at idealized positions and retained as rigid atoms. Final $wR2$=0.1051 for all data and 190 parameters; $R1$=0.0938 for 1604 $F_o>4\sigma$ (F_o).

4.2.44. 2-Ethyl-3-methylquinoline (8l).[74] Mp 49–51 °C; t_R 12.2; R_f 0.5 (hexane/ethyl acetate: 8/2); ν (KBr) 3058, 1665, 1626, 1600 cm^{-1} (C=CH); δ_H 1.35 (3H, t, J=7.5 Hz, C*H*$_3$CH$_2$), 2.40 (3H, s, CH$_3$C), 2.95 (2H, q, J=7.5 Hz, CH$_2$CH$_3$), 7.35–7.45 and 7.55–7.65 (1 and 2H, respectively, 2m, H_{5-7}-quinoline), 7.74 (1H, s, H_4-quinoline), 8.03 (1H, d, J=8.4 Hz, H_8-quinoline); δ_C 12.7, 18.9, 29.3, 125.4, 126.5, 127.15, 128.1, 128.3, 129.2, 135.55, 146.45, 163.05; *m/z* 171 (M^+, 63%), 171 (100), 143 (27), 115 (14).

4.2.45. 1,2,3,4-Tetrahydroacridine (8m).[75] t_R 14.4; R_f 0.43 (hexane/ethyl acetate: 4/1); ν (film) 3054, 1626, 1596 cm^{-1} (C=CH); δ_H 1.80–1.90 and 1.90–2.00 [2H each one, 2m, CH$_2$(C*H*$_2$)$_2$CH$_2$], 2.90–2.95 and 3.10–3.15 [2H each one, 2m, C*H*$_2$(CH$_2$)$_2$C*H*$_2$], 7.40–7.45 and 7.55–7.65 (1 and 2H, respectively, 2m, H_{6-8}-acridine), 7.74 (1H, s, H_9-acridine), 7.98 (1H, d, J=8.4 Hz, H_5-acridine); δ_C 22.75, 23.05, 29.1, 33.35, 125.4, 126.75, 127.0, 128.05, 128.35, 130.8, 134.85, 146.35, 159.1; *m/z* 184 (M^++1, 13%), 183 (M^+, 100), 182 (95), 168 (26), 167 (28), 155 (14), 154 (18).

4.2.46. 3-Azatetracyclo[10.2.1.0^{2,11}.0^{4,9}]pentadeca-2(11),3,5,7,9-pentaene (8n).[76] t_R 14.7; R_f 0.35 (hexane/ethyl acetate: 4/1); ν (film) 3062, 1640 cm^{-1} (C=CH); δ_H 1.20–1.45, 1.65–1.70, and 1.88–1.92 (2, 1, and 1H, respectively, 3m, CH$_2$CH$_2$), 2.00–2.10 (2H, m, C*H*$_2$CH), 3.45–3.55 (2H, m, C*H*CH$_2$C*H*), 7.35–7.45, 7.55–7.65, 7.65–7.70, and 8.02 (1, 1, 2, and 1H, respectively, 3m and d, respectively, J=8.4 Hz, ArH); δ_C 25.5, 27.25, 41.95, 45.2, 46.55, 125.15, 125.4, 127.4, 127.6, 127.75, 128.45, 139.75, 146.45, 170.3; *m/z* 195 (M^+, 60%), 194 (51), 180 (15), 168 (16), 167 (100), 166 (18).

4.2.47. 1,15,15-Trimethyl-3-azatetracyclo-[10.2.1.0^{2,11}.0^{4,9}]pentadeca-2(11),3,5,7,9-pentaene (8o).[41] t_R 15.4; R_f 0.57 (hexane/ethyl acetate: 4/1); $[\alpha]_D^{20}$ +34.9 (c 9.6, CHCl$_3$); ν (film) 3068, 1641 cm^{-1} (C=CH); δ_H 0.56, 1.05, and 1.43 [3H each one, 3s, (CH$_3$)$_2$CCCH$_3$], 1.20–1.40, 1.90–2.00, and 2.10–2.20 (2, 1, and 1H, respectively, 3m, CH$_2$CH$_2$), 2.94 (1H, d, J=4.1 Hz, CH$_2$C*H*), 7.40–7.45, 7.55–7.60, 7.65–7.70, and 8.05–8.10 (1, 1, 2, and 1H, respectively, 4m, ArH); δ_C 10.55, 18.9, 20.15, 26.35, 31.8, 51.15, 54.05, 55.2, 125.05, 125.95, 127.35, 127.5, 127.85, 128.7, 140.0, 146.7, 172.05; *m/z* 237 (M^+, 29%), 222 (21), 208 (12), 195 (19), 194 (100), 193 (14), 180 (16).

4.2.48. *N*-Benzyl-15,15-dimethyl-3-azatetracyclo-[10.2.1.0^{2,11}.0^{4,9}]pentadeca-2(11),3,5,7,9-pentaen-1-ylmethanesulfonamide (8p). R_f 0.54 (hexane/ethyl acetate: 3/2); $[\alpha]_D^{20}$ +76.9 (c 8.5, CHCl$_3$); ν (film) 3068, 1634, 1581 cm^{-1} (C=CH); δ_H 0.50 and 1.01 (3 and 3H, respectively, 2s, 2×CH$_3$), 1.20–1.30, 2.00–2.05, and 2.15–2.25 (1, 1, and 2H, respectively, 3m, CH$_2$CH$_2$), 2.97 (1H, d, J=3.3 Hz, C*H*CH$_2$), 3.22 and 3.55 (1 and 1H, respectively, 2d, J=15.2 Hz, CH$_2$SO$_2$), 4.35–4.45 and 4.55–4.60 (1 and 1H, 2m, CH$_2$N), 7.25–7.45 and 7.70–7.75 (8 and 2H, respectively, 2m, ArH), 9.51 (1H, t, J=6.3 Hz, NH); δ_C 19.0, 20.4, 26.5, 30.25, 48.25, 50.55, 51.75, 55.45, 57.6, 126.15, 127.6, 127.65, 127.7, 127.75, 128.35, 128.7 (2C), 128.75 (2C), 128.8, 137.4, 139.4, 145.15, 168.45; *m/z* 238 (M^+−168, 10%), 237 (70), 236 (100), 220 (11), 209 (18), 208 (14), 195 (19), 194 (50), 193 (14), 192 (14), 180 (21); HRMS: M^+ found 406.1722. $C_{24}H_{26}SN_2O_2$ requires 406.1715.

4.2.49. *N*-Benzyl-19,19-dimethyl-3-azapentacyclo-[14.2.1.0^{4,13}.0^{5,10}]nonadeca-2(15),3,5(10),6,8,11,13-heptaen-1-ylmethanesulfonamide (8q). R_f 0.52 (hexane/ethyl acetate: 6/4); $[\alpha]_D^{20}$ +28.0 (c 13.5, CHCl$_3$); ν (film) 3295 (NH), 3060, 1613, 1563 cm^{-1} (C=CH); δ_H 0.48 and 1.04 (3 and 3H, respectively, 2s, 2×CH$_3$), 1.22–1.32, 1.95–2.00, and 2.20–2.40 (1, 1, and 2H, respectively, 3m, CH$_2$CH$_2$), 3.00 (1H, d, J=3.7 Hz, C*H*CH$_2$), 3.30 and 3.67 (2H, 2d, J=15.1 Hz, CH$_2$SO$_2$), 4.48–4.63 (2H, m, CH$_2$N), 7.15–7.40, 7.50–7.65, 7.75–7.85, and 8.78 (6, 2, 3, and 1H, respectively, 3m and d, respectively, J=8.3 Hz, ArH), 8.82 (1H, t, J=6.6 Hz, NH); δ_C 19.3, 20.15, 26.25, 29.0, 47.5, 50.5, 52.35, 55.75, 58.05, 123.35, 125.4, 125.6, 126.8, 127.05, 127.3, 127.4, 128.0 (2C), 128.2, 128.3 (2C), 128.45, 130.75, 133.25, 137.35, 139.95, 143.3, 166.85; *m/z* 288 (M^+−168, 11%), 287 (68), 286 (100), 285 (14), 258 (14), 245 (17), 244 (45), 243 (18), 242 (25), 230 (21), 106 (11), 91 (10); HRMS: M^+−$C_7H_8NO_2S$ found 286.1593. $C_{21}H_{20}N$ requires 286.1596.

CCDC-296061 and CCDC-296062 contain the supplementary crystallographic data for compounds **6e** and **7a**, respectively, reported in this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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