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Catalytic conjugate addition of heterocyclic compounds to α,β-unsaturated carbonyl compounds by hafnium salts and scandium salts

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Abstract—The hafnium chloride ($HfCl_4$) and scandium chloride ($ScCl_3$) catalyzed conjugate additions of heterocyclic compounds, such as indoles, pyrrole, pyrazole, and imidazole, have been demonstrated. Hafnium chloride effectively catalyzed the conjugate addition of indoles to α,β-unsaturated carbonyl compounds, and the addition product was obtained in high yield. The reaction of pyrrole was also catalyzed by $HfCl_4$ or $ScCl_3$, and produced 2,6-dialkylated pyrroles up to 99% yields. Furthermore, the conjugate addition of the 1-position of the pyrazoles and imidazole occurred, and produced several substituted heterocyclic compounds in good yields.

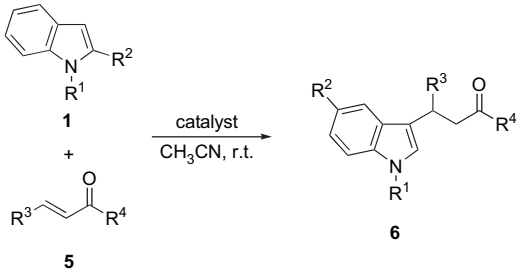
1. Introduction

Nitrogen-containing heterocycles are the key components of some pharmacologically and biologically active compounds,[1] and the development of new and efficient transformations of heterocyclic compounds into several derivatives has attracted much attention in organic synthesis. Recently, several Lewis acids were found to catalyze the conjugate addition of heterocyclic compounds to electron deficient olefins, and Bi,[2] In,[3] Yb,[4] Sc,[5] Al,[6] Cu,[7] Au,[8] Zn,[9] Sm,[10] and Ce[11] salts were used for the addition of indole to α,β-enones. We also reported that hafnium(IV) trifluoromethanesulfonate {$Hf(OTf)_4$} and scandium trifluoromethanesulfonate {$Sc(OTf)_3$} are effective Lewis acids for the conjugated addition of indoles to α,β-enones.[12] On the other hand, there are only a few reports about the Lewis acid catalyzed conjugated addition of pyrrole, pyrazole, and imidazole to α,β-unsaturated carbonyl compounds.[13] In this paper, we report the hafnium(IV) chloride ($HfCl_4$) and scandium(III) chloride ($ScCl_3$) catalyzed conjugated addition of heterocyclic compounds to α,β-unsaturated carbonyl compounds.

2. Result and discussion

2.1. Conjugate addition of indoles to α,β-enones

Based on our previous research, we further examined the conjugate addition of the 3-position of indoles to α,β-enones, which can be catalyzed by other Lewis acids (Scheme 1). As we have previously reported, the reaction of indole (**1a**) to methyl vinyl ketone (**5a**) was effectively catalyzed by $Hf(OTf)_4$ and $Sc(OTf)_3$ (Table 1, entries 1 and 3). After our screening of several hafnium and scandium salts, we found that hafnium chloride ($HfCl_4$) and scandium chloride ($ScCl_3$) are also effective catalysts for this reaction. The reaction catalyzed by $HfCl_4$ and $ScCl_3$ proceeded smoothly in an acetonitrile solvent at room temperature and gave the addition product (**6a**) in a 93 and 92% isolated yields, respectively (entries 2 and 4). The $HfCl_4$ catalyzed addition reaction of **1a** to phenyl 1-propenyl ketone (**5b**) also occurred in a quantitative yield even though it needed a longer reaction time (entry 6). However, the reaction of **1a** with a cyclic enone (**5c**) gave **6c** in low yield (entry 8). The addition reaction of 1-methylindole (**1b**) to **5a** catalyzed by $Hf(OTf)_4$ and $HfCl_4$ gave the product (**6d**) in a 50 and 99% yields, respectively (entries 9 and 10). This result indicate that $HfCl_4$ is a superior catalyst compared to $Hf(OTf)_4$ for this reaction. The $HfCl_4$ catalyzed reaction of 2-methylindole



Scheme 1.

Keywords: Conjugate addition; Heterocyclic compound; Hafnium chloride; Scandium chloride; Lewis acid.
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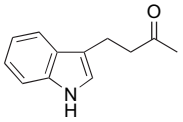
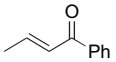
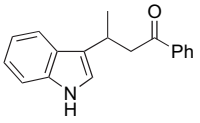
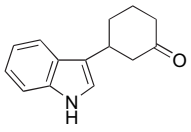
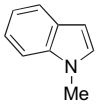
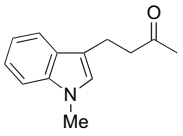
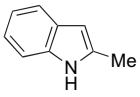
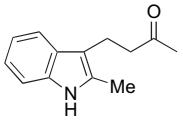
Table 1. Conjugate addition of indoles **1a–c** to α,β-enones **5a–c**[a]

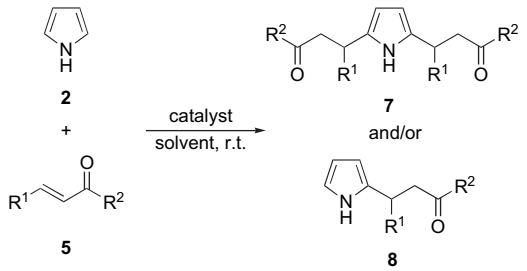
Entry	Indole (**1**)	Enone (**5**)	Catalyst	Time	Product **6**	Yield[b] (%)
1	 **1a**	 **5a**	$Hf(OTf)_4$	10 min	 **6a**	85
2			$HfCl_4$	15 min		93
3			$Sc(OTf)_3$	2 h		90
4			$ScCl_3$	6 h		92
5		 **5b**	$Hf(OTf)_4$	15 min	 **6b**	80
6			$HfCl_4$	2 h		99
7		 **5c**	$Hf(OTf)_4$	30 min	 **6c**	70
8			$HfCl_4$	12 h		30
9	 **1b**	**5a**	$Hf(OTf)_4$	15 min	 **6d**	50
10			$HfCl_4$	20 min		99
11	 **1c**	**5a**	$Hf(OTf)_4$	10 min	 **6e**	80
12			$HfCl_4$	4 h		99

[a] All reactions were carried out at rt: indoles (1.0 mmol), enones (1.5 mmol), catalyst (0.1 mmol), and CH_3CN (5.0 mL).
[b] Isolated yield by silica gel column chromatography.

(**1c**) also smoothly occurred even though it requires a longer reaction time than the reaction by $Hf(OTf)_4$, but the reaction still produced a 99% yield of product **6e** (entries 11 and 12). In these reactions, we confirmed that $Hf(OTf)_4$ forms a by-product from the dimerization and/or polymerization of indoles, but $HfCl_4$ will not form such a by-product under the catalytic conditions. This result explains the reason why the reaction by $HfCl_4$ is much slower, but produced a higher yield compared to the reaction using $Hf(OTf)_4$.

2.2. Reaction of pyrrole to α,β-enones

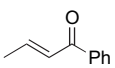
We extended this $HfCl_4$ catalyst system to the reaction of other heterocyclic compounds, and examined the conjugate addition of pyrrole (**2**) to α,β-enones **5a–c** (Scheme 2). The



Scheme 2.

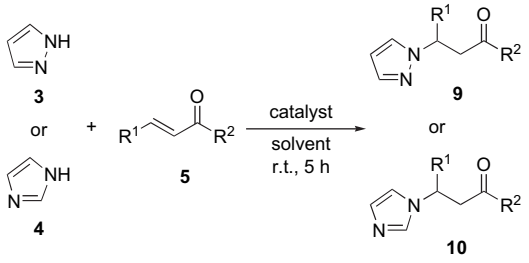
$Hf(OTf)_4$ catalyzed conjugate addition reaction of **2** to methyl vinyl ketone (**5a**) was very slow, but gave a mixture of 2,5-dialkylated pyrrole **7a** and 2-alkylated pyrrole **8a** in 19 and 13% yields, respectively (Table 2, entry 1). Changing of the solvent from CH_3CN to CH_2Cl_2 effectively increased the yield, but the ratio of **7a** and **8a** was almost the same (entry

Table 2. Reaction of pyrrole (**2**) to α,β-enones **5a–c**[a]

Entry	Enone (**5**)	Catalyst	Solvent	Time (h)	Yield[b] (%) of **7** and **8**	
1	 **5a**	$Hf(OTf)_4$	CH_3CN	20	19 (**7a**)	13 (**8a**)
2		$Hf(OTf)_4$	CH_2Cl_2	20	34 (**7a**)	27 (**8a**)
3		$HfCl_4$	CH_3CN	5	34 (**7a**)	7 (**8a**)
4		$HfCl_4$	CH_2Cl_2	5	63 (**7a**)	6 (**8a**)
5		$HfBr_4$	CH_2Cl_2	5	43 (**7a**)	0 (**8a**)
6		$Sc(OTf)_3$	CH_3CN	96	10 (**7a**)	6 (**8a**)
7		$ScCl_3$	CH_2Cl_2	5	48 (**7a**)	7 (**8a**)
8	 **5b**	$HfCl_4$	CH_2Cl_2	5	65 (**7b**)	0 (**8b**)
9		$ScCl_3$	CH_2Cl_2	5	99 (**7b**)	0 (**8b**)
10	 **5c**	$HfCl_4$	CH_2Cl_2	5	0 (**7c**)	0 (**8c**)
11		$ScCl_3$	CH_2Cl_2	5	15 (**7c**)	0 (**8c**)

[a] All reactions were carried out at rt: pyrrole (1.0 mmol), enones (3.0 mmol), catalyst (0.1 mmol), and solvent (5.0 mL).
[b] Isolated yield by silica gel column chromatography.

2). Again, we discovered that $HfCl_4$ is a better catalyst for the conjugate addition of **2** to **5a**. The reaction, which was catalyzed by $HfCl_4$, in CH_3CN decreased the formation of 2-alkylated pyrrole **8a**, but the yield of the 2,5-dialkylated pyrrole **7a** did not change (entry 3). However, changing the reaction solvent from CH_3CN to CH_2Cl_2 increased the yield of **7a** to 63% (entry 4). The use of $HfBr_4$ allowed the selective formation of **7a**, but the isolated yield was low (entry 5). Scandium chloride ($ScCl_3$) in CH_2Cl_2 also effectively catalyzed this reaction, but the yield was lower than the result from the $HfCl_4$ catalyzed reaction (entry 7). On the other hand, the addition reaction of pyrrole (**2**) to phenyl 1-propenyl ketone (**5b**) selectively formed the 2,5-dialkylated pyrrole **7b** by using $HfCl_4$ (entry 8). Interestingly, the reaction by $ScCl_3$ exhibited the selective formation of **7b** in a 99% isolated yield (entry 9). Unfortunately, the addition to a cyclic enone (**5c**) did not occur by using $HfCl_4$, and even the use of $ScCl_3$ resulted in a very low yield (entries 10 and 11).

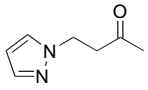
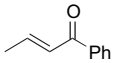
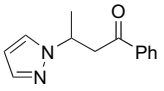
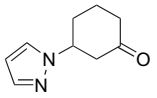
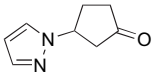
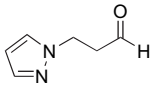
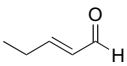
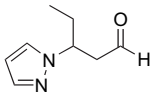
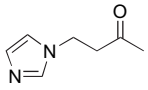
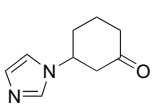


Scheme 3.

2.3. Conjugate addition of pyrazole and imidazole to α,β-unsaturated carbonyl compounds

We next demonstrated the reaction of pyrazole (**3**) and imidazole (**4**) with α,β-unsaturated carbonyl compounds (Scheme 3), and results are summarized in Table 3. Usually,

Table 3. $HfCl_4$ or $ScCl_3$ catalyzed conjugate addition of pyrazole (**3**) and imidazole (**4**) to α,β-unsaturated carbonyl compounds **5a–f**[a]

Entry	**3** or **4**	Enone or enal (**5**)	Catalyst	Solvent	Product **9** or **10**	Yield[b] (%)
1			$HfCl_4$	CH_2Cl_2		72
2			$ScCl_3$	CH_2Cl_2		51
	3	**5a**			**9a**	
3			$HfCl_4$	CH_2Cl_2		94
4			$ScCl_3$	CH_2Cl_2		21
		5b			**9b**	
5			$HfCl_4$	CH_2Cl_2		90
6			$ScCl_3$	CH_2Cl_2		99
		5c			**9c**	
7			$ScCl_3$	CH_2Cl_2		99
		5d			**9d**	
8			$Hf(OTf)_4$	CH_2Cl_2		0
9			$HfCl_4$	CH_2Cl_2		77
10			$Sc(OTf)_3$	CH_2Cl_2		0
11		**5e**	$ScCl_3$	CH_2Cl_2	**9e**	51
12			$HfCl_4$	CH_2Cl_2		72
		5f			**9f**	
13			$HfCl_4$	CH_2Cl_2		0
14			$ScCl_3$	CH_2Cl_2		0
	4	**5a**			**10a**	
15			$HfCl_4$	CH_2Cl_2		50
16			$HfCl_4$	CH_3CN		79
17		**5c**	$ScCl_3$	CH_2Cl_2	**10b**	6

[a] All reactions were carried out at rt: pyrazole or imidazole (1.0 mmol), electron deficient olefins (2.4 mmol), catalyst (0.1 mmol), and solvent (5.0 mL).
[b] Isolated yield by silica gel column chromatography.

the Michael addition of **3** at the 1-position to electron deficient olefins requires a high temperature and/or base, but we found that $HfCl_4$ and $ScCl_3$ effectively catalyzed the reaction at room temperature. The reaction catalyzed by $HfCl_4$ occurred with several α,β-enones and gave *N*-alkylated products (**9a–c**) in good to excellent yields (Table 3, entries 1, 3, and 5). The catalyst activity of $ScCl_3$ was lower than that of $HfCl_4$ for the reaction of pyrazole to **5a** and **b** (entries 2 and 4). However, the coupling reaction of pyrazole with cyclic enone such as 2-cyclohexen-1-one (**5c**) suggested that $ScCl_3$ was a slightly better catalyst than $HfCl_4$, and the reaction gave *N*-alkylation product **9c** in a quantitative isolated yield (entries 5 and 6). We also demonstrated the addition of pyrazole to α,β-unsaturated aldehydes (**5e** and **f**), and the reaction of **9d** and **f** produced the corresponding addition product in good yield as we expected (entries 9, 11, and 12). In this reaction, $Hf(OTf)_4$ and $Sc(OTf)_3$ didn't catalyze the reaction (entries 8 and 10). The addition reaction at the 1-position of imidazole to α,β-enones was also demonstrated. Unfortunately, the addition reaction of imidazole (**4**) to methyl vinyl ketone (**5a**) didn't occur (entries 13 and 14), but $HfCl_4$ effectively catalyzed the reaction of imidazole to a cyclic enone **5c** in CH_3CN, and gave a 79% yield of product **10b** (entry 16).

3. Conclusion

In conclusion, we demonstrated that $HfCl_4$ and $ScCl_3$ catalyzed conjugate addition of indoles, pyrrole, pyrazole, and imidazole to α,β-unsaturated carbonyl compounds. The reactivity depends on the substrates and solvents, but $HfCl_4$ exhibited excellent catalyst reactivity. Furthermore, we confirmed that $ScCl_3$ was also a good catalyst for some combination of heterocyclic compounds to α,β-unsaturated carbonyl compounds.

4. Experimental section

4.1. General methods

All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5. NMR spectra were recorded on a JEOL JNM-AL300 spectrometer (300 MHz for ^1H and 75 MHz for ^{13}C). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^1H NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as an internal reference for ^{13}C NMR. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 25 °C. All reagents and solvents were purchased from common commercial sources and were used as received or purified by distillation from appropriate drying agents.

4.2. General procedure of conjugate addition of heterocyclic compounds to α,β-enones: typical procedure (entry 2 in Table 1)

A mixture of indole **1** (117 mg, 1.0 mmol), methyl vinyl ketone **2** (105 mg, 1.5 mmol), and $HfCl_4$ (32 mg, 0.1 mmol) in CH_3CN (5 mL) was stirred at room temperature for 15 min. After complete conversion, as indicated by TLC, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (hexane/EtOAc=4/1) to give 174 mg (93%) of 4-(1*H*-indole-3-yl)butan-2-one (**6a**)[3b]. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.94 (br s, 1H), 7.58 (d, *J*=7.9 Hz, 1H), 7.34 (d, *J*=7.9 Hz, 1H), 7.19 (td, *J*=7.9, 1.3 Hz, 1H), 7.11 (td, *J*=7.9, 1.3 Hz, 1H), 6.98 (d, *J*=2.4 Hz, 1H), 3.05 (t, *J*=7.4 Hz, 2H), 2.84 (t, *J*=7.4 Hz, 2H), 2.13 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.8, 136.3, 127.1, 121.9, 121.4, 119.2, 118.6, 115.1, 111.1, 44.0, 30.0, 19.3. White powder. R_f=0.13 (20% EtOAc in hexane).

4.2.1. 3-(1*H*-Indole-3-yl)-1-phenylbutan-1-one (6b). ^1H NMR (300 MHz, $CDCl_3$), δ: 7.93–7.96 (m, 2H), 7.67 (dt, *J*=7.9, 0.7 Hz, 1H), 7.50–7.56 (m, 1H), 7.33–7.40 (m, 3H), 7.19 (ddd, *J*=7.9, 7.0, 1.1 Hz, 1H), 7.11 (ddd, *J*=7.9, 7.0, 1.1 Hz, 1H), 7.02 (d, *J*=2.0 Hz, 1H), 3.77–3.88 (m, 1H), 3.47 (dd, *J*=16.3, 4.9 Hz, 1H), 3.23 (dd, *J*=16.3, 8.8 Hz, 1H), 1.45 (d, *J*=7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 199.8, 137.3, 136.6, 132.9, 128.5 (2C), 128.1 (2C), 126.3, 122.0, 121.5, 120.2, 119.2 (2C), 111.3, 46.5, 27.2, 21.0. IR (KBr) cm^{-1}: 3422 (N–H), 1680 (C=O). EIMS *m/z*: 263 $[M]^+$. EIHRMS *m/z*: 263.1314 (Calcd for $C_{18}H_{17}NO$: 263.1310). Anal. Calcd for $C_{18}H_{17}NO$: C, 82.10; H, 6.51; N, 5.32. Found: C, 81.95; H, 6.41; N, 5.12. White powder. R_f=0.26 (20% EtOAc in hexane). Mp 88–92 °C.

4.2.2. 3-(1*H*-Indole-3-yl)cyclohexanone (6c).[11a] ^1H NMR (300 MHz, $CDCl_3$), δ: 7.95 (br s, 1H), 7.54–7.57 (m, 1H), 7.29 (dt, *J*=7.9, 1.1 Hz, 1H), 7.10 (ddd, *J*=7.9, 7.0, 1.1 Hz, 1H), 7.05 (ddd, *J*=7.9, 7.0, 1.1 Hz, 1H), 6.91 (dd, *J*=2.4, 0.7 Hz, 1H), 3.42–3.33 (m, 1H), 2.73 (ddt, *J*=14.1, 4.8, 1.7 Hz, 1H), 2.56 (ddd, *J*=14.1, 10.5, 1.1 Hz, 1H), 2.28–2.43 (m, 2H), 2.17–2.20 (m, 1H), 2.09–1.70 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.8, 136.5, 126.1, 122.2, 120.3, 119.7, 119.3, 119.0, 111.3, 48.1, 41.5, 35.9, 31.7, 24.9.

4.2.3. 4-(1-Methylindole-3-yl)butan-2-one (6d).[4b] ^1H NMR (300 MHz, $CDCl_3$), δ: 7.56 (d, *J*=8.0 Hz, 1H), 7.27 (d, *J*=8.0 Hz, 1H), 7.20 (td, *J*=8.0, 1.3 Hz, 1H), 7.09 (td, *J*=8.0, 1.3 Hz, 1H), 6.83 (s, 1H), 3.72 (s, 3H), 3.03 (t, *J*=7.4 Hz, 2H), 2.82 (t, *J*=7.4 Hz, 2H), 2.13 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.7, 137.0, 127.5, 126.3, 121.5, 118.7 (2C), 113.6, 109.2, 44.3, 32.5, 30.0, 19.2. Yellow oil. R_f=0.27 (20% EtOAc in hexane).

4.2.4. 4-(1*H*-2-Methylindole-3-yl)butan-2-one (6e).[3b] ^1H NMR (300 MHz, $CDCl_3$), δ: 7.68 (br s, 1H), 7.39 (d, *J*=8.8 Hz, 1H), 7.19–7.15 (m, 1H), 7.05–6.95 (m, 2H), 2.89 (t, *J*=7.7 Hz, 2H), 2.68 (t, *J*=7.7 Hz, 2H), 2.29 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.9, 135.3, 131.1, 128.3, 121.0, 119.1, 117.7, 110.2 (2C), 44.2, 30.2, 18.4, 11.5. Yellow oil. R_f=0.25 (20% EtOAc in hexane).

4.2.5. 2,5-Bis(3-oxobutyl)pyrrole (7a).[14] ^1H NMR (300 MHz, $CDCl_3$), δ: 2.14 (s, 6H), 2.71–2.81 (m, 8H), 5.69 (d, *J*=2.6 Hz, 2H), 8.43 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 21.6 (2C), 30.0 (2C), 44.0 (2C), 104.8 (2C), 130.4 (2C), 209.1 (2C). Yellow oil. R_f=0.38 (50% EtOAc in hexane).

4.2.6. 4-(1*H*-Pyrrol-2-yl)butan-2-one (8a). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.14 (s, 3H), 2.77–2.83 (m, 4H), 5.86 (s, 1H), 6.06 (d, J=2.6 Hz, 1H), 6.63 (d, J=2.6 Hz, 1H), 8.46 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 21.3, 30.1, 44.2, 105.3, 107.8, 116.7, 136.6, 209.6. Yellow oil. R_f=0.15 (50% EtOAc in hexane). EIHRMS m/z: 137.0844 (Calcd for $C_{24}H_{24}NO_2$: 137.0841).

4.2.7. 2,5-Bis(1-methyl-3-phenyl-3-oxopropyl)pyrrole (7b). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.27 (d, J=7.0 Hz, 3H), 1.28 (d, J=7.0 Hz, 3H), 3.01–3.24 (m, 4H), 3.43 (quint, J=7.0 Hz, 2H), 5.74 (d, J=2.6 Hz, 2H), 7.29–7.49 (m, 6H), 7.78–7.87 (m, 4H), 8.67 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 19.9, 20.0, 27.8, 27.9, 47.1, 47.2, 102.6, 102.7, 128.1 (4C), 128.5 (2C), 128.6 (2C), 133.0, 133.1, 135.6 (2C), 137.1 (2C), 200.2 (2C). Yellow oil. R_f=0.35 (20% EtOAc in hexane). EIHRMS m/z: 358.1810 (Calcd for $C_{24}H_{24}NO_2$: 358.1807).

4.2.8. 1-Phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (9a).[15] ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.14 (s, 3H), 3.05 (t, J=6.4 Hz, 2H), 4.39 (t, J=6.4 Hz, 2H), 6.20 (t, J=2.2 Hz, 1H), 7.42 (d, J=2.2 Hz, 1H), 7.48 (d, J=2.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 19.0, 26.1, 32.2, 106.6, 126.5, 138.8, 207.9. Yellow oil. R_f=0.27 (50% EtOAc in hexane).

4.2.9. 1-Phenyl-3-(1*H*-pyrazol-1-yl)butan-1-one (9b). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.62 (d, J=6.8 Hz, 3H), 3.32 (dd, J=17.4, 6.8 Hz, 1H), 3.79 (dd, J=17.4, 6.8 Hz, 1H), 5.06 (sextet, J=6.8 Hz, 1H), 6.18 (t, J=2.0 Hz, 1H), 7.40–7.57 (m, 5H), 7.90–7.93 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 21.4, 45.3, 53.6, 104.8, 128.1 (2C), 128.6 (2C), 133.4 (2C), 136.7, 139.4, 197.4. Yellow oil. R_f=0.30 (20% EtOAc in hexane). EIHRMS m/z: 214.1108 (Calcd for $C_{13}H_{14}N_2O$: 214.1106).

4.2.10. 3-(1*H*-Pyrazol-1-yl)cyclohexanone (9c). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.66–1.81 (s, 1H), 2.01–2.12 (m, 1H), 2.22–2.29 (m, 2H), 2.41–2.46 (m, 2H), 2.82 (dd, J=14.5, 5.0 Hz, 1H), 2.99 (dd, J=14.5, 10.0 Hz, 1H), 4.50–4.60 (m, 1H), 6.25 (t, J=2.2 Hz, 1H), 7.41 (d, J=2.2 Hz, 1H), 7.54 (d, J=2.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 21.7, 31.8, 40.6, 47.7, 69.75, 105.3, 127.5, 139.4, 207.9. Yellow oil. R_f=0.50 (50% EtOAc in hexane). EIHRMS m/z: 164.0948 (Calcd for $C_9H_{12}N_2O$: 164.0950).

4.2.11. 3-(1*H*-Pyrazol-1-yl)cyclopentanone (9d). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.23–2.85 (m, 5H), 2.76 (dd, J=9.5, 7.7 Hz, 1H), 4.94 (quint, J=6.6 Hz, 1H), 6.24 (t, J=2.6 Hz, 1H), 7.41 (d, J=2.6 Hz, 1H), 7.51 (d, J=2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 30.3, 36.8, 44.8, 58.6, 105.7, 127.9, 139.7, 215.0. Yellow oil. R_f=0.40 (50% EtOAc in hexane). EIHRMS m/z: 150.0795 (Calcd for $C_8H_{10}N_2O$: 150.0793).

4.2.12. 3-(1*H*-Pyrazol-1-yl)propanal (9e).[15] ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.05 (t, J=6.2 Hz, 2H), 4.43 (t, J=6.2 Hz, 2H), 6.19 (s, 1H), 7.41 (d, J=2.2 Hz, 1H), 7.46 (s, 1H), 9.78 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 43.8, 44.8, 105.5, 129.8, 139.7, 199.3. Yellow oil. R_f=0.25 (50% EtOAc in hexane).

4.2.13. 3-(1*H*-Pyrazol-1-yl)pentanal (9f). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.71 (t, J=7.7 Hz, 3H), 1.68–1.81 (m, 1H), 1.84–1.99 (m, 1H), 2.81 (ddd, J=17.6, 4.8, 1.1 Hz, 1H), 3.16 (ddd, J=17.6, 8.4, 1.1 Hz, 1H), 4.53 (septet, J=4.8 Hz, 1H), 6.13 (t, J=2.2 Hz, 1H), 7.36 (d, J=2.2 Hz, 1H), 7.45 (s, 1H), 9.61 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 10.4, 28.5, 48.6, 58.2, 104.8, 129.4, 139.6, 199.5. Yellow oil. R_f=0.50 (50% EtOAc in hexane). EIHRMS m/z: 152.0951 (Calcd for $C_8H_{12}N_2O$: 152.0950).

4.2.14. 3-(1*H*-Imidazol-1-yl)cyclohexanone (10b).[2a] ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.67–1.79 (m, 1H), 1.98–2.13 (m, 2H), 2.27–2.47 (m, 3H), 2.68 (dd, J=13.9, 11.0 Hz, 1H), 2.80 (ddt, J=13.9, 4.8, 1.5 Hz, 1H), 4.30–4.39 (m, 1H), 7.04 (s, 1H), 7.24 (s, 1H), 7.51 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 21.9, 32.4, 40.4, 48.7, 55.5, 116.7, 129.7, 135.2, 206.7. Yellow oil. R_f=0.29 (EtOAc).

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