with CH_2Cl_2/MeOH (95/5). Evaporation of the third fraction yielded 15 mg (11 %) of **3b** as a brown-violet powder. ^{1}H NMR (250 MHz, CD_2Cl_2, 27 °C, TMS): $\delta = 6.35$ (m, 8H, ArH), 8.34 (brs, 16H, pyrrole β-H), 8.60 (m, 8H, ArH), 9.45 (m, 22H, ArH); MS (positive SI-MS): m/z calcd for $C_{86}H_{54}N_{10}Ce$: 1368 [M^+]; found: 1368; elemental analysis calcd for $C_{80}H_{48}N_{16}Ce$: C 75.53, H 3.98, N 10.24; found: C 74.92, H 3.70, N 10.06; UV/Vis (CH_2Cl_2): λ_{max} ($\lg\varepsilon$) = 398 nm (5.22), 543 nm (4.20), 650 nm (3.57), 722 nm(3.48).

CD spectroscopy: A stock solution of dicarboxylic acid in ethyl acetate was added to a 0.1 mM solution of **3a** or **3b** in dichloromethane. The dichloromethane/ethyl acetate ratio of the sample was adjusted to 30/1. The CD spectra were recorded from 250 nm to 500 nm for different concentrations of guest molecules at 25 °C.

Instruments: Shimadzu UV-160A (absorption spectra), JASCO J-720WI (CD spectra), and JEOL 400 MHz FT-NMR (GSX-400) (^{1}H NMR spectra).

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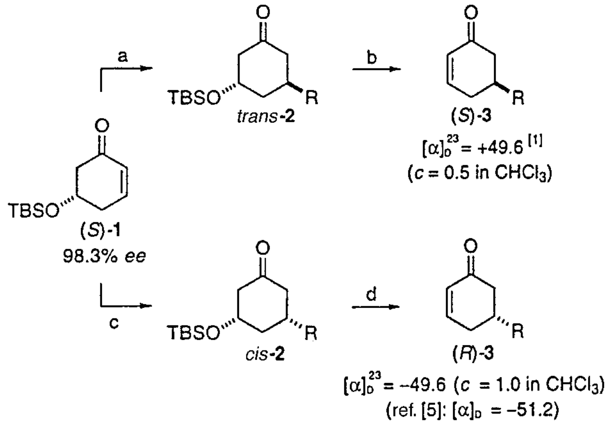
[15] Elemental analysis of the precipitate: calcd for **3a** · (L-tartaric acid)$_{4.0}$: C 58.42, H 3.68, N 11.35; for **3a** · (L-tartaric acid)$_{3.8}$: C 58.83, H 3.67, N 11.53; for **3a** · (L-tartaric acid)$_{3.0}$: C 60.59, H 3.65, N 12.29; found: C 58.76, H 3.68, N 11.49. Thus, the experimental result is closest to **3a** · (L-tartaric acid)$_{3.8}$. The slight deviation from the 1:4 stoichiometry is due to immediate precipitation after mixing.

Unexpected *cis*-Selective 1,4-Addition Reaction of Lower Order Cyanocuprates to Optically Active 5-(*tert*-Butyldimethylsiloxy)-2-cyclohexenone[**]

Georges Hareau-Vittini, Shinichi Hikichi, and Fumie Sato[*]

We have recently reported an efficient and practical synthesis of the 5-(*tert*-butyldimethylsiloxy)-2-cyclohexenone (**1**; 98.3 % *ee*) as a convenient chiral 2,5-cyclohexadienone synthon.[1, 2] The enone **1**, as expected, undergoes highly selective *anti*-1,4-additions with organocopper reagents such as [R_2CuLi] or [$R_2Cu(CN)Li_2$] to yield *trans*-**2** as the major products. These can be easily converted into the optically active 5-substituted-2-cyclohexenone **3** upon treatment with DBU or toluenesulfonic acid (Scheme 1).[1]



Scheme 1. Preparation of both enantiomers of **3** starting from *(S)*-**1**. a) [nBu$_2$Cu(CN)Li$_2$], 92 %, 98 % *dr*; b) DBU (3 equiv), DMF, 20 °C, 5 h, 93 %; c) [nBuCu(CN)Li], 91 %, 99 % *dr*; b) DBU (5 equiv), DMF 100 °C, 1 h, 74 %. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, TBS = *tert*-butyldimethylsilyl.

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[*] Prof. Dr. F. Sato, Dr. G. Hareau-Vittini, S. Hikichi
Department of Biomolecular Engineering
Tokyo Institute of Technology
4259 Nagatsuta-cho, Midori-ku, Yokohama,
Kanagawa 226-8501 (Japan)
Fax: (+81) 45-924-5826
E-mail: fsato@bio.titech.ac.jp

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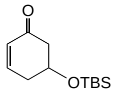
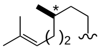
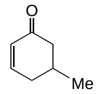
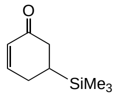
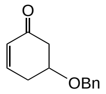
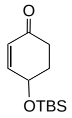
In the course of a further study of the 1,4-addition reaction, we have found that **1** reacts with lower order butylcyanocuprate [BuCu(CN)Li][3] to yield with high selectivity *cis*-**2** (R = *n*Bu). This is the first *cis*-selective 1,4-addition of organocopper reagents to 5-substituted 2-cyclohexenones,[4] and enables the preparation of both enantiomers of **3** (R = *n*Bu) starting from a single enantiomer of **1** (Scheme 1).

The significance of this result from the viewpoint of synthetic chemistry, as well as organocopper chemistry, prompted us to carry out further study. The objective of our work was centered on the examination of the generality of the reaction by changing the R group in [RCu(CN)Li], and also to reveal whether this phenomenon was characteristic of the particular substrate **1** or not.

Table 1 summarizes the results of the reaction of **1** with a variety of lower order cyanocuprates ([RCu(CN)Li]) and, for comparison, those obtained when the higher order dilithium cyanocuprate [R$_2$Cu(CN)Li$_2$] was used.[1, 6] The reaction in Et$_2$O with a variety of lower order cyanocuprates, except for the vinyl derivative, proceeds with high *cis* selectivity, although the phenylcyanocuprate gives the 1,4-addition product only in a moderate yield. Especially noteworthy is the very high selectivity observed with the methyl derivative (entry 1), primary alkyl derivatives (entries 2 and 4), and secondary alkyl derivatives (entry 6); in these cases the corresponding *cis*-**2** product can be obtained in an almost pure form after usual workup of the reaction mixture. The reaction of tertiary-alkyl and phenyl derivatives, however, proceeded with lower diastereomeric ratio (*dr*), 75:25 – 80:20 (entries 8 and 9). Even if the selectivity was somewhat diminished, the lower order cyanocuprate [RCu(CN)MgX] derived from Grignard reagents also yielded mainly the *cis*-addition product (entries 3, 5, and 7). The only exception to the *cis*-selective addition of lower order cyanocuprates to **1** is the case of the vinyl derivative which gave the *trans*-addition product selectively (entry 10); the explanation for this result must await further study.

To see whether this highly *cis*-selective 1,4-addition of [RCu(CN)Li] was characteristic of **1**, we carried out the reaction of [*n*BuCu(CN)Li] with 5-methyl- and 5-trimethyl-

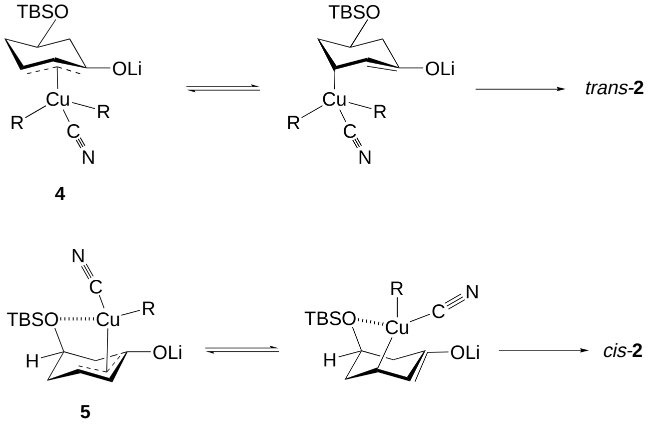
Table 1. 1,4-Addition of lower order cyanocuprates [RCu(CN)M] onto 2-cyclohexenones.

Entry	Enone	R	M	Conditions[a]	Yield [%][b]	*cis*:*trans*[c]	Reaction with [R$_2$Cu(CN)Li$_2$]	
							Yield [%][b]	*cis*:*trans*[c]
1		Me	Li	A	77[d]	> 99:1[e]	83[d]	3:97[e]
2		*n*Bu	Li	B[f]	91[d]	> 99.5:0.5[e]	92[d]	2:98[e]
3		*n*Bu	MgBr	C[g]	73	90:10	–	–
4			Li	B	87[d]	98:2	–	–
5			MgBr	B	–[h]	70:30	–	–
6		*s*Bu	Li	A	84[d]	> 98:2	[h]	< 2:98
7		cyclohexyl	MgCl	D	75	65:35	–	–
8		*t*Bu	Li	A	78	75:25	92	< 2:98
9		Ph	Li	D	25	80:20	80[d]	3:97[e]
10		H$_2$C=CH	Li	D	45	25:75	75	5:95
11		*n*Bu	Li	B	95	< 1:99[e]	–	–
12		*n*Bu	Li	B	–[h]	< 1:99[e]	–	–
13		*n*Bu	Li	B	80	> 98:2	87	10:90[e]
14		*n*Bu	Li	D	91[d]	3:97[e]	–	–

[a] All reactions were performed with 2.40 equiv of lower order cyanocuprate, unless otherwise stated. A: Et$_2$O, $-78\,^{\circ}\text{C} \rightarrow 0\,^{\circ}\text{C}$, 1 h; B: Et$_2$O, $-78\,^{\circ}\text{C}$, 1 h; C: THF, $-78\,^{\circ}\text{C}$, 1 h; D: Et$_2$O, $-78\,^{\circ}\text{C} \rightarrow 0\,^{\circ}\text{C}$, 2 h. [b] *cis*/*trans* mixture, determined by NMR spectroscopy. [c] Determined by NMR spectroscopy. [d] Yield of isolated product. [e] Determined by gas chromatography. [f] 1.2 Equiv of [*n*BuCu(CN)MgBr] yielded 82 % of the product with a *cis*:*trans* ratio of > 98:2. [g] 1.2 Equiv of [*n*BuCu(CN)Li] were used. [h] Not determined.

silyl-2-cyclohexenone: the reactions yielded almost exclusively the corresponding *trans*-3,5-disubstituted cyclohexanones (entries 11 and 12). This result strongly indicates that the alkoxy functionality in the substrate **1** plays a crucial role in the control of the stereochemistry of the 1,4-addition. We confirmed this assumption by carrying out the reaction of 5-benzyloxy-2-cyclohexenone[8] with [*n*BuCu(CN)Li], which yielded almost exclusively the corresponding *cis* adduct (entry 13). With the evidence that an alkoxy group is essential to attain excellent *cis* selectivity, we then turned our attention to the reaction of [*n*BuCu(CN)Li] with the 4-(*tert*-butyldimethylsiloxy)-2-cyclohexenone[9] to examine the effect of the position of the alkoxy group on the diastereoselectivity of the addition.[10] The reaction furnished the *trans*-addition product almost exclusively (entry 14), indicating that the selectivity is also highly dependent on the position of the alkoxy group on the cyclohexenone ring.

The foregoing results may be explained by assuming that the reaction proceeds via a d,π*-complex intermediate as suggested by Corey et al.[11] Based on this model, the reaction with the higher order cuprates [$R_2Cu(CN)Li_2$] proceeds by via the d,π*-complex **4**, which has the TBSO functionality in a pseudo-equatorial position, while the reaction with the lower order cuprate [BuCu(CN)Li] proceeds via **5** in which the copper atom is coordinated by the oxygen atom of the alkoxy group (Scheme 2).[12]



Scheme 2. Proposed intermediates for the reaction of **1** with higher (top) and lower order (bottom) cyanocuprates. TBS = *tert*-butyldimethylsilyl.

In conclusion, the reaction of **1** with lower order cyanocuprates (except for the vinyl derivative) gives the *cis*-1,4-addition products with high selectively. This is the first *cis*-selective 1,4-addition of organocopper compounds to a 5-substituted-2-cyclohexenone and opens up an easy and practical access to both enantiomers of 5-alkyl-2-cyclohexenones **3** from the readily available **1**.[13]

Experimental Section

Entry 2 in Table 1: CuCN[14] (1.2 mmol, 107 mg) and dry Et_2O (10 mL) were introduced into a flame-dried Schlenk tube flushed with argon. The mixture was cooled to −78 °C under magnetic agitation and *n*BuLi (1.59 M in *n*-hexane, 1,2 mmol; 0.75 mL) was slowly added. The resulting mixture was stirred for 30 min at −78 °C (until complete dissolution of the copper salt; the mixture can be warmed up to 0 °C if needed), and enone **1** (0.5 mmol, 113 mg) in ether (1 mL) was added dropwise at −78 °C (addition time: about 5 min). Stirring was continued for a further hour before the mixture was quenched with saturated NH_4OH. After extraction with Et_2O, the combined organic layers were dried over $MgSO_4$. Evaporation of the solvent gave a colorless oil, *cis:trans* = >99.5:0.5 by GC measurement, purification by flash chromatography (SiO_2; hexanes:Et_2O (9:1)) yielded the corresponding product as a colorless oil (130 mg, 91 %). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.80$ (dddd, $J = 10.6$, 10.6, 4.8, 4.8 Hz, 1 H), 2.60–2.50 (m, 1 H); 2.35–2.23 (m, 2 H), 2.08–1.98 (m, 1 H), 1.88 (dd, $J = 13.2$, 13.2 Hz, 1 H), 1.62–1.44 (m, 1 H), 1.40–1.15 (m, 7 H), 0.95–0.70 (m, 12 H), 0.02 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 209.6(4)$, 69.6(3), 51.5(2), 46.9(2), 41.5(2), 36.1(2), 32.7(3), 28.6(2), 25.6(1), 22.5(2), 17.8(4), 13.8(1), −4.96(1), −4.98(1).

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