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ADDITION OF 2-OXAZOLIDINONES TO ARYLIDENECYCLOPROPANES: A HIGHLY EFFICIENT METHOD FOR THE PREPARATION OF *GEM*-ARYL DISUBSTITUTED HOMOALLYLIC OXAZOLIDINONES

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(Dedicated to the great contribution to organic chemistry of the late professor Kenji Koga)

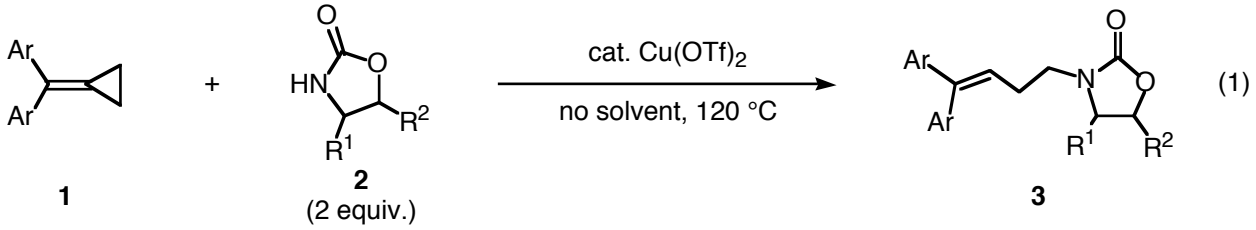
Abstract – The copper-catalyzed reaction of arylidenecyclopropanes (**1**) with 2-oxazolidinone (**2**) gave the corresponding homoallylic oxazolidinones (**3**) in good to high yields. For example, the reaction of diphenylmethylenecyclopropane (**1a**), {bis(*p*-tolyl)methylenecyclopropane (**1b**), and {bis(*p*-anisyl)methylene}-cyclopropane (**1d**) in the presence of 10 mol% of $Cu(OTf)_2$ without solvent proceeded at 120 °C, giving the corresponding homoallylic oxazolidinones (**3a**, **3b**, and **3d**) in 89, 80, and 58% yields, respectively.

INTRODUCTION

Synthesis of homoallylic oxazolidinones has been of great interest for organic chemists since the structural framework of homoallylic amines is often found in biologically important natural products and the synthetic intermediates leading to them.[1] However, the synthesis of these compounds is limited by the lack of a general synthetic method; previously homoallylic amides have been prepared by substitution reactions from the corresponding homoallylic halides or alcohols[2] or McMurry coupling with the corresponding β-amidocarbonyl compounds.[3]

During the last decade, methylenecyclopropanes have become readily accessible and found application in organic synthesis as versatile building brocks.[4] The high chemical reactivity of methylenecyclopropanes

is due to a high level of ring strain, although they are stable and easy to handle. Recently, we reported that the convenient synthesis of homoallylic halides[5] and alcohols through methylenecyclopropanes.[6] These results prompted us to investigate a possibility of the direct synthesis of homoallylic oxazolidinones through methylenecyclopropanes. Recently, Shi *et al*. reported synthesis of homoallylic anilides by $Sn(OTf)_2$-catalyzed reaction of methylenecyclopropanes with anilines.[7] Quite recently, Huang *et al*. reported the Brønsted acid-mediated reaction of methylenecyclopropanes with nitriles which gives the corresponding homoallylic amides.[8] Herein, we report that the copper-catalyzed reaction of arylidenecyclopropanes with oxazolidinones (**2**) produces the corresponding *gem*-aryl disubstituted homoallylic oxazolidinones (**3**) in good to high yields (eq. 1).



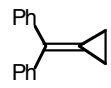
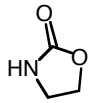
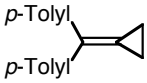
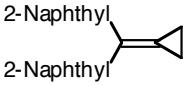
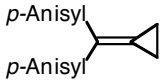
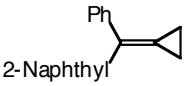
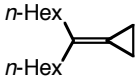
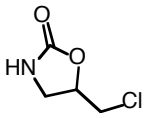
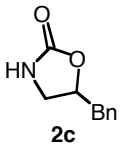
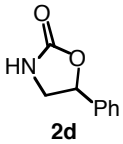
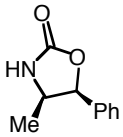
RESULTS AND DISCUSSION

The results are summarized in Table 1. The reaction of diphenylmethylenecyclopropane (**1a**) and 2 equivalents of 2-oxazolidinone (**2a**) in the presence of 10 mol % of $Cu(OTf)_2$ without solvent proceeded at 120 °C and the corresponding homoallylic oxazolidinone (**3a**) was obtained in 89% yield (entry 1). When 1 equivalent of **2a** was used, **3a** was obtained in 43% yield along with a small amount of recovered **1a**. The reaction using $Sn(OTf)_2$ instead of $Cu(OTf)_2$ did not proceed at all. The reaction of **1a** and **1b** using solvent, such as benzene, 1,4-dioxane, THF, and DMF, gave **3a** in lower yields. The reaction of {bis(*p*-tolyl)methylene}cyclopropane (**1b**), {bis(2-naphthyl)methylene}cyclopropane (**1c**), and {bis(*p*-anisyl)methylene}cyclopropane (**1d**) produced **2b**, **2c**, and **2d** in 80, 47, 58% yields, respectively (entries 2-4). The reaction of unsymmetrical arylidenecyclopropane (**1e**) gave an inseparable mixture of E/Z isomers of **3e** in 63% yield (entry 5). The reaction of dihexylmethylenecyclopropane (**1f**) with **2a** did not afford the desired product and the starting materials were decomposed (entry 6). The reaction of **1a** with 2-oxazolidinones (**2b**, **2c**, **2d**, and **2e**), which had one or two substituents on the oxazolidinone ring, afforded the corresponding homoallylic oxazolidinones (**3f**, **3g**, **3h**, and **3i**) in good to high yields (entries 7-10).

A plausible mechanism of the present reaction is illustrated in Scheme 1.[6,7] Addition of $Cu(OTf)_2$ to the arylidenecyclopropane (**1**) most probably lead to the tertiary carbocation (**4**). Cyclopropylcarbinyl-

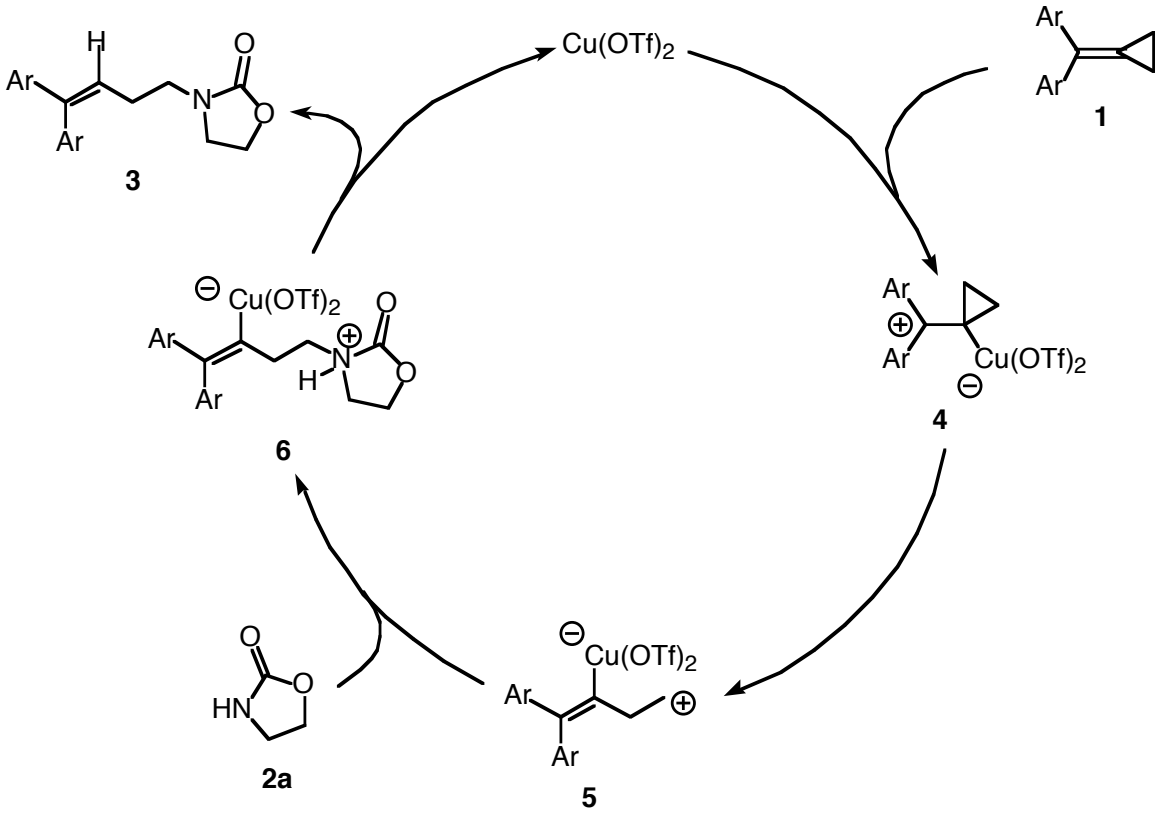
homoallyl rearrangement would take place.[9] Nucleophilic attack of 2-oxazolidinone (**2a**) to the resulting homoallyl cation (**5**) would give the *N*-homoallylic ammonium derivative (**6**). Protonolysis of **6** gives the product (**3**).

Table 1. Addition of oxazolidinone (**2**) to arylidenecyclopropane (**1**) catalyzed by $Cu(OTf)_2$ [a]

entry	1	2	3	yield / % [b]
1	 **1a**	 **2a**	**3a**	89
2	 **1b**	**2a**	**3b**	80
3	 **1c**	**2a**	**3c**	47
4	 **1d**	**2a**	**3d**	58
5	 **1e**	**2a**	**3e**	63 [c]
6	 **1f**	**2a**		decomposition
7	**1a**	 **2b**	**3f**	52
8	**1a**	 **2c**	**3g**	58
9	**1a**	 **2d**	**3h**	60
10	**1a**	 **2e**	**3i**	54

[a] The reaction of **1** (0.5 mmol) with **2** (1.0 mmol) was carried out in the presence of 10 mol % of $Cu(OTf)_2$ without solvent at 120 °C for 3 days. [b] Isolated yield. [c] An inseparalble mixture of E/Z isomers was obtained.

Scheme 1



CONCLUSION

We are now in a position to synthesize *gem*-diaryl substituted homoallylic oxazolidinones catalytically in good to high yields. This methodology provides highly useful homoallylic oxazolidinones in a catalytic and an atom economic manner. The related reaction of di- and mono-alkyl substituted methylenecyclopropanes is under investigation in our laboratory.

EXPERIMENTAL

General Procedure. A mixture of an arylidenecyclopropane (**1**) (0.5 mmol), 2-oxazolidinone (**2**) (1.0 mmol), and $Cu(OTf)_2$ (18.1 mg, 0.05 mmol) was stirred at 120 °C for 3 days. The reaction mixture was passed through short silica gel column. The crude product was purified by silica gel column chromatography using hexane / ethyl acetate (20/1) as eluent to give the product (**3**).

3-(4,4-Diphenyl-but-3-enyl)oxazolidodin-2-one (3a). IR (neat) 3398, 2925, 2854, 1747, 1598, 1492, 1443, 1426, 1366, 1262, 1176, 1109, 1060, 1039, 971, 785, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.40 (q, J = 6.8 Hz, 2H), 3.29 (q, J = 6.8 Hz, 2H), 3.37 (t, J = 6.8 Hz, 2H), 4.19 (q, J = 8.0 Hz, 2H), 6.03 (t, J = 3.8 Hz, 1H), 7.16-7.20 (m, 3H), 7.22-7.28 (m, 4H), 7.29-7.34 (m, 1H), 7.37-7.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.80, 43.92, 44.14, 61.57, 125.00, 127.12, 127.14, 127.26, 128.04, 128.19, 129.57,

139.63, 142.05, 144.14, 158.29; HRMS (EI) Calcd for $C_{19}H_{19}NO_2$: m/z 293. 1308. Found: m/z 293.1310.

3-(4,4-Di-*p*-tolylbut-3-enyl)oxazolidin-2-one (3b). IR (neat) 2917, 1764, 1608, 1510, 1428, 1365, 1266, 1108, 1062, 971, 817, 761, 730, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.26-2.43 (m, 8H), 3.29-3.38 (m, 4), 4.22 (t, J = 8.0 Hz, 2H), 5.97 (t, J = 7.6 Hz, 1H), 7.06 (dd, J = 3.6, 4.0 Hz, 4H), 7.10 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.89, 21.09, 21.26, 44.02, 44.20, 61.60, 123.92, 127.21, 128.73, 128.85, 129.49, 136.73, 136.81, 136.85, 139.52, 143.92, 158.32; HRMS (EI) Calcd for $C_{21}H_{23}NO_2$: m/z 321. 1621. Found: m/z 321.1622.

3-(4,4-Dinaphthalen-2-yl-but-3-enyl)oxazolidin-2-one (3c). IR (neat) 3398, 3060, 2925, 2855, 1740, 1599, 1495, 1453, 1228, 1159, 1121, 1071, 1033, 1010, 817, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.52 (q, J = 6.8 Hz, 2H), 3.27 (q, J = 6.8 Hz, 2H), 3.44 (t, J = 6.8 Hz, 2H), 4.18-4.22 (m, 2H), 6.27 (t, J = 7.2 Hz, 1H), 7.31 (dd, J = 1.2, 2.0 Hz, 1H), 7.40-7.43 (m, 2H), 7.47-7.57 (m, 4H), 7.68-7.80 (m, 4H), 7.83-7.90 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.11, 44.04, 44.23, 61.60, 125.38, 125.81, 126.03, 126.06, 126.09, 126.27, 126.70, 127.41, 127.68, 127.73, 127.90, 127.95, 128.15, 128.58, 132.52, 132.63, 137.12, 139.37, 144.11, 158.35; HRMS (EI) Calcd for $C_{20}H_{32}N_2$: m/z 393. 1621. Found: m/z 393.1622.

3-[4,4-Bis-(4-methoxyphenyl)but-3-enyl]oxazolidin-2-one (3d). IR (neat) 3036, 2953, 2836, 1607, 1576, 1513, 1464, 1406, 1292, 1244, 1183, 1115, 1087, 1026, 935, 888, 838, 786, 763, 729 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.41 (q, J = 6.8 Hz, 2H), 3.30-3.38 (m, 4H), 3.79 (s, 3H), 3.84 (s, 3H), 4.21-4.25 (m, 2H), 5.88 (t, J = 7.2 Hz, 1H), 6.80 (d, J = 3.0 Hz, 2H), 6.90 (d, J = 2.9 Hz, 2H), 7.09 (d, J = 3.0 Hz, 2H), 7.14 (d, J = 3.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.87, 44.09, 44.19, 55.26, 55.29, 61.62, 113.45, 113.57, 123.09, 128.51, 130.77, 132.18, 135.22, 143.20, 158.84; HRMS (EI) Calcd for $C_{21}H_{23}NO_4$: m/z 353. 1519. Found: m/z 353.1520.

3-(4-Naphthalen-2-yl-4-phenylbut-3-enyl)oxazolidin-2-one (3e). An inseparable mixture of stereoisomers A and B. IR (neat) 3054, 3018, 2922, 1748, 1597, 1483, 1443, 1429, 1362, 1266, 1225, 1175, 1103, 1061, 1040, 970, 901, 862, 819, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.43-2.49 (m, 2H, A, B), 3.24 (t, J = 8.4 Hz, 2H, A), 3.33 (t, J = 8.0 Hz, 2H, B), 3.41 (q, J = 6.4 Hz, 2H, A and B), 6.12 (t, J = 7.4 Hz, 1H, A), 6.18 (t, J = 7.4 Hz, 1H, B), 7.22-7.87 (m, 12H, A and B); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.96, 27.99, 43.98, 44.04, 44.18, 44.25, 61.59, 61.63, 125.28, 125.48, 125.61, 125.76, 125.99, 126.04, 126.23, 126.49, 127.26, 127.29, 127.39, 127.46, 127.63, 127.65, 127.81, 127.84, 128.14, 128.45, 129.72, 132.44, 133.17, 137.13, 139.42, 142.03, 144.14, 144.17, 158.35; HRMS (EI) Calcd for $C_{23}H_{21}NO_2$: m/z 343. 1465. Found: m/z 343.1466.

5-Chloromethyl-3-(4,4-diphenylbut-3-enyl)oxazolidin-2-one (3f). IR (neat) 3398, 3056, 3024, 2926, 1748, 1658, 1598, 1489, 1445, 1341, 1266, 1179, 1114, 1048, 912, 757, 732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.35-2.49 (m, 2H), 3.25 (q, J = 5.6 Hz, 1H), 3.37-3.44 (m, 3H), 3.35 (q, J = 6.8 Hz, 1H), 3.64 (q, J = 3.6 Hz, 1H), 4.61 (s, 1H), 7.16-7.23 (m, 4H), 7.24-7.27 (m, 2H), 7.31-7.36 (m, 2H), 7.37-7.41 (m,

2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.78, 43.84, 44.54, 47.17, 71.26, 124.84, 127.22, 127.26, 128.09, 128.25, 129.63, 139.52, 141.99, 144.35, 156.88; HRMS (EI) Calcd for $C_{20}H_{20}ClNO_2$: m/z 341. 1075. Found: m/z 341.1074.

5-Benzyl-3-(4,4-diphenylbut-3-enyl)oxazolidin-2-one (3g)

IR (neat) 3028, 2925, 1754, 1599, 1494, 1444, 1414, 1224, 1158, 1108, 1031, 912, 761 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.39-2.47 (m, 3H), 2.91 (dd, J = 4.4, 4.4 Hz, 1H), 3.08-3.14 (m, 1H), 3.62-3.69 (m, 1H), 3.73 (q, J = 7.6 Hz, 1H), 3.87 (q, J = 6.4 Hz, 1H), 4.01 (t, J = 8.4 Hz, 1H), 6.89 (d, J = 1.8 Hz, 2H), 7.15-7.26 (m, 10H), 7.32-7.42 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.67, 38.24, 41.58, 55.38, 66.84, 124.94, 126.99, 127.19, 127.25, 127.31, 128.09, 128.30, 128.72, 128.77, 129.69, 135.29, 139.67, 142.01, 144.34, 158.05; HRMS (EI) Calcd for $C_{26}H_{25}NO_2$: m/z 383. 1778. Found: m/z 383.1778.

3-(4,4-Diphenylbut-3-enyl)-5-phenyloxazolidin-2-one (3h). IR (neat) 3351, 3028, 2925, 1754, 1660, 1599, 1494, 1477, 1457, 1444, 1414, 1358, 1223, 1158, 1108, 1063, 912, 762, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.22-2.31 (m, 1H), 2.33-2.41 (m, 1H), 2.74-2.80 (m, 1H), 3.62-3.69 (m, 1H), 3.99 (t, J = 7.4 Hz, 1H), 4.35 (t, J = 7.4 Hz, 1H), 4.46 (t, J = 8.6 Hz, 1H), 7.02-7.05 (m, 2H), 7.13-7.15 (m, 2H), 7.19-7.22 (m, 3H), 7.23-7.26 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.29, 41.50, 59.19, 69.79, 125.15, 126.96, 127.16, 127.17, 127.22, 127.39, 128.09, 128.24, 128.92, 129.13, 129.71, 137.25, 137.38, 139.68, 139.69, 142.15, 142.15, 144.13, 158.22; HRMS (EI) Calcd for $C_{25}H_{23}NO_2$: m/z 369. 1621. Found: m/z 369.1622.

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