Supplementary Material (ESI) for Chemical Communications

Electronic supplementary information

The cascade carbo-carbonylation of unactivated alkenes catalyzed by an organocatalyst and a transition metal catalyst: a facile approach to γ-diketones and γ-carbonyl aldehydes from arylalkenes under air

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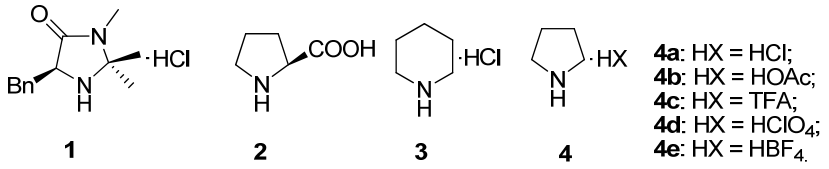
Experimental section

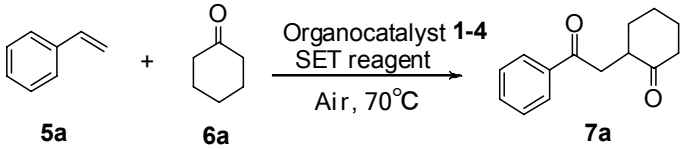
All substituted styrenes **5a-f** were prepared according to the literature procedures.[1] MacMillan-type catalyst salt **1** was synthesized according to the literature method.[2] Piperidine salt **3** and pyrrolidine salt **4** were obtained by the protocol similar to that for organocatalyst **1**.



1 **2** **3** **4**

Scheme 1 Organocatalysts **1-4**

Table 1 Screening of reaction conditions for the reaction of cyclohexanone with styrene mediated by organocatalyst **1-4** and transition metal salt [a]



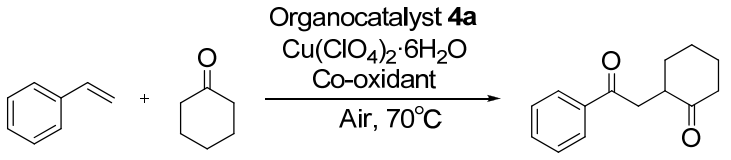
5a **6a** **7a**

Entry	SET reagent (mol %)	Organocatalyst (30 mol %)	Time/hr	Solvent	Yield (%)[b]
1	$FeCl_3$(100%)	**1**	60	DMF	trace
2	$FeCl_3$(100%)	**2**	60	DMF	0
3	$FeCl_3$(100%)	**3**	60	DMF	8
4	$FeCl_3$(100%)	**4a**	48	DMF	16
5[c]	$FeCl_3 \cdot 6H_2O$(100%)	**4a**	48	DMF	13
6	$FeCl_3$(100%)	**4b-e**	48	DMF	9-11
7	$FeCl_3$(100%)	**--**	60	DMF	0
8	**--**	**4a**	60	DMF	0
9[c]	$FeCl_3$(100%)	**4a**	60	DMF	0
10[d]	$FeCl_3$(100%)	**4a**	60	DMF	0
11[e]	$FeCl_3$(100%)	**4a**	60	DMF	10
12[f]	$FeCl_3$(100%)	**4a**	168	DMF	trace
13[g]	$FeCl_3$(100%)	**4a**	72	DMF	<5
14	$FeCl_3$(100%)	**4a**	60	THF	0
15	$FeCl_3$(100%)	**4a**	60	CH_3CN	0
16	$FeCl_3$(100%)	**4a**	60	1,4-Dioxane	0
17	$FeCl_3$(100%)	**4a**	60	DCE[h]	0
18[i]	$FeCl_3$(100%)	**4a**	60	**--**	0
19	$CuCl_2$(100%)	**4a**	48	DMF	16
20	$CuSO_4$(100%)	**4a**	48	DMF	32

21	$Cu(OTf)_2$(100%)	**4a**	48	DMF	30
22	$Cu(ClO_4)_2·6H_2O$(100%)	**4a**	48	DMF	40
23	$Cu(OAc)_2·H_2O$(100%)	**4a**	48	DMF	24
24	$Pd(OAc)_2$(100%)	**4a**	60	DMF	0
25	$Cu(ClO_4)_2·6H_2O$ (100%)	**1**	60	DMF	trace
26	$Cu(ClO_4)_2·6H_2O$ (100%)	**2**	60	DMF	0
27	$Cu(ClO_4)_2·6H_2O$ (100%)	**3**	60	DMF	25
28[c]	$Cu(ClO_4)_2·6H_2O$ (100%)	**3**	60	DMF	18
29	$Cu(ClO_4)_2·6H_2O$ (100%)	**4b**	48	DMF	21
30	$Cu(ClO_4)_2·6H_2O$ (100%)	**4c**	48	DMF	26
31	$Cu(ClO_4)_2·6H_2O$ (100%)	**4d**	48	DMF	30
32	$Cu(ClO_4)_2·6H_2O$ (100%)	**4e**	48	DMF	28
33	$Cu(ClO_4)_2·6H_2O$ (100%)	**--**	60	DMF	0
34	**--**	**4a**	60	DMF	0
35[c]	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	48	DMF	30
36[d]	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	60	DMF	0
37[f]	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	168	DMF	8
38[g]	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	72	DMF	13
39	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	60	THF	0
40	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	60	CH_3CN	0
41	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	60	1,4-Dioxane	trace
42	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	60	DCE[h]	0
43[i]	$Cu(ClO_4)_2·6H_2O$ (100%)	**4a**	60	--	0

[a] The reaction of styrene (0.5 mmol), cyclohexanone (3.0 mmol), 30 mol% organocatalyst **1-4** and SET reagent in the mixed solvent of DMF (2.5 mL) and H_2O (0.15 mL) was performed at 70□ under air. [b] Isolated yiled. [c] The reaction was carried out without H_2O. [d] The reaction was performed under nitrogen. [e] Using EtOH instead of H_2O. [f] The reaction was conducted at room temperature. [g] The reaction was carried out at 90□. [h] DCE=1,2-dichloroethane. [i] The reaction was conducted without organic solvent.

Table 2 Screening of co-oxidant for the reaction of cyclohexanone with styrene catalyzed by organocatalyst **4a** and $Cu(ClO_4)_2·6H_2O$ [a]



5a **6a** **7a**

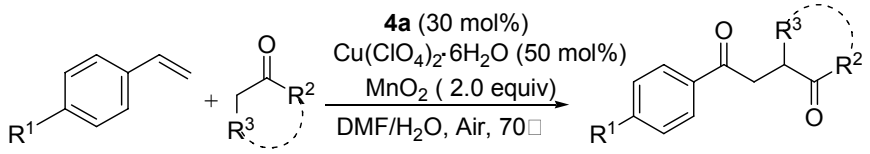
Entry	SET reagent (mol %)	Co-oxidant	Time/hr	Yield(%)[b]
1[c]	$Cu(ClO_4)_2·6H_2O$ (50 %)	O_2 (1 atm)	48	10
2	$Cu(ClO_4)_2·6H_2O$ (50 %)	TBHP(2.0 equiv)	48	13
3	$Cu(ClO_4)_2·6H_2O$ (50 %)	m-CPBA (2.0 equiv)	60	<5
4	$Cu(ClO_4)_2·6H_2O$ (50 %)	H_2O_2 (2.0 equiv)	48	trace
5	$Cu(ClO_4)_2·6H_2O$ (50 %)	MnO_2 (2.0 equiv)	48	61
6	$Cu(ClO_4)_2·6H_2O$ (50 %)	$Na_2S_2O_8$ (2.0 equiv)	48	50
7	$Cu(ClO_4)_2·6H_2O$ (50 %)	$K_2S_2O_8$ (2.0 equiv)	60	40

8	$Cu(ClO_4)_2·6H_2O$ (50 %)	$KClO_3$ (2.0 equiv)	48	43
9	$Cu(ClO_4)_2·6H_2O$ (30 %)	MnO_2(2.0 equiv)	48	45
10	$Cu(ClO_4)_2·6H_2O$ (15 %)	MnO_2(2.0 equiv)	48	36
11	$Cu(ClO_4)_2·6H_2O$ (0 %)	MnO_2(2.0 equiv)	48	trace

[a] The reaction of styrene (0.5 mmol), cyclohexanone (3.0 mmol), 30 mol% **4a**, $Cu(ClO_4)_2·6H_2O$ and a co-oxidant in the mixed solvent of DMF (2.5 mL) and H_2O (0.15 mL) was performed at 70□ under air. [b] Isolated yield. [c] The mixture of cyclohexanone (3.0 mmol), pyrrolidine salt **4a** (0.15 mmol, 30 mol%) in a mixed solvent (2.5 mL DMF and 0.15 mL H_2O) was stirred at 70□ for 5-10 min. Then, $Cu(ClO_4)_2·6H_2O$ (0.25 mmol, 50 mol%) and styrene (0.5 mmol) were added and the reaction mixture was stirred at 70□ for 48 hr under pure oxygen (1 atm). The experiment showed that most cyclohexanone was consumed. We inferred that pure oxygen might accelarate the oxidation of enamine. The similar phenomenon, which the yield of a reaction performed under pure oxygen atmosphere was decreased remarkably as compared to the reaction under air was also reported in: Y. Nobe, K. Arayama and H. Urabe, *J. Am. Chem. Soc.*, 2005, **127**, 18006.

General procedure for the synthesis of γ-diketones and γ-carbonyl aldehydes (7a-k)

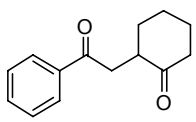
A mixture of ketone or aldehyde **6a-f** (3.0 mmol), organocatalyst **4a** (16.1 mg, 0.15 mmol, 30 mol%) in a mixed solvent (2.5 mL DMF and 0.15 mL H_2O) was stirred at 70℃ for 5-10 min. Then $Cu(ClO_4)_2·6H_2O$ (92.6 mg, 0.25mmol, 50 mol%), activated MnO_2 (86.9 mg, 1.0 mmol, 2.0 equiv) and arylalkene **5a-f** (0.5 mmol) were added. Under air, the reaction mixture was stirred at 70℃ for the time indicated in Table 2 of text (monitored by TLC). When the reaction was completed, the mixture was filtered through a pad of SiO_2 with petroleum/EtOAc as an eluent. To the filtrate was added saturated aqueous NH_4Cl (30 mL), and the aqueous layer was extracted with EtOAc (30 mL × 6). The combined organic layers were dried over Na_2SO_4, and filtered. The filtrate was concentrated in vacuo, and the resulting residue was purified by column chromatography (silica-gel, petroleum ether / EtOAc as eluent) to afford the desired γ-diketones or γ-carbonyl aldehydes **7a-k**.



5a-f **6a-f** **7a-k**

5a: R^1=H; **5b**: R^1=CH_3; **5c**: R^1=OCH_3; **5d**: R^1=Cl; **5e**: R^1=Br; **5f**: R^1=NO_2.
6a: R^2, R^3 = $(CH_2)_4$; **6b**: R^2, R^3 = $(CH_2)_3$; **6c**: R^2 = CH_3,R^3 = H; **6d**: R^2 = H, R^3 = CH_3; **6e**: R^2 = H, R^3 = $(CH_3)_2CH$; **6f**: R^2 = H, R^3 = $CH_3(CH_2)_5$.

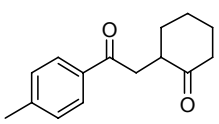
2-Phenacylcyclohexanone (7a)[3]



7a

Oil; 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.99 (d, *J*=7.2 Hz, 2 H), 7.56 (t, *J* = 7.2 Hz, 1 H), 7.46 (t, *J* = 7.2 Hz, 2 H), 3.61 (dd, *J* = 17.9, 6.6 Hz, 1 H), 3.24-3.11 (m, 1 H), 2.69 (dd, *J*=17.9, 5.7 Hz, 1 H), 2.50-2.39 (m, 2 H), 2.25-2.09 (m, 2 H), 1.95-1.60 (m, 3 H), 1.55-1.39 (m, 1 H). MS (ESI, positive) m/z Calcd for $C_{14}H_{16}O_2Na$ ($[M+Na]^+$) 239.10, found 239.42.

2-(4-Methylphenacyl)cyclohexanone (7b)[4,5]

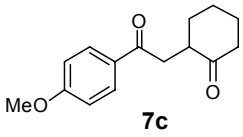


7b

Solid, mp. 67-69 ℃ (Lit.[6] 65-70 ℃); 58% yield. ^{1}H NMR (300 MHz,

$CDCl_3$) δ (ppm): 7.88 (d, *J* = 8.4 Hz, 2 H), 7.29-7.19 (m, 2 H), 3.56 (dd, *J* = 17.6, 6.5 Hz, 1 H), 3.21-3.09 (m, 1 H), 2.66 (dd, *J*=17.6, 5.9 Hz, 1 H), 2.50-2.35 (m, 5 H), 2.25-2.08 (m, 2 H), 1.95-1.57 (m, 3 H), 1.51-1.35 (m, 1 H). MS (ESI, positive) *m/z* Calcd for $C_{15}H_{18}O_2Na$ ($[M+Na]^+$) 253.12, found 253.25.

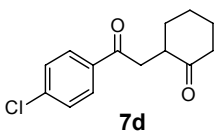
2-(4-Methoxyphenacyl)cyclohexanone (7c)[5]



7c

Solid, mp. 99-100 ℃ (Lit.[6] 98-99 ℃); 64% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.95 (d, *J* = 9.0 Hz, 2 H), 6.91 (d, *J* = 9.0 Hz, 2 H), 3.84 (s, 3 H), 3.53 (dd, *J* = 17.6, 6.3 Hz, 1 H), 3.20-3.09 (m, 1 H), 2.63 (dd, *J*=17.6, 6.0 Hz, 1 H), 2.45-2.37 (m, 2 H), 2.22-2.05 (m, 2 H), 1.95-1.57 (m, 3 H), 1.50-1.33 (m, 1 H). MS (ESI, positive) *m/z* Calcd for $C_{15}H_{18}O_3Na$ ($[M+Na]^+$) 269.12, found 269.50.

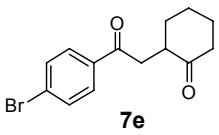
2-(4-Chlorophenacyl)cyclohexanone (7d)[5]



7d

Solid, mp. 57-58 ℃ (Lit.[6] 56-58 ℃); 62% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.91 (d, *J* = 8.7 Hz, 2 H), 7.41 (d, *J* = 8.7 Hz, 2 H), 3.54 (dd, *J*= 17.7, 7.1 Hz, 1 H), 3.21-3.09 (m, 1 H), 2.61 (dd, *J* = 17.7, 5.4 Hz, 1 H), 2.49-2.39 (m, 2 H), 2.23-2.07 (m, 2 H), 1.95-1.59 (m, 3 H), 1.55-1.35 (m, 1 H). MS (ESI, positive) *m/z* Calcd for $C_{14}H_{15}ClO_2Na$ ($[M+Na]^+$) 273.07, found 273.42.

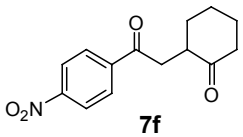
2-(4-Bromophenacyl)cyclohexanone (7e)[5]



7e

Solid, mp. 77-79 ℃ (Lit.[6] 78-80 ℃); 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.83 (d, *J* = 8.7 Hz, 2 H), 7.58 (d, *J* = 8.7 Hz, 2 H), 3.53 (dd, *J*= 17.5, 6.9 Hz, 1 H), 3.21-3.08 (m, 1 H), 2.60 (dd, *J* = 17.5, 5.3 Hz, 1 H), 2.45-2.35 (m, 2 H), 2.22-2.07 (m, 2 H), 1.95-1.55 (m, 3 H), 1.53-1.35 (m, 1 H). MS (ESI, positive) *m/z* Calcd for $C_{14}H_{15}BrO_2Na$ ($[M+Na]^+$) 317.02, found 317.33.

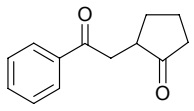
2-(4-Nitrophenacyl)cyclohexanone (7f)[5]



7f

Solid, mp. 62-65 ℃ (Lit.[6] 61-63 ℃); 40% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.30 (d, *J* = 9.0 Hz, 2 H), 8.13 (d, *J* = 9.0 Hz, 2 H), 3.59 (dd, *J*= 17.7, 7.5 Hz, 1 H), 3.25-3.13 (m, 1 H), 2.64 (dd, *J* = 17.7, 4.8 Hz, 1 H), 2.48-2.40 (m, 2 H), 2.28-2.10 (m, 2 H), 1.99-1.61 (m, 3 H), 1.59-1.41 (m, 1 H). MS (ESI, positive) *m/z* Calcd for $C_{14}H_{15}NO_4Na$ ($[M+Na]^+$) 284.09, found 284.17.

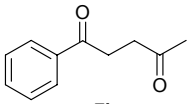
2-Phenacylcyclopentanone (7g)[4,7]



Oil; 43% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.96 (d, *J*=7.0 Hz, 2 H), 7.59-7.55 (m, 1 H), 7.49-7.45 (m, 2 H), 3.53 (dd, *J* = 18.0, 3.0 Hz, 1 H), 3.05 (dd, *J*= 18.0, 8.0 Hz, 1 H), 2.69-2.61 (m, 1 H), 2.45-2.35 (m, 2 H), 2.33-2.23

(m, 1 H), 2.15-2.05 (m, 1 H), 1.91-1.80 (m, 1 H), 1.65-1.55 (m, 1 H). MS (ESI, positive) m/z Calcd for $C_{13}H_{14}O_2Na$ ($[M+Na]^+$) 225.09, found 225.42.

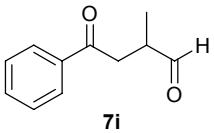
1-Phenylpentane-1,4-dione (7h)[8,9]



7h

Oil; 55% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.97 (d, *J* = 6.9 Hz, 2 H), 7.55 (t, *J* = 7.5 Hz, 1 H), 7.45 (t, *J* = 7.5 Hz, 2 H), 3.27 (t, *J* = 6.4 Hz, 2 H), 2.88 (t, *J* = 6.4 Hz, 2 H), 2.25 (s, 3 H). MS (ESI, positive) *m/z* Calcd for $C_{11}H_{12}O_2Na$ ($[M+Na]^+$) 199.07, found 199.25.

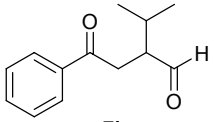
2-Methyl-4-oxo-4-phenylbutanal (7i)[10]



7i

Oil; 50% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.79 (s, 1 H), 7.97 (d, *J* = 7.0 Hz, 2 H), 7.58 (t, *J* = 7.7 Hz, 1 H), 7.47 (t, *J* = 7.7 Hz, 2 H), 3.49 (dd, *J* = 17.9, 6.5 Hz, 1 H), 3.22-3.08 (m, 1 H), 3.01 (dd, *J* = 17.9, 5.3 Hz, 1 H), 1.24 (d, *J*=7.5 Hz, 3 H). MS (ESI, positive) *m/z* Calcd for $C_{11}H_{12}O_2Na$ ($[M+Na]^+$) 199.07, found 199.42.

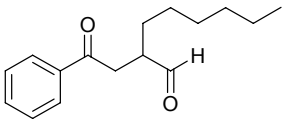
2-Isopropyl-4-oxo-4-phenylbutanal (7j)[10]



7j

Oil; 62% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.86 (s, 1 H), 7.99 (d, *J*=7.0 Hz, 2 H), 7.56 (t, *J*=7.7 Hz, 1 H), 7.47 (t, *J*=7.7 Hz, 2 H), 3.52 (dd, *J*=18.2, 8.8 Hz, 1 H), 3.15-3.10 (m, 1 H), 2.91 (dd, *J*=18.2, 3.8 Hz, 1 H), 2.30-2.21 (m, 1 H), 1.06 (d, *J*=7.3 Hz, 3 H), 1.01 (d, *J*=7.3 Hz, 3 H). MS (ESI, positive) *m/z* Calcd for $C_{13}H_{16}O_2Na$ ($[M+Na]^+$) 227.10, found 227.42.

2-Phenacyloctanal (7k)[11]



7k

Oil; 56% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.82 (s, 1 H), 7.97 (d, *J* = 7.2 Hz, 2 H), 7.57 (t, *J* = 7.4 Hz, 1 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 3.47 (dd, *J* = 17.3, 7.4 Hz, 1 H), 3.15-2.99 (m, 2 H), 1.85-1.71 (m, 1 H), 1.61-1.45 (m, 1 H), 1.42-1.21 (m, 8 H), 0.88 (t, *J* = 6.8 Hz, 3 H). MS (ESI, positive) *m/z* Calcd for $C_{16}H_{22}O_2Na$ ($[M+Na]^+$) 269.15, found 269.50.

References:

1. (a) G. P. Marsh, P. J. Parsons, C. McCarthy and X. G. Corniquet, *Org. Lett.,* 2007, **9**, 2613. (b) M. Davi and H. Lebel, *Org. Lett.*, 2009, **11**, 41. (c) C. A. Faler and M. M. Joullie, *Org. Lett.,* 2007, **9**, 1987. (d) K. Kuma, O. Sakai and K. Shioji, *Bull. Chem. Soc. of Japan,* 2003, **76**, 1675.

2. K. A. Ahrendt, C. J. Borths and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2000, **122**,4243.
3. G. A. Russell and S. V. Kulkarni, *J. Org. Chem.*, 1993, **58**, 2678.
4. V. V. Zhdankin, M. Mullikin, R. Tykwinski, B. Berglund and R. Caple, *J. Org. Chem.*, 1989, **54,** 2605.
5. V. B. Anderson, M. N. Agnew and R. C. Allen, *J. Med. Chem.*, 1976, **19,** 318.
6. R. C. Allen and V. B. Anderson, *U.S. Pat.*, 1976, No. 3931407.
7. H. Stitter and W. Haese, *Chem. Ber.,* 1984, **117**, 682.
8. J. Barluenga, H. Fanlo, S. Lopez and J. Florez, *Angew. Chem. Int. Ed.*, 2007, **46**, 4136.
9. S. Xue, L.-Z. Li, Y.-K. Liu and Q.-X. Guo, *J. Org. Chem.,* 2006, **71**, 215.
10. G. A. Molander and K. O. Cameron, *J. Am. Chem. Soc.*, 1993, **115**, 830.
11. H.-Y. Jang, J.-B. Hong and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2007, **129**, 7004.