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ARTICLE TYPE

Efficient Catalytic-free Method to α-Aryl Cycloalkanones through High Chemoselective Coupling of Aryl Compounds with Oxyallyl Cations

Juan Luo,[a,b] Hui Zhou,[a] Jiwei Hu,[a] Rui Wang [c] and Qiang Tang*[a,b]

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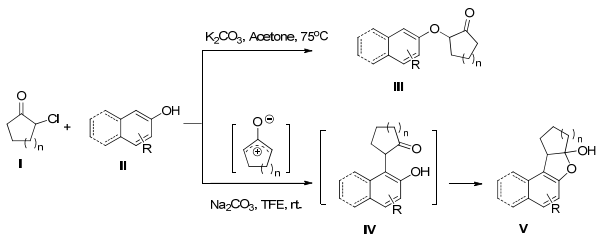
Reported here is cataltic-free coupling of aryl compounds and α-halo cycloketones *via in situ* generated oxyallyl cation intermediates. The reactions efficiently afford α-naphthol cycloalkanones with moderate to excellent yields. Electron-rich aromatic compounds are also used to produce the corresponding α-aryl cycloalkanones, and in some cases, analytically pure products are obtained after simple filtrations followed by evaporations.

Introduction

α-Aryl cycloalkanones are important building blocks for concise preparation of medicine or organic functional materials, such as naphthonone,[1] brazan,[2] and electroluminescence devices.[3] The synthesis of α-aryl cycloalkanones, particularly α-naphthol cycloalkanones, can be realized by nucleophilic substitution of α-hydroxylketones with oxygen protected naphthols *via* Grignard reagents and final deprotection,[4] or by direct electrophilic substitution of α-hydroxylketones with phenols under an acidic condition.[5] α-Arylation of β-dicarbonyl compounds, as a powerful technology, needs to be catalyzed by transitional metals,[6] organocatalysts[7] or enzymes[8]. Pappo group recently has reported an efficient cross dehydrogenative coupling reaction between phenols and α-substituted β-ketoesters catalyzed by iron trichloride.[9]



Scheme 1.Different Reaction Pathways of α-Halo ketones with Naphthols.

[a] *Department of Medical Chemistry, College of Pharmacy, Chongqing Medical University, Chongqing 400016, P. R. China. E-mail: tangqiang @cqmu.edu.cn*

[b] *The Faculty of Laboratory Medicine, Chongqing Medical University, Chongqing 401331, P. R. China.*

[c] *School of Pharmacy & Bioengineering, Chongqing University of Technology, Chongqing 400054, China*

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It has been reported that reaction of β-naphthol with α-cyclohexanone in xylene under refluxing temperature produces compound **V** directly.[10] However, high temperature is necessary, the yield is moderate (22%-57%), and a large amount of byproduct **III** is evolved. It is worth noting that direct substitution of α-haloketones with naphthols under basic conditions produces phenol ethers **III** (Scheme 1) as the main product.[11]

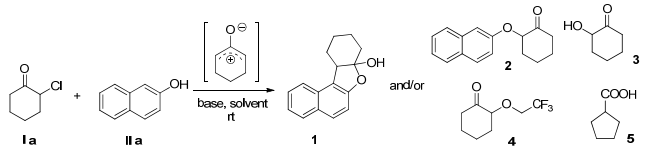
Here we report an efficient catalyst-free coupling of unprotected naphthols and oxyallyl cation intermediates generated from α-halocycloketones at room temperature. Oxyallyl cations have been extensively explored for more than half century.[12] Literature is replete with examples of cycloaddition reactions of such species, especially (4+3) cycloaddition reactions.[13] Moreover, aromatic groups have been extensively used to trap oxyallyl cations in the context of Nazarov cyclization.[14] However, there are only a few reports on the interrupted cycloaddition reactions of aromatic compounds with oxyallyl cations derived from α-halo ketones.[15] Recently, MacMillan group and we respectively reported an efficient synthesis of α-indole carbonyl compounds *via* electrophilic aromatic substitution of unprotected indoles to *in situ* generated oxyallyl cations.[16] To further expand the reaction scope, we start to use naphthols as nucleophile to react with oxyallyl cations generated from α-halo cycloalkanones. To our delight, the reaction proceeds smoothly and evolves α-naphthol cycloalkanones **IV** (Scheme 1) which are eventually transformed to product **V** (Scheme 1) with high yield.

Results and Discussion

We first explored the reaction between 2-chlorocyclohexanone (**Ia**) and 2-naphthol (**II b**). At room temperature, most of the starting materials remain unreacted in common organic solvents such as DMF, DMSO, THF, toluene, Et_2O, CH_2Cl_2, EtOAc, CH_3CN, toluene and xylene (Table 1, entries 1 & 2). Although cough medicine, product **1,** is evolved when xylene is used as solvent under high temperature, 33% yield of ether byproduct **2** which is not transform to product **1** within the prolonged reaction

time, is also obtained, (Table 1, entry 3). In the case that water was used as a solvent, hydrolysis of 2-chlorocyclohexanone becomes the preferred reaction pathway to produce compound **3** serving as a main product,[17] while little compound **1** could be isolated (Table 1, entry 4). Owing to high ionizing power and low nucleophilicity, fluorinated alcohols, such as trifluoroethanol (TFE) and hexafluoro isopropanol (HFIP) are the best solvents for generation of oxyallyl cations.[18] So the fluorinated alcohols were then evaluated (Table 1, entries 5-11). In the reaction condition of Na_2CO_3 in TFE at room temperature, a clean reaction with high yield is realized (Table 1, entry 5). Higher temperature (Table 1, entry 6) or higher ionizing power (Table 1, entry 7) is benefitial for the reaction rate rather than the reaction efficiency. With TFE as the solvent, the choice of bases showes significant effect on the reaction cleanliness and yield. Organic bases, i.e. pyrrolidine and Et_3N, effectively initiate the reaction (Table 1, entries 10-11). However, when a relatively weak base, i.e. sodium bicarbonate, was chosen, nearly no reaction takes place (Table 1, entry 8). On the contrary, when a strong base, i.e. NaOH, was used, the reaction becomes messy with formation of Favorskii rearrangement adduct **5** among side products (Table 1, entry 9). [19]

Table 1. Model Reaction Optimization.[a]

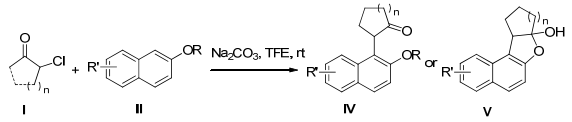


Entry	Base	Solvent	Temperature (^{0}C)	Time (h)	Product (yield %)[b]
1	Na_2CO_3	solvents[c]	25	48	**1** (<5)
2	Na_2CO_3	xylene	25	48	**1** (<5)
3	Na_2CO_3	xylene	140	24	**1/2** (42/33)[d]
4	Na_2CO_3	H_2O	25	12	**1/3** (8/85)[d]
5	Na_2CO_3	TFE	25	12	**1** (91)[e]
6	Na_2CO_3	TFE	80	10	**1/4** (88/5)[d]
7	Na_2CO_3	HFIP	25	10	**1** (86)[e]
8	$NaHCO_3$	TFE	25	48	**1** (<5)
9	NaOH	TFE	25	4	**1/5** (48/5)[d]
10	pyrrolidine	TFE	25	48	**1/4** (71/6)[d]
11	Et_3N	TFE	25	48	**1/4** (80/6)[d]

[a] Reaction condition: **I** (0.5 mmol), **II** (0.5 mmol), base (0.6 mmol) in solvent (1 mL). [b] Isolated yields. [c] DMF, DMSO, THF, Et_2O, toluene, CH_2Cl_2, EtOAc, CH_3CN. [d] Yield of minor product was determined by crude NMR integration. [e] No other product was isolated. TFE = 2,2,2-trifluoroethanol; HFIP = hexafluoro-2-propanol.

Then, we examined various naphthols in reaction with 2-chlorocyclopentanone. Both protected and unprotected β-naphthols are alkylated at C-1 to produce compounds **IV** or **V** in moderate to excellent yields (Table 2, entries **1-6**). Bromo-substituted naphthols show excellent outcomes no matter what the substitution position of bromo is (Table 2, entries **3-5**). For α-naphthols, the reaction shows excellent chemoselectivity, naphthols are regioselectively alkylated at C-4, no C-2 alkylated product is obtained (Table 2, entries **7-8**). To further examine the regioselectivity, 4-chloro-1-naphthol was selected as substrate (Table 2, entry 8). No C-2 alkylated product is detected under our standard reaction conditions. Most of the starting material is recovered after reacting for twelve hours.

Table 2. Addition of Naphthols to α-Halo Alkanones.[a,b]



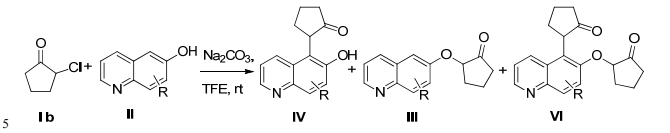
Entry	Haloketone	Naphthol	Product	Yield
1	Ia	IIa	1	91% (dr>20:1)[c]
2	Ib	IIa	6	92% (dr=10:1)[c]
3	Ib	IIb	7	93% (dr=10:1)[c]
4	Ib	IIc	8	93% (dr=8:1)[c]
5	Ib	IId	9	94% (dr=8:1)[c]
6	Ib	IIe	10	88%
7	Ib	IIf	11	89%[d,e]
8	Ib	IIg	12	--[f]
9	Ib	IIh	13	87%[d,g]
10	Ic	IIi	14	11%[h,i]

[a] **I** (0.5 mmol), **II** (0.5 mol), Na_2CO_3 (0.6 mmol) in TFE (1 mL). [b] Isolated yields. [c] Ratio of diastereomers was determined by integration of benzylic proton signals in ^{1}H NMR spectrum. [d] No another isomer was detected. [e] The structure is confirmed by 2D NMR spectra (COSY, HMQC and HMBC). [f] No desired product is obtained. [g] The ^{1}H and ^{13}C NMR spectra are the same as that reported in literature[4a]. [h] **I c** (1.0 mmol), **II i** (0.5 mol), Na_2CO_3 (1.1mmol) in HFIP (1 mL). [i] The ether product (**15**), 2-(naphthalen-2-yloxy)pentan-3-one , is also isolated.

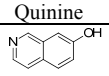
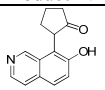
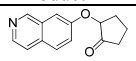
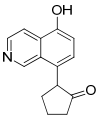
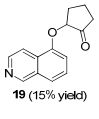
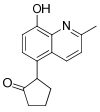
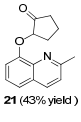
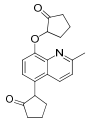
Noncyclic haloketones were also examined. Unfortunately, when 1,1-dichloropropan-2-one or 1,3-dichloropropan-2-one was used, we found most of 2-naphthol remains unreacted. Similarly, for substrates 1,3-dibromo-3-methylbutan-2-one and 1-chloro-1,3-diphenylpropan-2-one, a small amount of 2-naphthol is

consumed without isolating any desired products. Only 2-bromo-3-pentanone produces a little condensed product **14** in the presence of excessive halo ketone (Table 2, entry 10).

Table 3. Addition of Hydroxylquinines to α-Chloropentanone. [a]



I b **II** **IV** **III** **VI**

Entry	Quinine	Product **IV**	Product **III**	Product **VI**
1 [b]	 **II j**	 **16** (33% yield)	 **17** (16% yield) [d]	—— [e]
2 [b]	 **II k**	 **18** (36% yield)	 **19** (15% yield)	—— [e]
3 [c]	 **II l**	 **20** (13% yield)	 **21** (43% yield)	 **22** (11% yield) [f,g] (dr=1:1)

[a] Isolated yield. [b] **I** (0.5 mmol), **II** (0.5 mol), Na_2CO_3 (0.6 mmol) in TFE (1 mL). [c] **I** (1.5 mmol), **II** (0.5 mol), Na_2CO_3 (1.6 mmol) in TFE (1 mL). [d] Yield of product **15** was determined by integration of proton signals in ^{1}H NMR spectrum. [e] Not detected. [f] Ratio of diastereomers was determined by integration of proton signals in ^{1}H NMR spectrum. [g] The structure is confirmed by 2D NMR spectra (COSY, HMQC and HMBC).

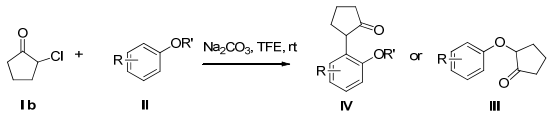
To further explore the reaction scope, we screened different hydroxyquinolines, wherein 5-hydroxy and 7-hydroxy isoquinoline give acceptable yield of α-aryl cycloalkanones along with their corresponding ether products **III** (Table 3, entries 1 & 2). It should be noted that product **16** is the ketone isomer, not the hemiketal form. When excessive halo ketone **I b** was used, disubstituted product **22** is obtained as a mixture of stereoisomers (Table 3, entry 3).

We think that the reaction mechanism is just like that of Friedel–Crafts alkylation, so we used different types of aromatic compounds to react with 2-chlorocyclopentanone. We found that an electron-rich system of aromatic compounds plays an important role in the reaction efficiency. When phenol (**II m)** was used as a substrate, only ether product **23** is obtained (Table 4, entry 1). For the reaction of substrates **II n** and **II o**, the main products are respectively ether **24** and amine **25,** both of which are accompanied with a few other complex compounds. However, when more electron-rich compound **II p** was used, nearly quantitative reaction takes place. After simple filtrations followed by evaporizations, analytically pure product **26** is obtained (Table 4, entry 4). The reaction efficiency is dramatically lowered if there is an electron-withdrawing group on the arene ring. Moderate yield is obtained in the presence of substrate **II q**, while no reaction occurs for substrate **II r** (Table 4, entries 5-6).

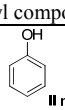
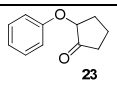
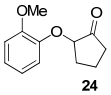
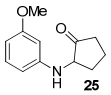
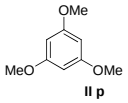
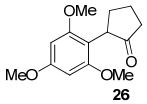
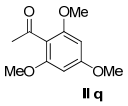
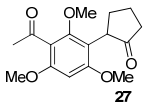
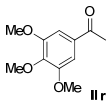
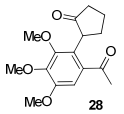
Conclusions

We developed a high efficient and practical method for chemoselective coupling of α-halo cycloalkanones with electon-rich aromatic compounds, especially naphthols, at room temperature. No protection of naphthol substrates and no catalysts are required in our protocol. α-Aryl cycloalkanone **26** is obtained in quantitative yield, and analytically pure products are obtained after simple filtrations followed by evaporations. An electron-rich system of aryl compounds plays an important role in the reaction efficiency. Further research for the interrupted cycloaddition reaction of oxyallyl cations is being pursued in our lab.

Table 4. Addition of Aryl Compounds to α-Chloropentanone. [a,b]



I b **II** **IV** **III**

Entry	Aryl compounds	Product	Yield
1	 **II m**	 **23**	46%
2	 **II n**	 **24**	38%
3	 **II o**	 **25**	32%
4	 **II p**	 **26**	99%
5	 **II q**	 **27**	48%
6	 **II r**	 **28**	--[c]

[a] **I** (0.5 mmol), **II** (0.5 mol), Na_2CO_3 (0.6 mmol) in TFE (1 mL). [b] Isolated yields. [c] Not detected.

Experimental Section

General Information

Nuclear magnetic resonance spectra (^{1}H and ^{13}C) were recorded on a JEOL ECA400 (400 MHz), Bruker AV300 (300 MHz), AV400 (400 MHz), AV500 (500 MHz) or BBFO400 (400 MHz) spectrometers. ^{1}H NMR chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or DMSO (δ = 2.50, singlet), and the splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). High resolution mass spectral analysis (HRMS) was performed on Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation). Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp or

chemical stains like $KMnO_4$ and 2,4-dinitrophenyl hydrazine solutions.

Commercially available materials purchased from Alfa Aesar or Aldrich were used as received, except α-haloketones that were further purified via distillation or column chromatography over silica gel prior to use. Some of the α-chloroketones (2-bromo-3-pentanone and 1,3-dibromo-3-methylbutan-2-one) were prepared using literature method.[20]

Typical procedure for metal-free coupling of aromatic compounds with α-haloketones.

A 4 mL vial equipped with a magnetic stir bar was charged with fresh distilled α-halo ketone **I** (0.5-1.5 mmol), aromatic compound **II** (0.5 mmol) and TFE or HFIP (1.0 mL). Anhydrous Na_2CO_3 (0.6 -1.6 mmol) was added to the reaction mixture and stirred at room temperature. After completion of the reaction (about 12-24h, monitored by TLC or crude ^1H NMR analysis), the reaction mixture was filtered through a celite pad using Et_2O or CH_2Cl_2 and the filtrate was concentrated under reduced pressure. The crude residue was further purified by silica gel flash chromatography using EtOAc/hexanes as eluent to give pure products. In some cases, analytically pure products could be obtained merely by simple filtration and evaporation under reduced pressure.

7a,8,9,10,11,11a-hexahydronaphtho[2,1-b]benzofuran-7a-ol (1): White solid, Mp: 136-137 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.81 (d, J = 8.3 Hz, 1H), 7.69 (t, J = 9.2 Hz, 2H), 7.45 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 7.31 (ddd, J = 8.1, 6.8, 1.1 Hz, 1H), 7.17 (d, J = 8.7 Hz, 1H), 3.41 (dd, J = 10.2, 6.8 Hz, 1H), 3.26 (d, J = 3.1 Hz, 1H), 2.46 – 2.27 (m, 2H), 1.90 (ddd, J = 14.1, 12.3, 5.2 Hz, 1H), 1.85 – 1.74 (m, 1H), 1.64 – 1.28 (m, 4H), 1.15 (dddd, J = 14.0, 12.0, 10.3, 3.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.23, 130.61, 129.91, 129.04, 126.72, 124.64, 123.18, 122.79, 113.05, 109.78, 46.62, 33.37, 30.86, 21.79, 21.76 ppm. HRMS (ESI) calcd for $C_{16}H_{17}O_2$ $(M+1)^+$: 241.1229, Found: 241.1233.

2-(naphthalen-2-yloxy)cyclohexanone (2)[11a]: White solid, Mp: 104-106 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.66 (dd, J = 2.8, 9.2 Hz, 2H), 7.58 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.2 Hz, 1H), 7.23 (t, J = 7.2 Hz, 1H), 7.10 (dd, J = 2.4, 8.8 Hz, 1H), 6.93 (d, J = 2.0 Hz, 1H), 4.72−4.65 (m, 1H), 2.59−2.52 (m, 1H), 2.34−2.21 (m, 2H), 2.01−1.89 (m, 3H), 1.74−1.62 (m, 2H) ppm.

2-hydroxycyclohexanone (3)[21]: White solid; Mp:110-112 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ = 4.13 (dd, J = 11.9, 7.0 Hz, 1H), 3.64 (s, 1H), 2.57 (ddt, J = 13.8, 4.3, 2.3 Hz, 1H), 2.52 – 2.43 (m, 1H), 2.36 (tdd, J = 13.7, 6.4, 1.5 Hz, 1H), 2.16 – 2.06 (m, 1H), 1.96 – 1.84 (m, 1H), 1.81 – 1.68 (m, 1H), 1.68 – 1.58 (m, 2H), 1.56 – 1.40 (m, 2H) ppm.

2-(2,2,2-trifluoroethoxy)cyclohexanone (4)[22]: Corlorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ = 4.20 (dq, J = 12.7, 9.0 Hz, 1H), 4.01 (dd, J = 10.4, 5.8 Hz, 1H), 3.76 (dq, J = 12.7, 8.5 Hz, 1H), 2.58 – 2.45 (m, 1H), 2.30 (dtd, J = 12.3, 5.4, 2.4 Hz, 2H), 2.08 – 1.88 (m, 2H), 1.85 – 1.62 (m, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.47, 128.00, 125.23, 122.45, 119.68, 83.86, 67.88, 67.54, 67.20, 66.86, 40.53, 34.23, 27.25, 23.22 ppm. HRMS (ESI) calcd for $C_8H_{12}F_3O_2$ $(M+1)^+$: 197.0789, Found: 197.0784.

8,9,10,10a –tetrahydro- 7aH -cyclopenta [b] naphtha [1,2-d] furan7a-ol (6): White solid; Mp: 128-129 ℃; Further purification could be realized by recrystallization using ethanol. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.80 (d, J = 8.2 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.46 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 7.31 (ddd, J = 8.1, 6.9, 1.1 Hz, 1H), 7.09 (d, J = 8.8 Hz, 1H), 3.84 (dd, J = 9.3, 3.0 Hz, 1H), 3.33 (s, 1H), 2.49 – 2.19 (m, 2H), 2.11 (ddd, J = 13.0, 10.9, 6.4 Hz, 1H), 1.93 (dddd, J = 8.6, 6.5, 5.4, 3.3 Hz, 1H), 1.81 (dtd, J = 9.6, 6.3, 3.0 Hz, 1H), 1.72 – 1.58 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl3) δ = 155.38, 130.48, 129.62, 129.35, 128.96, 126.78, 123.01, 122.44, 121.74, 121.24, 111.83, 51.48, 40.03, 32.71, 24.84 ppm. HRMS (ESI) calcd for $C_{15}H_{15}O_2$ $(M+1)^+$: 227.1072, Found: 227.1069.

3-bromo-8,9,10,10a-tetrahydro-7aH-cyclopenta[b]naphtha [1,2-d]furan-7a-ol (7): White solid; Mp: 86-87 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.94 (s, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.49 (q, J = 8.7 Hz, 2H), 7.08 (d, J = 8.8 Hz, 1H), 3.79 (d, J = 8.9 Hz, 1H), 3.60-3.30 (brs, 1H), 2.48 – 2.17 (m, 2H), 2.10 (dd, J = 18.1, 11.9 Hz, 1H), 1.94 – 1.73 (m, 2H), 1.74 – 1.52 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.76, 130.87, 130.72, 130.03, 128.93, 128.53, 124.11, 121.86, 121.58, 116.51, 112.87, 51.38, 40.07, 32.78, 24.87 ppm. HRMS (ESI) calcd for $C_{15}H_{14}BrO_2$ $(M+1)^+$: 306.1745, Found: 306.1744.

2-bromo-8,9,10,10a-tetrahydro-7aH-cyclopenta[b]naphtha [1,2-d]furan-7a-ol (8): Colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.75 (s, 1H), 7.65 (dd, J = 8.6, 3.6 Hz, 2H), 7.37 (dd, J = 8.7, 1.8 Hz, 1H), 7.07 (dd, J = 8.7, 3.4 Hz, 1H), 3.81 – 3.70 (m, 1H), 3.50-3.40 (brs, 1H), 2.49 – 2.34 (m, 1H), 2.34 – 2.20 (m, 1H), 2.19 – 2.04 (m, 1H), 1.94 – 1.72 (m, 2H), 1.64 (dq, J = 10.6, 6.3 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.09, 131.62, 130.61, 129.39, 127.93, 126.38, 124.57, 122.02, 121.22, 120.68, 112.18, 51.13, 40.02, 32.70, 24.80 ppm. HRMS (ESI) calcd for $C_{15}H_{14}BrO_2$ $(M+1)^+$: 306.1745, Found: 306.1742.

6-bromo-8,9,10,10a-tetrahydro-7aH-cyclopenta[b]naphtha [1,2-d]furan-7a-ol (9): Colorless oil, 94% yield. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.90 (s, 1H), 7.71 (t, J = 10.8 Hz, 1H), 7.60 (d, J = 8.3 Hz, 1H), 7.47 (dd, J = 8.1, 7.1 Hz, 1H), 7.33 (dd, J = 8.1, 7.0 Hz, 1H), 3.99 – 3.88 (m, 1H), 3.51 (d, J = 10.4 Hz, 1H), 2.52 – 2.35 (m, 2H), 2.19 – 2.08 (m, 1H), 1.99 – 1.88 (m, 1H), 1.83 (ddd, J = 12.7, 6.4, 3.5 Hz, 1H), 1.76 – 1.64 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 152.39, 131.06, 130.53, 129.43, 128.02, 127.00, 123.93, 122.92, 122.61, 122.23, 104.75, 52.34, 40.20, 32.80, 24.94 ppm. HRMS (ESI) calcd for $C_{15}H_{14}BrO_2$ $(M+1)^+$: 306.1745, Found: 306.1740.

2-(2-methoxynaphthalen-1-yl)cyclopentanone (10): White solid; Mp: 92-93 ℃;. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.79 (dd, J = 8.5, 4.4 Hz, 2H), 7.47 (t, J = 7.3 Hz, 1H), 7.39 – 7.30 (m, 1H), 7.30 – 7.22 (m, 2H), 3.85 (s, 3H), 2.60 (ddd, J = 18.4, 11.9, 8.6 Hz, 1H), 2.45 (ddd, J = 19.3, 12.4, 8.0 Hz, 2H), 2.33 – 2.10 (m, 2H), 2.09 – 1.84 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 219.87, 129.62, 128.98, 128.76, 126.69, 123.51, 122.48, 114.12, 56.07, 47.79, 38.22, 30.83, 22.08 ppm. HRMS (ESI) calcd for $C_{15}H_{17}O_2$ $(M+1)^+$: 241.1229, Found: 241.1230

2-(1-hydroxynaphthalen-4-yl)cyclopentanone (11): Yellow solid; Mp: 102-103 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.22 – 8.08 (m, 1H), 7.78 (dd, J = 8.4, 3.4 Hz, 1H), 7.57 – 7.34 (m, 2H), 6.96 (dd, J = 9.8, 7.9 Hz, 1H), 6.59 (dd, J = 15.7, 7.8 Hz, 1H), 5.99 (brs, 1H), 4.06 – 3.88 (m, 1H), 2.71 – 2.53 (m, 2H), 2.53 – 2.36 (m, 1H), 2.30 – 2.10 (m, 2H), 2.10 – 1.89 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 221.02, 151.09, 132.87, 127.01, 126.41, 125.37, 125.12, 124.74, 123.33, 122.64, 108.31, 52.34,

39.10, 32.48, 21.06 ppm. HRMS (ESI) calcd for $C_{16}H_{17}O_2$ $(M+1)^+$: 241.1229, Found: 241.1231

2- (4- methoxy naphthalen -2-yl) cyclopentanone (13)[4a]: Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.31 (dd, J = 8.3, 1.2 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.60 – 7.38 (m, 2H), 7.14 (d, J = 8.0 Hz, 1H), 6.77 (d, J = 8.0 Hz, 1H), 4.01-3.93 (m, 1H), 3.98 (s, 3H), 2.68 – 2.51 (m, 2H), 2.51 – 2.35 (m, 1H), 2.30 – 2.12 (m, 2H), 2.04 (dddd, J = 14.1, 12.2, 7.1, 3.3 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 219.12, 154.76, 132.88, 127.33, 126.58, 126.16, 125.12, 125.02, 123.46, 122.78, 103.47, 55.54, 52.03, 38.94, 32.45, 21.08 ppm. HRMS (ESI) calcd for $C_{15}H_{17}O_2$ $(M+1)^+$: 241.1229, Found: 241.1234.

2-ethyl-1-methyl-1,2-dihydronaphtho[2,1-b] furan-2-ol (14): Freshly distilled 2-chloro-3-pentanone (1.0 mmol) was added into the solution of 2-naphthol (0.5 mmol), anhydrous Na_2CO_3 (0.6 mmol) and HFIP (1.0 mL). The mixture was stirred at r.t. over two days, and then filtered through a celite pad using CH_2Cl_2. The filtrate was concentrated under reduced pressure and separated by silica gel flash chromatography to give two pure products. Product **13** was white solid, Mp: 101-103 ℃, 11% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.38 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.66-7.50 (m, 3H), 7.44(t, J = 7.6 Hz, 1H), 2.84 (dd, J = 15.2, 7.6 Hz, 2H), 2.57 (s, 3H), 1.33 (t, J = 7.6Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.04, 157.26, 130.32, 128.43, 127.51, 125.75, 124.22, 124.10, 123.09, 122.21, 121.72, 113.01, 27.90, 25.00, 23.93 ppm. HRMS (ESI) calcd for $C_{17}H_{19}O_2$ $(M+1)^+$: 211.1123, Found: 211.1125.

2-(naphthalen-2-yloxy)pentan-3-one (15): Brown oil, 7% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.81 – 7.72 (m, 2H), 7.69 (d, J = 8.2 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.39 – 7.30 (m, 1H), 7.17 (dd, J = 8.9, 2.5 Hz, 1H), 6.98 (d, J = 2.4 Hz, 1H), 4.80 (q, J = 6.9 Hz, 1H), 2.73 (dq, J = 18.9, 7.2 Hz, 1H), 2.47 (dq, J = 18.9, 7.3 Hz, 1H), 2.20 – 2.04 (m, 1H), 1.56 (d, J = 7.0 Hz, 3H), 1.01 (t, J = 7.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 213.20, 155.48, 134.33, 129.94, 129.26, 127.63, 126.89, 126.63, 124.10, 118.75, 107.42, 79.13, 29.89, 18.07, 7.11 ppm. HRMS (ESI) calcd for $C_{15}H_{17}O_2$ $(M+1)^+$: 229.1229, Found: 229.1224.

2-(7-hydroxyisoquinolin-8-yl)cyclopentanone (16): Yellow solid; Mp: 92-93 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.28 (s, 1H), 8.50 (d, J = 5.8 Hz, 1H), 8.14 (d, J = 5.8 Hz, 1H), 7.16 (dd, J = 17.2, 8.2 Hz, 1H), 7.07 – 6.96 (m, 1H), 4.14 – 4.02 (m, 1H), 2.71 – 2.52 (m, 2H), 2.52 – 2.34 (m, 1H), 2.22 (tt, J = 17.4, 6.0 Hz, 2H), 2.12 – 2.03 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 218.72, 152.19, 147.69, 140.26, 129.17, 128.13, 127.12, 126.39, 116.83, 112.65, 51.10, 38.65, 32.18, 20.98 ppm. HRMS (ESI) calcd for $C_{14}H_{14}NO_2$ $(M+1)^+$: 228.1025, Found: 228.1022.

2-(5-hydroxyisoquinolin-8-yl)cyclopentanone (18): White solid, Mp: 103-104 ℃, 36% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.92 (s, 1H), 8.15 (d, J = 5.6 Hz, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.45 (d, J = 5.6 Hz, 1H), 7.21 (d, J = 5.6 Hz, 1H), 3.87 (t, J = 6.8 Hz, 1H), 2.43 – 2.34 (m, 2H), 2.23 – 2.18 (m, 1H), 1.84 – 1.81 (m, 2H), 1.71 -1.52 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 205.73, 157.01, 146.54, 138.91, 131.63, 130.83, 130.24, 127.65, 121.76, 108.57, 50.42, 39.91, 33.32, 24.56 ppm. HRMS (ESI) calcd for $C_{14}H_{14}NO_2$ $(M+1)^+$: 228.1025, Found: 228.1026.

2-(isoquinolin-5-yloxy)cyclopentanone (19): Colorless oil, 15% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.14 (s, 1H), 8.42 (d, J = 5.7 Hz, 1H), 7.75 (d, J = 9.0 Hz, 1H), 7.59 (d, J = 5.7 Hz, 1H), 7.42 (dd, J = 8.9, 2.5 Hz, 1H), 7.34 (d, J = 2.4 Hz, 1H), 4.79 (t, J = 8.4 Hz, 1H), 2.70 – 2.57 (m, 1H), 2.51 – 2.31 (m, 2H), 2.31 – 2.17 (m, 1H), 2.13 – 1.88 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 213.42, 156.68, 151.17, 141.44, 131.80, 129.63, 128.24, 123.89, 120.26, 107.63, 79.54, 35.28, 29.42, 17.33 ppm. HRMS (ESI) calcd for $C_{14}H_{14}NO_2$ $(M+1)^+$: 228.1025, Found: 228.1027.

2-(8-hydroxy -2-methylquinolin -5-yl) cyclopentanone (20): With large excess amount of α-haloketone, three products were obtained. Product **19** was white solid, Mp: 114-115 ℃, 15% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 (d, J = 8.7 Hz, 1H), 7.32 (d, J = 8.7 Hz, 1H), 7.15 (d, J = 7.9 Hz, 1H), 7.08 (d, J = 7.9 Hz, 1H), 3.88 (dd, J = 10.4, 8.7 Hz, 1H), 2.72 (s, 3H), 2.63 – 2.48 (m, 2H), 2.41 (ddd, J = 19.1, 10.4, 8.6 Hz, 1H), 2.32 – 2.13 (m, 2H), 2.13 – 1.95 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 218.07, 156.53, 150.89, 138.08, 133.04, 125.50, 124.98, 124.87, 122.50, 109.19, 51.27, 38.51, 31.50, 24.73, 21.04 ppm. HRMS (ESI) calcd for $C_{15}H_{16}NO_2$ $(M+1)^+$: 242.1181, Found: 242.1177.

2-((2-methylquinolin-8-yl)oxy)cyclopentanone (21): White solid, Mp: 87-89 ℃, 43% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (d, J = 8.4 Hz, 1H), 7.47 – 7.33 (m, 2H), 7.33 – 7.28 (m, 1H), 7.22 (dd, J = 7.5, 1.2 Hz, 1H), 5.09 – 4.89 (m, 1H), 2.77 (s, 3H), 2.72 – 2.58 (m, 1H), 2.46 – 2.36 (m, 1H), 2.28 (dddd, J = 14.1, 10.3, 6.6, 4.7 Hz, 2H), 2.13 – 1.79 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 214.01, 158.31, 153.25, 140.07, 136.16, 127.82, 125.49, 122.51, 121.08, 112.90, 81.11, 35.38, 29.37, 25.60, 17.20 ppm. HRMS (ESI) calcd for $C_{15}H_{16}NO_2$ $(M+1)^+$: 242.1181, Found: 242.1180.

2-((2-methyl -5- (2-oxocyclopentyl) quinolin-8-yl)oxy) cyclo pentanone (22): White solid, Mixture of two diastereomers (dr = 1:1), Mp: 76-79 ℃, 11% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 (dd, J = 11.5, 8.8 Hz, 1H), 7.31 (dd, J = 8.7, 3.2 Hz, 1H), 7.20 – 7.08 (m, 2H), 5.07 – 4.82 (m, 1H), 3.92 (dd, J = 18.8, 8.8 Hz, 1H), 2.76 (d, J = 2.1 Hz, 3H), 2.67 – 2.49 (m, 3H), 2.49 – 2.33 (m, 3H), 2.33 – 2.13 (m, 4H), 2.13 – 1.98 (m, 1H), 1.98 – 1.80 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 218.07, 217.80, 214.13, 213.94, 157.91, 157.86, 152.57, 152.51, 140.74, 140.52, 132.69, 132.52, 128.47, 128.26, 126.70, 126.58, 124.15, 123.85, 122.30, 122.21, 113.27, 112.37, 81.38, 81.16, 51.47, 51.07, 38.71, 38.61, 35.44, 35.39, 31.80, 31.69, 29.40, 25.40, 21.04, 21.02, 17.22 ppm. HRMS (ESI) calcd for $C_{20}H_{22}NO_3$ $(M+1)^+$: 324.1600, Found: 324.1603.

2-phenoxycyclopentanone (23)[11a]: White solid; Mp: 69-71℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.28 (t, J =8.1 Hz, 2H) , 6.96−7.00 (m, 3H), 4.58−4.63 (m, 1H) ,2.46−2.55 (m, 1H) , 2.33−2.41 (m, 2H), 2.11−2.19 (m, 1H),1.89−2.04 (m, 2H).

2-(2-methoxyphenoxy)cyclopentanone (24): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.08 – 6.94 (m, 2H), 6.94 – 6.82 (m, 2H), 4.60 (dd, J = 9.2, 8.0 Hz, 1H), 3.85 (s, 3H), 2.51 – 2.40 (m, 1H), 2.35 (dt, J = 9.5, 6.8 Hz, 2H), 2.21 – 2.08 (m, 1H), 2.10 – 1.98 (m, 1H), 1.95 – 1.76 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 213.77, 150.31, 147.32, 122.81, 120.82, 117.09, 112.34, 81.00, 55.95, 35.24, 29.53, 17.20 ppm. HRMS (ESI) calcd for $C_{12}H_{15}O_3$ $(M+1)^+$: 207.1021, Found: 207.1024.

2-((3- methoxyphenyl) amino) cyclopentanone (25): White solid; Mp: 121-122 ℃ ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.10 (t, J = 8.1 Hz, 1H), 6.37 – 6.27 (m, 2H), 6.22 (t, J = 2.3 Hz, 1H), 4.42 (s, 1H), 3.77 (s, 3H), 3.69 (dd, J = 11.4, 7.9 Hz, 1H), 2.76 (ddd, J

= 12.5, 7.6, 6.3 Hz, 1H), 2.56 – 2.41 (m, 1H), 2.21 (dd, *J* = 19.5, 9.4 Hz, 1H), 2.17 – 2.07 (m, 1H), 1.99 – 1.84 (m, 1H), 1.58 (qd, *J* = 12.3, 6.8 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 215.63, 160.86, 148.85, 130.09, 106.57, 103.21, 99.66, 61.96, 55.15, 34.68, 31.83, 17.79 ppm. HRMS (ESI) calcd for $C_{12}H_{16}NO2$ $(M+1)^+$: 206.1181, Found: 206.1180.

2-(2,4,6- trimethoxyphenyl) cyclopentanone (26): Freshly distilled α-chlorocyclopentanone (0.5 mmol) was added into the solution of 1,3,5-trimethoxybenzene (0.5 mmol), anhydrous Na_2CO_3 (0.6 mmol) and TFE (1.0 mL). After stirred at r.t. for 8h, a white solid was obtained merely by filtration through a celite pad using dicholoromethane and evaporation under reduced pressure. Mp: 117-118 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.12 (s, 2H), 3.79 (s, 3H), 3.74 (s, 6H), 3.68 (dd, *J* = 11.0, 8.7 Hz, 1H), 2.37 (dd, *J* = 9.6, 5.5 Hz, 2H), 2.28 – 2.17 (m, 1H), 2.09 (ddt, *J* = 16.8, 11.7, 4.2 Hz, 2H), 1.93 – 1.75 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 220.63, 160.28, 158.55, 109.34, 91.18, 55.61, 55.35, 45.06, 38.05, 29.92, 21.82 ppm. HRMS (ESI) calcd for $C_{14}H_{19}O_4$ $(M+1)^+$: 251.1283, Found: 251.1280.

2- (3-acetyl- 2,4,6- trimethoxyphenyl) cyclopentanone (27): White solid, Mp: 86-87 ℃, 48% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.25 (s, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.67 (s, 3H), 3.57 (dd, *J* = 10.6, 9.0 Hz, 1H), 2.50 (s, 3H), 2.38 (dd, *J* = 9.8, 4.5 Hz, 2H), 2.31 – 2.20 (m, 1H), 2.20 – 2.08 (m, 2H), 1.95 – 1.81 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 219.98, 201.97, 159.24, 157.22, 157.11, 114.77, 91.82, 55.90, 55.63, 45.66, 37.96, 32.51, 30.25, 21.72 ppm. HRMS (ESI) calcd for $C_{16}H_{21}O_5$ $(M+1)^+$: 293.1389, Found: 293.1390

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Notes and references

1. (a) Mousseron, M. J., *US2882201A* 1959; (b) Campaigne, E.; Weddleton, R. F., *J. Heterocycl. Chem.* 1986, **23**, 1625-1628.
2. (a) Martínez, A.; Fernández, M.; Estévez, J. C.; Estévez, R. J.; Castedo, L., *Tetrahedron* 2005, **61**, 1353-1362; (b) Chatterjea, J. N.; Banerji, K. D., *Chem. Ber.* 1965, **98**, 2738-2741; (c) Callighan, R. H.; Morgan, M. S., *J. Org. Chem.* 1964, **29**, 983-985; (d) Chatterjea, J. N., *Experientia* 1956, **12**, 371-372; (e) Robinson, R. A.; Mosettig, E., *J. Am. Chem. Soc.* 1939, **61**, 1148-1151.
3. (a) Kawamura, M.; Chiba, S.-s., *EP2436679A1* 2009; (b) Mitschke, U.; Bauerle, P., *J. Mater. Chem.* 2000, **10**, 1471-1507; (c) Salbeck, J., *Ber.Bunsenges.Phys. Chem.* 1996, **100**, 1667-1677; (d) Campaigne, E.; Osborn, S. W., *J. Heterocycl. Chem.* 1968, **5**, 655-661; (e) Chaitanya, T. K.; Nagarajan, R., *Org. Biomol. Chem.* 2011, **9**, 4662-4670.
4. (a) Góra, M.; Łuczyński, M. K.; Sepioł, J. J., *Synthesis* 2005, **2005**, 1625-1630; (b) Rettig, M.; Sigrist, A.; Rétey, J., *Helv. Chim. Acta* 2000, **83**, 2246-2265; (c) Nachtsheim, C. M.; Frahm, A. W., *Arch. Pharm.* 1989, **322**, 187-197.
5. (a) Belapure, S. A.; Beamer, Z. G.; Bartmess, J. E.; Campagna, S. R., *Tetrahedron* 2011, **67**, 9265-9272; (b) Prabhakar, K. R.; Veerapur, V. P.; Bansal, P.; Vipan, K. P.; Reddy, K. M.; Barik, A.; Reddy, B. K. D.; Reddanna, P.; Priyadarsini, K. I.; Unnikrishnan, M. K., *Biorg. Med. Chem.* 2006, **14**, 7113-7120; (c) Kundu, S. K.; Pramanik, *Indian. J .chem. Sec. B* 2004, **43**, 595-603; (d) Kundu, S. K.; Patra, A.; Pramanik, A., *Indian. J .chem. Sec. B* 2004, **43**, 604-611; (e) Das, S.; Pramanik, A.; Fröhlich, R.; Patra, A., *Tetrahedron* 2004, **60**, 10197-10205.
6. (a) Motti, E.; Della Ca, N.; Xu, D.; Armani, S.; Aresta, B. M.; Catellani, M., *Tetrahedron* 2013, **69**, 4421-4428; (b) Bhat, V.; Mackay, J. A.; Rawal, V. H., *Org. Lett.* 2011, **13**, 3214-3217; (c) Sastry Mudiganti, N. V.; Claessens, S.; De Kimpe, N., *Tetrahedron* 2009, **65**, 1716-1723; (d) Guo, X.; Yu, R.; Li, H.; Li, Z., *J. Am. Chem. Soc.* 2009, **131**, 17387-17393; (e) DeMartino, M. P.; Chen, K.; Baran, P. S., *J. Am. Chem. Soc.* 2008, **130**, 11546-11560; (f) Christoffers, J.; Werner, T.; Frey, W.; Baro, A., *Eur. J. Org. Chem.* 2003, **2003**, 4879-4886.
7. (a) Alemán, J.; Richter, B.; Jørgensen, K. A., *Angew. Chem. Int. Ed.* 2007, **46**, 5515-5519; (b) Kobbelgaard, S.; Bella, M.; Jørgensen, K. A., *J. Org. Chem.* 2006, **71**, 4980-4987.
8. Pietruszka, J.; Wang, C., *Green Chemistry* 2012, **14**, 2402-2409.
9. Parnes, R.; Kshirsagar, U. A.; Werbeloff, A.; Regev, C.; Pappo, D., *Org. Lett.* 2012, **14**, 3324-3327.
10. (a) Osdene, T. S.; Russell, P. B., *J. Org. Chem.* 1966, **31**, 2646-2648; (b) Ebel, F., *Helv. Chim. Acta* 1929, **12**, 3-16.
11. (a) Bai, W.-J.; Xie, J.-H.; Li, Y.-L.; Liu, S.; Zhou, Q.-L., *Adv. Synth. Catal.* 2010, **352**, 81-84; (b) Murphy, J. A.; Commeureuc, A. G. J.; Snaddon, T. N.; McGuire, T. M.; Khan, T. A.; Hisler, K.; Dewis, M. L.; Carling, R., *Org. Lett.* 2005, **7**, 1427-1429; (c) Orovecz, O.; Kovács, P.; Kolonits, P.; Kaleta, Z.; Párkányi, L.; Szabó, É.; Novák, L., *Synthesis* 2003, **2003**, 1043-1048; (d) Lauktien, G.; Volk, F.-J.; Frahm, A. W., *Tetrahedron: Asymmetry* 1997, **8**, 3457-3466; (e) Dürbeck, H. W.; Frischkorn, C. G. B.; Hilpert, K., *Tetrahedron* 1971, **27**, 2927-2937; (f) Dirania, M. K. M.; Hill, J., *J. Chem. Soc. C:* 1969, 2144-2147; (g) Williamson, K. L.; Keller, R. T.; Fonken, G. S.; Szmuszkovicz, J.; Johnson, W. S., *J. Org. Chem.* 1962, **27**, 1612-1615; (h) Bordwell, F. G.; Carlson, M. W., *J. Am. Chem. Soc.* 1970, **92**, 3370-3377.
12. (a) Lohse, A. G.; Hsung, R. P., *Chem. Eur. J.* 2011, **17**, 3812-3822; (b) Harmata, M., *Chem. Commun.* 2010, **46**, 8886-8903; (c) Harmata, M., *Chem. Commun.* 2010, **46**, 8904-8922; (d) Foley, D. A.; Maguire, A. R., *Tetrahedron* 2010, **66**, 1131-1175; (e) Harmata, M., *Adv. Synth. Catal.* 2006, **348**, 2297-2306; (f) Battiste, M. A.; Pelphrey, P. M.; Wright, D. L., *Chem. Eur. J.* 2006, **12**, 3438-3447; (g) Huang, J.; Hsung, R. P., *ChemTracts* 2005, **18**, 207-214; (h) Tamaru, Y., *Eur. J. Org. Chem.* 2005, **2005**, 2647-2656; (i) Niess, B.; Hoffmann, H. M. R., *Angew. Chem. Int. Ed.* 2005, **44**, 26-29; (j) Hartung, I. V.; Hoffmann, H. M. R., *Angew. Chem. Int. Ed.* 2004, **43**, 1934-1949; (k) Harmata, M.; Rashatasakhon, P., *Tetrahedron* 2003, **59**, 2371-2395; (l) Harmata, M., *Acc. Chem. Res.* 2001, **34**, 595-605; (m) Rigby, J. H.; Pigge, F. C., *Organic Reactions* 1997, **51**, 351-478; (n) Harmata, M., *Tetrahedron* 1997, **53**, 6235-6280; (o) Mann, J., *Tetrahedron* 1986, **42**, 4611-4659; (p) Tidwell, T. T., *Angew. Chem. Int. Ed.* 1984, **23**, 20-32; (q) Hoffmann, H. M. R., *Angew. Chem.* 1984, **96**, 29-48; (r) Hoffmann, H. M. R., *Angew. Chem. Int. Ed.* 1984, **23**, 1-19; (s) Noyori, R.; Hayakawa, Y., *Organic Reactions* 1983, **29**, 163-344; (t) Noyori, R., *Acc. Chem. Res.* 1979, **12**, 61-66; (u) Takaya, H.; Makino, S.; Hayakawa, Y.; Noyori, R., *J. Am. Chem. Soc.* 1978, **100**, 1765-1777; (v) Hoffmann, H. M. R., *Angew. Chem. Int. Ed.* 1973, **12**, 819-835.
13. (a) Föhlisch, B.; Flogaus, R.; Henle, G. H.; Sendelbach, S.; Henkel, S., *Eur. J. Org. Chem.* 2006, **2006**, 2160-2173; (b) MaGee, D. I.; Godineau, E.; Thornton, P. D.; Walters, M. A.; Sponholtz, D. J., *Eur. J. Org. Chem.* 2006, **2006**, 3667-3680; (c) Föhlisch, B.; Korfant, H.; Meining, H.; Frey, W., *Eur. J. Org. Chem.* 2000, **2000**, 1335-1344; (d) Lo, B.; Lam, S.; Wong, W.-T.; Chiu, P., *Angew. Chem. Int. Ed.* 2012, **51**, 12120-12123.
14. (a) Kwon, Y.; McDonald, R.; West, F. G., *Angew. Chem. Int. Ed.* 2013, **52**, 8616-8619; (b) Bonderoff, S. A.; Grant, T. N.; West, F. G.; Tremblay, M., *Org. Lett.* 2013, **15**, 2888-2891; (c) Boudreau, J.; Courtemanche, M.-A.; Marx, V. M.; Jean Burnell, D.; Fontaine, F.-G., *Chem. Commun.* 2012, **48**, 11250-11252; (d) Lebœuf, D.; Gandon, V.; Ciesielski, J.; Frontier, A. J., *J. Am. Chem. Soc.* 2012, **134**, 6296-6308; (e) Ma, Z.-X.; He, S.; Song, W.; Hsung, R. P., *Org. Lett.* 2012, **14**, 5736-5739; (f) Spencer, W. T.; Levin, M. D.; Frontier, A. J., *Org. Lett.* 2010, **13**, 414-417; (g) Huang, J.; Lebœuf, D.; Frontier, A. J., *J. Am. Chem. Soc.* 2011, **133**, 6307-6317; (h) Grant, T. N.; Rieder, C. J.; West, F. G., *Chem. Commun.* 2009, 5676-5688; (i) Jin, T.; Yamamoto, Y., *Org. Lett.* 2008, **10**, 3137-3139; (j) Rieder, C. J.;

Fradette, R. J.; West, F. G., *Heterocycles* 2010, **80**, 1413-1427; (k) Marx, V. M.; Burnell, D. J., *J. Am. Chem. Soc.* 2010, **132**, 1685-1689; (l) Cao, P.; Sun, X.-L.; Zhu, B.-H.; Shen, Q.; Xie, Z.; Tang, Y., *Org. Lett.* 2009, **11**, 3048-3051; (m) Rieder, C. J.; Fradette, R. J.; West, F. G., *Chem. Commun.* 2008, 1572-1574; (n) Grant, T. N.; West, F. G., *J. Am. Chem. Soc.* 2006, **128**, 9348-9349; (o) White, T. D.; West, F. G., *Tetrahedron Lett.* 2005, **46**, 5629-5632; (p) Yungai, A.; West, F. G., *Tetrahedron Lett.* 2004, **45**, 5445-5448; (q) Bender, J. A.; Blize, A. E.; Browder, C. C.; Giese, S.; West, F. G., *J. Org. Chem.* 1998, **63**, 2430-2431.

15. (a) Harmata, M.; Huang, C.; Rooshenas, P.; Schreiner, Peter R., *Angew. Chem. Int. Ed.* 2008, **47**, 8696-8699; (b) Leitich, J.; Heise, I., *Eur. J. Org. Chem.* 2001, **2001**, 2707-2718.
16. a) Tang, Q.; Chen, X.; Tiwari, B.; Chi, Y. R., *Org. Lett.* 2012, **14**, 1922-1925; b) Vander Wal, M. N.; Dilger, A. K.; MacMillan, D. W. C. Chem. Sci., 2013, **4**, 3075-3079.
17. (a) Utsukihara, T.; Nakamura, H.; Watanabe, M.; Akira Horiuchi, C., *Tetrahedron Lett.* 2006, **47**, 9359-9364; (b) Aitken, D. J.; Gauzy, C.; Pereira, E., *Tetrahedron Lett.* 2004, **45**, 2359-2361; (c) Schmittel, M.; Röck, M., *Chem. Ber.* 1992, **125**, 1611-1620; (d) Bartlett, P. D.; Woods, G. F., *J. Am. Chem. Soc.* 1940, **62**, 2933-2938.
18. (a) Berkessel, A.; Adrio, J. A.; Hüttenhain, D.; Neudörfl, J. M., *J. Am. Chem. Soc.* 2006, **128**, 8421-8426; (b) Bégué, J.-P.; Bonnet-Delpon, D.; Crousse, B., *Synlett* 2004, **2004**, 18,29; (c) Schaal, H.; Haber, T.; Suhm, M. A., *J. of Phy. Chem. A* 1999, **104**, 265-274; (d) Middleton, W. J.; Lindsey, R. V., *J. Am. Chem. Soc.* 1964, **86**, 4948-4952.
19. (a) Föhlisch, B.; Franz, T.; Kreiselmeier, G., *Eur. J. Org. Chem.* 2005, **2005**, 4687-4698; (b) Föhlisch, B.; Radl, A.; Schwetzler-Raschke, R.; Henkel, S., *Eur. J. Org. Chem.* 2001, **2001**, 4357-4365; (c) Fort, A. W., *J. Am. Chem. Soc.* 1962, **84**, 4979-4981.
20. (a) Tanemura, K.; Suzuki, T.; Nishida, Y.; Satsumabayashi, K.; Horaguchi, T., *Chem. Comm.* 2004, 470-471; (b) Brummond, K. M.; Gesenberg, K. D., *Tetrahedron Lett.* 1999, **40,** 2231-2234; (c) Fraser, R. R.; Kong, F., *Syn. Comm.* 1988, **18,** 1071-1077.
21. (a) Chung, K.; Banik, S. M.; De Crisci, A. G.; Pearson, D. M.; Blake, T. R.; Olsson, J. V.; Ingram, A. J.; Zare, R. N.; Waymouth, R. M., *J. Am. Chem. Soc.* 2013, **135**, 7593-7602; (b) Ramachary, D. B.; Barbas, C. F., *Org. Lett.* 2005, **7**, 1577-1580.
22. Foehlisch, B.; Joachimi, R.; Reiner, S., *J. Chem.l Res., Miniprint,* 1993, **7**, 1701 - 1730.