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Carbon–Carbon Double-Bond Formation from the Reaction of Organozinc Reagents with Aldehydes Catalyzed by a Nickel(II) Complex**

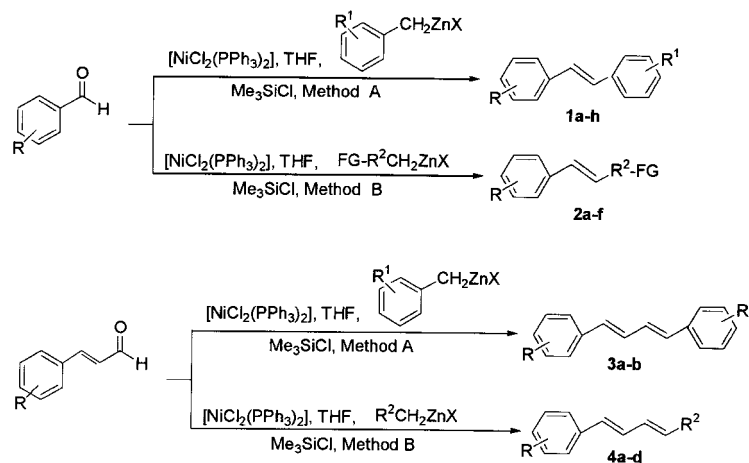
Jin-Xian Wang,* Ying Fu, and Yulai Hu

Reactions that form carbon–carbon bonds are of the utmost importance in modern organic synthesis, and the development of new methods to form such bonds is still a formidable challenge for organic chemists. It is well known that reactions forming C=C bonds have been extensively used in the synthesis of various polyfunctional unsaturated compounds and natural products, while some applications in combinatorial chemistry have also been described. Many methods have been developed for C=C bond formation such as Wittig reactions,^[1] reductive coupling of carbonyl compounds,^[2] self-coupling of α -lithiated benzylic sulfones,^[3] and condensation of aldehyde tosylhydrazones with stabilized carbanions.^[4] More recently, new procedures for the synthesis of stilbenes have been reported, in which aldehyde tosylhydrazones were treated with benzotriazole-stabilized carban-

ions,^[5] trimethyl borate/lithium *tert*-butoxide, trialkylboranes, and alkylboron chlorides.^[6]

Organozinc complexes are powerful reagents for the formation of carbon–carbon bonds.^[7] Recently, transition-metal-catalyzed coupling reactions of halides with organozinc complexes have been reported.^[8] In addition, we have reported that the nitro group of 1-aryl-2-nitroethenes can be substituted by organozinc halides, using $[\text{Ni}(\text{acac})_2]$ (acac = acetylacetonato) as a catalyst in the presence of a tertiary amine, to give 1-aryl-1-alkenes in excellent yields.^[9]

The reaction of alkylzinc reagents and carbonyl compounds represents one of the most reliable methods to prepare optically active secondary alcohols.^[10, 11] Herein we show that *E*-stilbenes can be formed by the reaction of organozinc halides with aryl aldehydes in the presence of a silylating agent and using $[\text{NiCl}_2(\text{PPh}_3)_2]$ as the catalyst. To our knowledge, the formation of C=C bonds by the reaction of aldehydes and organozinc reagents, using this catalyst in the presence of chlorotrimethylsilane, is yet to be reported. Herein, we report that a number of *E*-alkenes can be obtained by this route. To investigate the scope and limitations of this new reaction for the synthesis of *E*-alkenes, various aldehydes and organozinc reagents, including some functionalized species, have been utilized as substrates (Scheme 1). The results are summarized in Table 1.



Scheme 1.

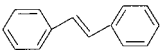
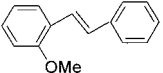
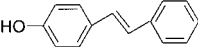
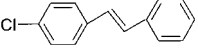
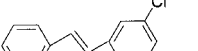
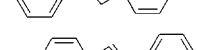
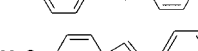
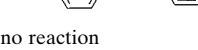
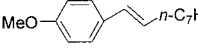
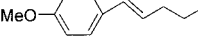
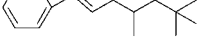
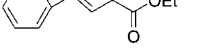
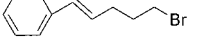
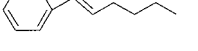
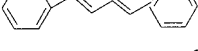
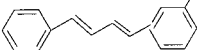
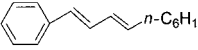
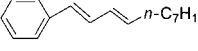
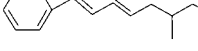
We observed that certain organozinc reagents worked best at particular reaction conditions. For the benzylic zinc halides, reactions at room temperature gave the corresponding *E*-stilbenes in good-to-excellent yields after 8 h (78–92%, entries 1–8). However, when alkylzinc iodides were used, yields of *E*-alkenes were optimized by carrying out reactions at -18°C , and then warming to room temperature (54–89%, entries 10–15, 18–21). Both electron-withdrawing and electron-donating substituents on the phenyl ring, such as methyl, chloro, bromo, benzyloxy, hydroxy, and methoxy, are tolerated in these reactions and generally have little effect on product yield, except for 2,4-dinitrobenzaldehyde which gave no olefination product (entries 2–11 and 17). Where organozinc halides were functionalized by chloro, bromo, and ester moieties, the corresponding *E*-alkenes also contained these groups (entries 11, 13, and 14). Interestingly, the unsaturated

[*] Prof. J.-X. Wang, Y. Fu, Dr. Y. Hu
Institute of Chemistry, Department of Chemistry
Northwest Normal University
Lanzhou 730070 (P. R. China)
Fax: (+86) 931-776-8159
E-mail: wangjx@nwnu.edu.cn

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Table 1. Nickel(II)-catalyzed alkenylation of functionalized organozinc reagents with aldehydes.[a]

Entry	Ar	FG-R or Aryl	X	Temp. [°C]	Time [h]	Product[b]	Yield[c] [%]
1	Ph	Ph	Cl	RT	8	 1a	88
2	2-MeOPh	Ph	Cl	RT	8	 1b	79
3	4-HOPh	Ph	Cl	RT	8	 1c	78
4	4-ClPh	Ph	Br	RT	8	 1d	87
5	Ph	3-ClPh	Br	RT	8	 1e	81
6	Ph	3-BrPh	Br	RT	8	 1f	63
7	Ph	4-BrPh	Br	RT	8	 1g	85
8	4-MeOPh	Ph	Cl	RT	8	 1h	92
9	2,4-(O ₂ N) ₂ Ph	Ph	Br	RT	8	no reaction	0
10	4-MeOPh	<i>n</i> -C ₇ H ₁₅ -	I	-18-RT	12	 2a	68
11	4-MeOPh	Cl(CH ₂) ₃ -	I	-18-RT	12	 2b	63
12	Ph	 2c	I	-18-RT	12		61
13	Ph	EtO ₂ CCH ₂ -	I	-18-RT	12	 2d	66
14	Ph	Br(CH ₂) ₃ -	I	-18-RT	12	 2e	65
15	Ph	<i>n</i> -C ₄ H ₉ -	I	-18-RT	12	 2f	68
16	PhCH=CH ₂ -	Ph	Cl	RT	8	 3a	89
17	PhCH=CH ₂ -	3-ClPh	Br	RT	8	 3b	74
18	PhCH=CH ₂ -	<i>n</i> -C ₆ H ₁₃ -	I	-18-RT	12	 4a	62
19	PhCH=CH ₂ -	<i>n</i> -C ₇ H ₁₅ -	I	-18-RT	12	 4b	60
20	PhCH=CH ₂ -	 4c	I	-18-RT	12		54
21	PhCH=CH ₂ -	<i>n</i> -C ₅ H ₁₁ -	I	-18-RT	12	 4d	65

[a] All reactions were conducted on the following scale: 10 mmol aldehydes, 11 mmol organozinc reagents, 0.3 mmol catalyst [NiCl₂(PPh₃)₂] in THF (20 mL).
 [b] All products were characterized by IR and ¹H NMR spectroscopy, as well as mass spectrometry. [c] Yields of isolated products.

double bond of phenylacrylic aldehyde could also be introduced into the products in moderate-to-good yields (entries 16–21). We also found that these reactions tolerated different molecular structures of RZnX; for example, under the same conditions, the use of sterically hindered complexes with branched functionalities gave the desired products in moderate yields (entries 12 and 20).

One advantage of this reaction, which makes it a particularly attractive synthetic procedure, is its regioselectivity. The double bond is formed between the carbonyl carbon atom of the aldehyde and the carbon atom of the organozinc reagent. The reaction is also stereoselective; in all cases only the *E*-alkenes were isolated after chromatography.

In the well-studied Wittig reaction, stilbenes are usually formed in moderate-to-high yield as a mixture of *E* and *Z* isomers, together with triphenylphosphine oxide as a by-product.^[1a] Although the *E*:*Z* ratio can be changed by varying some of the reaction conditions,^[12, 13] recent studies indicate that the *E*:*Z* ratio is unchanged by varying the concentration, mode of addition, or molar ratio of the aldehyde and ylide.^[14] Slight variations were seen by changing the substituents in the aldehyde and aryl alkylidenetriphenylphosphorane precursors. The use of an aldehyde as its enamine derivative can limit possible side reactions to give *E*-stilbenes in high yields.^[1a] Our experimental results showed that this reaction is highly stereoselective and only gives *E*-alkenes selectively.

Based on our experimental results and other related studies,^{[15], [16]} we propose the general reaction mechanism shown in Scheme 2. The first step of this mechanism is the reaction of $[\text{NiCl}_2(\text{PPh}_3)_2]$ (**1**) with the functionalized organozinc reagent **2**, to form $[\text{FG-ArCH}_2\text{NiCl}(\text{PPh}_3)_2]$ (**3**). The second step is 1,2-addition of **3** to an aromatic aldehyde **4**, which is activated by chlorotrimethylsilane,^[17] to give nickel complex **6**. The loss of **1** from **6**, in the presence of chlorotrimethylsilane, yields secondary silyl ethers **7**, which have been isolated.^[18] Compounds **7** can also be detected in the reaction by GC-MS. Loss of Me_3SiOH from **7** gives the final *E*-alkenes product **8**.

In conclusion, we have developed a new and convenient method for the efficient and highly stereoselective synthesis of *E*-alkenes from the corresponding aldehydes and functionalized organozinc reagents in the presence of a silylating agent and a catalytic quantity of $[\text{NiCl}_2(\text{PPh}_3)_2]$. The main advantages of this new method are high stereoselectivity, tolerance to unsaturated and polyfunctional groups, simple operation procedure, and excellent product yields, all under relatively mild reaction conditions.

Experimental Section

Typical procedure: Method A: Benzylzinc halides (11 mmol) were prepared following Knochel's procedure.^[19] $[\text{NiCl}_2(\text{PPh}_3)_2]$ (0.2 g, 0.3 mmol) in THF (2 mL) was added to a solution of benzylzinc halides in THF at 0 °C. After stirring the mixture for 2 min, the temperature was allowed to reach room temperature. A solution of benzaldehyde (1.06 g, 10 mmol) and Me_3SiCl (2.18 g, 20 mmol) in THF (10 mL) was then added dropwise. The reaction mixture was stirred at room temperature for 8 h. *E*-stilbenes were obtained by column chromatography on silica gel using petroleum/ethyl acetate as an eluent. All products were characterized by IR, ^1H NMR, and mass spectroscopy.

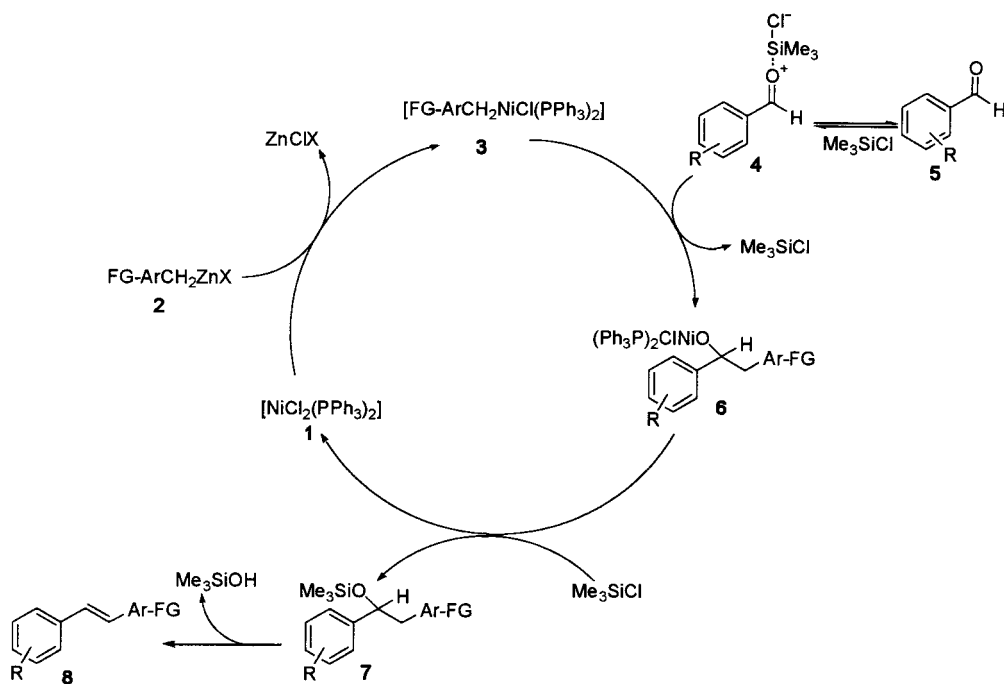
1b: ^1H NMR (400 MHz, CDCl_3): δ = 7.62–7.50 (m, 4H; Ar-H), 7.39–7.19 (m, 4H; Ar-H), 7.10 (d, $^3J(\text{H,H})$ = 16.6 Hz, 1H; =CH), 6.94 (dd, $^3J(\text{H,H})$ = 18.6 Hz, $^3J(\text{H,H})$ = 7.0 Hz, 2H; =CH, Ar-H), 3.88 ppm (s, 3H; OCH_3); IR (KBr): $\tilde{\nu}$ = 3017, 2969, 2841, 1600, 1591, 1569, 1483, 1466, 1241, 1030, 965, 753, 691 cm^{-1} ; MS (70 eV): m/z (%): 210 (100) [M^+], 195 (4) [$M^+ - \text{CH}_3$], 179 (13) [$M^+ - \text{OCH}_3$], 165 (40) [$M^+ - \text{OCH}_3 - \text{CH}_2$], 152 (12) [$M^+ - \text{OCH}_3 - \text{C}_2\text{H}_5$], 139 (4) [$M^+ - \text{OCH}_3 - \text{C}_3\text{H}_7$], 128 (2) [$M^+ - \text{OCH}_3 - \text{C}_4\text{H}_9$], 115 (3) [$M^+ - \text{OCH}_3 - \text{C}_5\text{H}_{11}$], 104 (17) [$M^+ - \text{OCH}_3 - \text{C}_6\text{H}_{13}$], 91 (24) [$\text{C}_6\text{H}_5\text{CH}^+ + 1$], 77 (3) [C_6H_5^+].

2a: ^1H NMR (400 MHz, CDCl_3): δ = 7.32 (dt, $^3J(\text{H,H})$ = 8.2 Hz, $^4J(\text{H,H})$ = 2.0 Hz, 2H; Ar-H), 6.80 (dt, $^3J(\text{H,H})$ = 8.8 Hz, $^4J(\text{H,H})$ = 1.8 Hz, 2H; Ar-H), 6.28 (d, $^3J(\text{H,H})$ = 15.8 Hz, 1H; H-1), 6.02 (dt, $^3J(\text{H,H})$ = 15.8 Hz, $^4J(\text{H,H})$ = 7.2 Hz, 1H; H-2), 3.77 (s, 3H, OCH_3), 2.17 (q, 2H, $^3J(\text{H,H})$ = 6.6 Hz), 1.41–1.08 (m, 10H, CH_2), 0.88 ppm (t, $^3J(\text{H,H})$ = 6.4 Hz, 3H; CH_3); IR (neat): $\tilde{\nu}$ = 2927, 2855, 1610, 1511, 1465, 1370, 1301, 1241, 1098, 964, 831, 725 cm^{-1} ; MS (70 eV): m/z (%): 232 (M^+ , 17.5), 147(100), 134 (22.5), 121, (46.8), 91 (24), 77 (7.0).

2b: ^1H NMR (400 MHz, CDCl_3): δ = 7.27 (dt, $^3J(\text{H,H})$ = 8.8 Hz, $^4J(\text{H,H})$ = 2.2 Hz, 2H; Ar-H), 6.84 (m, 2H; Ar-H), 6.37 (d, $^3J(\text{H,H})$ = 16.0 Hz, 1H; H-1), 6.01 (dt, $^3J(\text{H,H})$ = 15.8 Hz, $^4J(\text{H,H})$ = 7.0 Hz, 1H; H-2), 3.77 (s, 3H, OCH_3), 3.55 (t, $^3J(\text{H,H})$ = 6.6 Hz, 2H; CH_2), 2.35 (q, $^3J(\text{H,H})$ = 6.8 Hz, 2H; CH_2), 1.95–1.74 ppm (m, 2H, CH_2); IR (neat): $\tilde{\nu}$ = 2996, 2934, 2861, 1610, 1512, 1461, 1240, 1170, 1037, 960, 800, 725, 685, 651 cm^{-1} ; MS (70 eV): m/z (%): 214 (1) [$M^+ + 4$], 213 (3) [$M^+ + 3$], 212 (3) [$M^+ + 2$], 211 (9) [$M^+ + 1$], 210 (21) [M^+], 175 (2), 161 (2), 147 (100), 121 (51), 91 (35), 77 (14).

3b: ^1H NMR (400 MHz, CDCl_3): δ = 7.46 (t, $^3J(\text{H,H})$ = 7.6 Hz, 3H; Ar-H), 7.36 (t, $^3J(\text{H,H})$ = 7.6 Hz, 2H; Ar-H), 7.32–7.20 (m, 4H; Ar-H), 6.98 (ddd, $^3J(\text{H,H})$ = 19.8 Hz, $^4J(\text{H,H})$ = 10.6 Hz, $^4J(\text{H,H})$ = 4.1 Hz; 1H), 6.94 (ddd, $^3J(\text{H,H})$ = 19.8 Hz, $^4J(\text{H,H})$ = 10.6 Hz, $^4J(\text{H,H})$ = 4.1 Hz, 1H; CH=), 6.72 (ddd, $^3J(\text{H,H})$ = 20.5 Hz, $^4J(\text{H,H})$ = 11.4 Hz, $^4J(\text{H,H})$ = 5.3 Hz, 1H; CH=), 6.61 ppm (ddd, $^3J(\text{H,H})$ = 21.2 Hz, $^4J(\text{H,H})$ = 11.5 Hz, $^4J(\text{H,H})$ = 4.6 Hz, 1H; CH=); MS (70 eV): m/z (%): 243 (3.4) [$M^+ + 3$], 242 (19.8) [$M^+ + 2$], 241 (13.1) [$M^+ + 1$], 240 (62.1) [M^+], 205 (100) [$M - \text{Cl}$].

4c: ^1H NMR (400 MHz, CDCl_3): δ = 7.45–7.19 (m, 5H; Ar-H), 6.82 (dd, $^3J(\text{H,H})$ = 16.8 Hz, $^4J(\text{H,H})$ = 10.2 Hz, 1H; H-1), 6.53 (t, $^3J(\text{H,H})$ = 16.8 Hz, 1H; H-2), 6.25 (dd, $^3J(\text{H,H})$ = 15.2 Hz, $^4J(\text{H,H})$ = 10.2 Hz, 1H; H-3), 5.80 (dt, $^3J(\text{H,H})$ = 15.0 Hz, $^4J(\text{H,H})$ = 7.0 Hz, 1H; H-4), 2.10 (q, $^3J(\text{H,H})$ = 7.0 Hz, 2H; CH_2), 1.46–1.25 (m, 10H, CH_2), 0.88 ppm (t, $^3J(\text{H,H})$ = 6.2 Hz, 3H; CH_3); IR (neat): $\tilde{\nu}$ = 2926, 2855, 1636, 1606, 1511, 1465, 1370, 1250, 1037, 962, 838, 765 cm^{-1} ; MS (70 eV): m/z (%): 243 (1) [$M^+ + 1$], 242 (5) [M^+], 197 (2), 183 (1), 169 (1), 157 (1), 143 (47), 128 (28), 117 (7), 104 (2), 91 (13), 77 (5), 57 (100), 41 (57).



Scheme 2. General mechanism for a nickel(II)-catalyzed alkenylation of aldehydes with functionalized organozinc reagents. The compounds labeled **1**–**8** in this scheme are distinct from any other numbered species in either the main text, the Experimental Section, or the Supporting Information.

Method B: Under an argon atmosphere, a mixture of zinc dust (0.85 g, 13 mmol), 1,2-dibromoethane (0.19 g, 1.0 mmol), and THF (2 mL) was heated in a three-necked flask to 60–70 °C for 2–3 min and then cooled to room temperature. Chlorotrimethylsilane (0.1 mL) was added, and the mixture was stirred at room temperature for 15 min. A solution of RI (12 mmol) in THF (10 mL) was then added, and the mixture was stirred for 12 h at 35 °C. The resulting RZnI solution was then added to another three-necked flask, in which $[\text{NiCl}_2(\text{PPh}_3)_2]$ (0.2 g, 0.3 mmol) and THF (2 mL) had been previously heated at 60 °C for 2 min. The resulting mixture was cooled to –18 °C. A solution of aldehyde (10 mmol) and chlorotrimethylsilane (20 mmol) in THF (10 mL) was added over a few minutes and the mixture was allowed to warm to room temperature. After stirring the mixture for 12 h, saturated aqueous solution of NH_4Cl (10 mL) and Et_2O (10 mL) were added and the mixture was stirred for 10 min. The organic layer was separated, dried over anhydrous MgSO_4 , and concentrated. The product was isolated from the crude reaction mixture by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent.

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- [18] Spectroscopic data for **7**: ^1H NMR (400 MHz, CDCl_3): δ = 7.42 (dd, $^3J(\text{H,H})$ = 8.2 Hz, $^3J(\text{H,H})$ = 1.8 Hz; 1H), 6.89 (t, $^3J(\text{H,H})$ = 7.4 Hz; 1H), 6.77 (d, $^3J(\text{H,H})$ = 8.2 Hz; 1H), 5.09 (t, $^3J(\text{H,H})$ = 6.0 Hz; 1H), 3.77 (s, 3H), 1.58 (s, 2H), 1.24 (s, 8H), 0.84 (t, $^3J(\text{H,H})$ = 6.6 Hz; 3H), 0.06 ppm (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ = 155.4, 134.3, 127.4, 126.7, 120.4, 109.8, 68.3, 39.0, 31.8, 29.2, 26.0, 22.7, 14.1, 0.0 ppm; MS (70 eV): m/z (%): 296 (M^+ +2, 0.5), 281 (5), 211 (100), 181 (5), 136 (4), 122 (4), 92 (4), 74 (16).
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Mechanistic Features, Cooperativity, and Robustness in the Self-Assembly of Multicomponent Silver(I) Grid-Type Metalloarchitectures

Annie Marquis, Jean-Pierre Kintzinger, Roland Graff, Paul N. W. Baxter, and Jean-Marie Lehn*

Self-organization processes allow the spontaneous but controlled generation of complex organic or inorganic architecture on the basis of the molecular information stored in the components, and its processing through the interactional algorithms defined by specific molecular recognition events.^[1, 2] Such processes connect input components with output entity(ies), with a fidelity/reliability depending on the robustness of the program, that is, its ability to resist interference from factors other than the directing/dominant coding interactions.

While in equilibrium conditions, the process ideally leads to the preferential formation of a given entity under thermodynamic control/pressure; input and output species may be linked by complex mechanistic pathways and involve the generation of kinetic species that may or may not be direct intermediates. Such is the case, for instance, in the final formation of the thermodynamically favored circular helicates following kinetically favored triple-helical complexes.^[3]

Although it is crucial to gain insight into the mechanistic, thermodynamic, and kinetic features of the self-organization process, only few such studies have been reported.^[4] Whereas the preferential, ideally exclusive, formation of a given entity is usually pursued, various factors may interfere with the dominant code and complicate the issue. Thus, considering the self-assembly of inorganic grid architectures, which makes use of specifically designed ligands and of strong metal-ion coordination interactions, $[2 \times 2]$ -,^[5] $[3 \times 3]$ -,^[6] and $[4 \times 4]$ -^[7] type entities form exclusively. However, with a pentadentate ligand, both an incomplete $[4 \times 5]\text{Ag}^+_{20}$ grid and a quadruple helicate are simultaneously generated in place of the full $[5 \times 5]\text{Ag}^+_{25}$ entity, because of the interplay of various structural factors.^[8] On the other hand, such cases also stress that when different “Boltzmann species” are thus formed, provided they are well defined, diversity ensues, an attractive feature of multiple outputs^[9] in a self-assembly process. To gain understanding of the self-organization pathways, it is first necessary to identify the species that may form and then try to define their role in the process. In particular, features such as

[*] Prof. Dr. J.-M. Lehn, Dr. A. Marquis, Dr. P. N. W. Baxter

Laboratoire de Chimie Supramoléculaire
ISIS-Université Louis Pasteur
4, rue Blaise Pascal, 67000 Strasbourg (France)
Fax: (+33)390-241-117
E-mail: lehn@chimie.u-strasbg.fr

Dr. J.-P. Kintzinger
Laboratoire de RMN de la Matière Condensée
CNRS-Université Louis Pasteur
4, rue Blaise Pascal, 67000 Strasbourg (France)

Dr. R. Graff
Service Commun de RMN
Université Louis Pasteur
1, rue Blaise Pascal, 67000 Strasbourg (France)