

Reactions of Geminal Dication Synthons with Geminal Dianionic Species. Cross Coupling of Benzylic Dithioacetals with Nickela-Bimetallic Reagents

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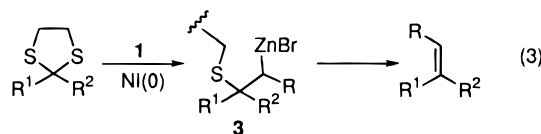
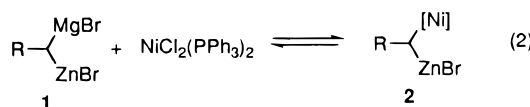
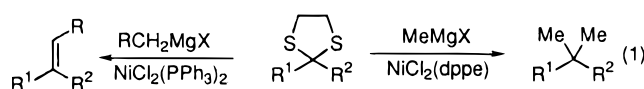
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Summary: Nickel-catalyzed cross-coupling reactions of dithioacetals derived from diaryl ketones with the geminal magna–zinc reagent give the corresponding olefination products in good yields. The less reactive dithioacetals derived from alkyl aryl ketones or aromatic aldehydes afford the similar olefination products when a stoichiometric amount of the nickel catalyst is used in the presence of 1 equiv of CuCN.

Introduction

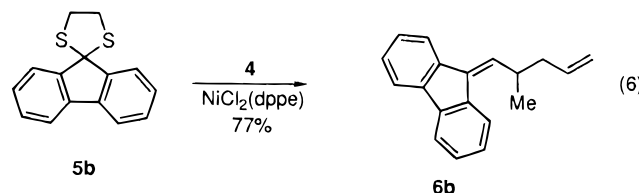
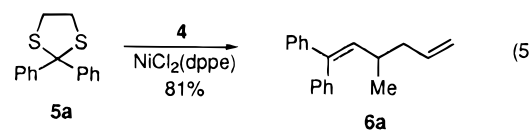
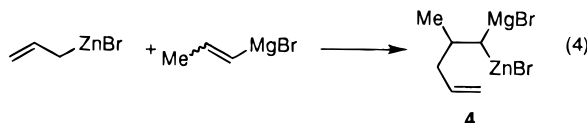
Geminal organobimetallic species have been demonstrated as valuable in ever burgeoning applications in fascinating organic transformations.² These geminal dianionic moieties are particularly useful in the alkylation of a carbonyl group as well as sequential couplings with two different electrophiles.² The reactivity of these bimetallic reagents can be tuned by variation of metals, certain transition metal analogs (e.g. zirconium) being exceedingly useful in organic synthesis. Transmetalation has often been employed for this purpose. It is noteworthy that such exchange of metallic species is one of the key steps in the transition metal-catalyzed cross-coupling reactions. However, similar reaction with a bimetallic species has not been successful. We recently reported a series of nickel-catalyzed olefination and geminal dimethylation of dithioacetals with Grignard reagents (eq 1).^{3–5} In these reactions, the dithioacetal group can be considered as a geminal dication synthon.³ The key step in these nickel-catalyzed cross coupling reactions may involve the reductive elimination of an organonickel species which is formed by transmetalation. Accordingly, when a geminal bimetallic reagent **1** is employed in the nickel-catalyzed reaction of a dithioacetal, a nickela-bimetallic intermediate **2** is envisaged (eq 2).⁶ The cross-coupling



reaction of the dithioacetal with an active Ni(0) species generated in situ from **2** will give **3** which can readily undergo Boord-type β -heteroatom elimination to yield the corresponding olefination product (eq 3).

Results and Discussion

The magna–zinc reagent **4** in THF was prepared according to the literature procedure (eq 4).^{7,8} The THF



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(1) Also known as Hsien-Jung Tseng.

(2) For a recent review, see: Farina, V. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995; Vol. 12, Chapter 3.4.

(3) For reviews, see: (a) Luh, T.-Y. *Acc. Chem. Res.* **1991**, *24*, 257. (b) Luh, T.-Y.; Ni, Z.-J. *Synthesis* **1990**, 89. (c) Luh, T.-Y.; Leung, M.-K. In *Advances in the Use of Synthons in Organic Chemistry*; Dondoni, A., Ed.; JAI: London, 1996; Vol. 2, p 129. (d) Luh, T.-Y. In *Modern Methodology in Organic Synthesis*; Shono, T., Ed.; Kodansha: Tokyo, 1992; p 229. (e) Luh, T.-Y. *Pure Appl. Chem.* **1996**, *68*, 105. (f) Luh, T.-Y. *Synlett* **1996**, 201.

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solvent of the slurry of **3** equiv of **4**⁹ was removed, and the residue was allowed to react with dithioacetal **5a** in benzene in the presence of a nickel catalyst [NiCl₂(PPh₃)₂ or NiCl₂(dppe)] while keeping the reaction

(6) There is also no evidence to show which metal (magnesium or zinc) has been transmetalated, and the exact nature of the nickela-bimetallic species **2** or **3** is not known. It is assumed that an organomagnesium compound may be more reactive than the corresponding zinc counterpart (cf. ref 8).

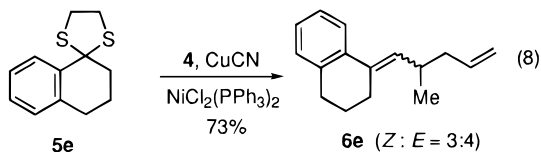
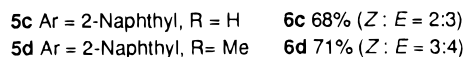
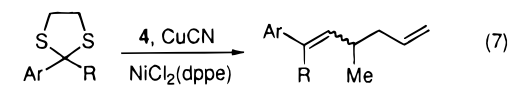
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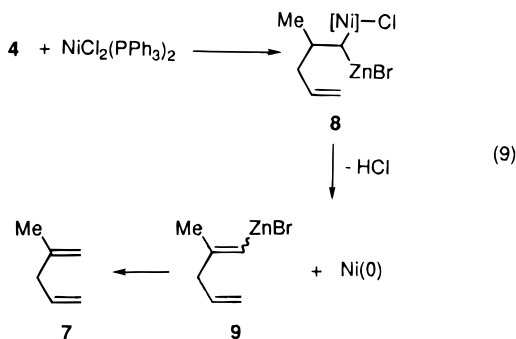
(9) Excess amount of the bimetallic reagent **4** was required to give the optimal yield of the coupling product.

temperature at 5–10 °C. After usual workup and chromatographic separation, the coupling product **6a** was obtained in 81% yield (eq 5). Similar reaction with fluorenone derivative **5b** gave **6b** in 77% yield (eq 6). It is interesting to note that dithioacetals derived from diaryl ketones gave the corresponding coupling products in good yield. In both cases, only a catalytic amount of the nickel catalyst was required. The reaction has to be carried out in aromatic hydrocarbon solvent, and a small amount of the ethereal solvent will inhibit the overall process. The reaction became extremely slow when the temperature was lower than –20 °C. On the other hand, when the reaction was carried at the refluxing benzene temperature, a mixture of unidentified products was obtained.

For less reactive substrates **5c–e**, a stoichiometric amount of the nickel catalyst was essential. In addition, 1 equiv of CuCN was necessary for these reactions (eqs 7 and 8). It is noteworthy that no reaction was observed



in the absence of the nickel catalyst. Presumably, transmetalation may occur and the active species could be a copper-containing bimetallic complex.⁸ Although the actual mode of this reaction has not been established, a similar mechanism as that for the nickel-catalyzed cross coupling of dithioacetals with the Grignard reagent may be involved (cf. eq 3).^{3–5} The generation of an active Ni(0) species from **2** will be responsible for the success of this cross-coupling reaction. Indeed, 2-methyl-1,4-pentadiene (**7**) was obtained from the reaction of **4** with 1 equiv of NiCl₂(PPh₃)₂.¹⁰ Presumably, the nickela-bimetallic intermediate **8**⁶ may undergo β-hydride elimination followed by an reductive elimination process to produce the active Ni(0) catalyst for the cross-coupling reaction. Protonolysis of the vinylic organometallic species **9** thus generated will give **7** (eq 9).



In summary, we have demonstrated the first olefination example using a geminal dianionic species to couple

with the dithioacetal which serves as a geminal dication synthon. Further applications of this new reaction in synthesis are in progress in our laboratory.

Experimental Section

Preparation of 1-Magnesium-1-zincio-2-methyl-4-pentene 4.^{7,8} To a THF solution of allylzinc bromide (6 mL of 1 M solution, 6.00 mmol) was added 1-propenylmagnesium bromide (12 mL, 0.5 M in THF, 6.00 mmol), and the mixture was stirred at room temperature for 30 min. The white precipitation was used directly for the next reaction.

1,1-Diphenyl-3-methyl-1,5-hexadiene (6a). A freshly prepared THF solution of **4** (6.00 mmol) was evacuated to remove the solvent. Under nitrogen atmosphere, a benzene (20 mL) solution of dithioacetal **5a** (516 mg, 2.00 mmol) was added. NiCl₂(dppe) (53 mg, 0.10 mmol) was then introduced, and the mixture was stirred at 5–10 °C for 12 h. The mixture was quenched with water (20 mL) and extracted with ether (20 mL × 2). The organic layer was dried (MgSO₄), and the solvent was removed in vacuo to give a brown oil which was chromatographed on silica gel (hexane) to give **6a** as a colorless oil (402 mg, 81%): ¹H NMR (400 MHz, CDCl₃) δ 1.01 (d, *J* = 6.6 Hz, 3 H), 2.07 (m, 2 H), 2.39 (doublet of sextet, *J* = 10.0, 6.6 Hz, 1 H), 4.93–5.00 (m, 2 H), 5.70 (ddt, *J* = 17.0, 10.0, 7.6 Hz, 1 H), 5.87 (d, *J* = 10.0 Hz, 1 H), 7.14–7.37 (m, 10 H); ¹³C NMR (80 MHz, CDCl₃) δ 20.8, 33.7, 41.9, 115.8, 126.8, 127.1, 128.0, 128.1, 129.8, 134.6, 135.4, 136.9, 140.3, 140.4, 142.6; IR (neat) 3056, 2960, 2923, 2866, 1640, 1493, 1443, 912, 762, 699 cm⁻¹; MS (70 eV) *m/z* (rel intensity) 248 (21), 207 (81), 178 (16), 165 (13), 129 (100), 105 (12), 91 (43), 77 (11); HRMS calcd for C₁₇H₁₈ *m/z* 248.1565, found *m/z* 248.1567.

5-(9-Fluorenylidene)-4-methyl-1-pentene (6b). According to the procedure described above, freshly prepared **4** (6.00 mmol) in benzene (20 mL) was treated with **5b** (512 mg, 2.00 mmol) in the presence of NiCl₂(dppe) (53 mg, 0.10 mmol) to give **6b** as a colorless oil (387 mg, 77%): ¹H NMR (300 MHz, CDCl₃) δ 1.28 (d, *J* = 6.6 Hz, 3 H), 2.27–2.25 (m, 2 H), 3.48 (doublet of sextet, *J* = 9.8, 6.6 Hz, 1 H), 5.04 (dd, *J* = 9.6, 1.9 Hz, 2 H), 5.12 (dd, *J* = 15.2, 1.9 Hz, 2 H), 5.88 (ddt, *J* = 15.2, 9.6, 7.2 Hz, 1 H), 6.58 (d, *J* = 9.8 Hz, 1 H), 7.29–7.41 (m, 4 H), 7.66–7.72 (m, 2H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.88 (d, *J* = 7.2 Hz, 1H); ¹³C NMR (80 MHz, CDCl₃) δ 20.1, 33.1, 41.6, 116.5, 119.4, 119.7, 119.8, 124.8, 126.8, 126.9, 127.4, 127.7, 134.2, 136.2, 136.3, 137.1, 138.5, 139.5, 140.9; IR (neat) 3059, 2958, 2921, 2866, 1641, 1476, 1444, 912, 773, 728 cm⁻¹; MS (70 eV) *m/z* (rel intensity) 246 (20), 205 (100), 190 (12), 165 (12).

1-(2-Naphthyl)-2-methyl-1,5-hexadiene (6c). A THF solution of **4** (6.00 mmol) was evacuated under reduced pressure to which a benzene (20 mL) solution of dithioacetal **5c** (464 mg, 2.00 mmol) was added. NiCl₂(dppe) (1.05 g, 2.00 mmol) and CuCN (176 mg, 2.00 mmol) were then added using the Schlenk technique. The mixture was stirred at 5–10 °C for 18 h. Water (20 mL) was then added, and the mixture was extracted with ether (20 mL × 2). The combined extracts were dried (MgSO₄), and the solvent was evaporated in vacuo to give a brown oil which was chromatographed on silica gel (hexane) to afford a mixture of (*Z*)-**6c** and (*E*)-**6c** (302 mg, 68%, *Z*:*E* = 2:3) a colorless oil. The two isomers were separated by preparative HPLC. (*Z*)-**6c**: ¹H NMR (200 MHz, CDCl₃) δ 1.08 (d, *J* = 6.6 Hz, 3 H), 2.19 (m, 2 H), 2.93 (doublet of sextet, *J* = 10.1, 6.6 Hz, 1 H), 4.94–5.07 (m, 2 H), 5.53 (dd, *J* = 10.2, 11.6 Hz, 1 H), 5.77 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 6.51 (d, *J* = 11.6 Hz, 1 H), 7.36–7.45 (m, 3 H), 7.70 (s, 1 H), 7.72–7.81 (m, 3 H); ¹³C NMR (80 MHz, CDCl₃) δ 20.7, 32.3, 41.8, 115.9, 125.6, 126.0, 127.1, 127.2, 127.5, 127.6, 127.7, 127.9, 132.2, 133.4, 135.3, 136.8, 139.0; IR (neat, cm⁻¹) 3056, 2958, 2923, 1640, 1454, 912, 857, 819, 738; MS (70 eV) *m/z* (rel intensity) 222 (16), 181 (100), 166 (43), 141 (9), 115 (6), 88 (9), 61 (27); HRMS calcd for C₁₇H₁₈ *m/z* 222.1408, found *m/z* 222.1403. (*E*)-**6c**: ¹H NMR (200 MHz, CDCl₃) δ 1.12 (d, *J* = 6.6 Hz, 3 H), 2.18 (m,

(10) Compound **7** exhibited identical mass spectral properties as those of the literature data. The ¹H NMR data for **7** are the same as those reported in the literature (cf. Aldrich Library of ¹³C and ¹H FT-NMR Spectra, Vol. 1, 42A).

2 H), 2.45 (septet, $J = 6.6$ Hz, 1 H), 4.97–5.10 (m, 2 H), 5.28 (ddt, $J = 17.2, 10.2, 6.8$ Hz, 1 H), 6.25 (dd, $J = 6.6, 16.0$ Hz, 1 H), 6.51 (d, $J = 16.0$ Hz, 1 H), 7.37–7.43 (m, 2 H), 7.56 (dd, $J = 2.0, 8.6$ Hz, 1 H), 7.67 (s, 1 H), 7.73–7.78 (m, 3 H); ^{13}C NMR (80 MHz, CDCl_3) δ 20.0, 37.0, 41.4, 115.0, 123.6, 125.4, 126.1, 127.6, 127.8, 128.0, 128.3, 132.3, 132.7, 133.7, 135.3, 136.5, 136.9; IR (neat) 3056, 2962, 2922, 1639, 1507, 1453, 964, 912, 809, 743 cm^{-1} ; MS (70 eV) m/z (rel intensity) 222 (18), 181 (100), 166 (39), 141 (8), 115 (6), 84 (2), 61 (11); HRMS calcd for $\text{C}_{17}\text{H}_{18}$ m/z 222.1408, found m/z 222.1406.

1-(2-Naphthyl)-1,3-dimethyl-1,5-hexadiene (6d). In a manner similar to that described above, a benzene (20 mL) solution of dithioacetal **5d** (492 mg, 2.00 mmol) was allowed to react with **4** (6.00 mmol) in the presence of $\text{NiCl}_2(\text{PPh}_3)_2$ (1.31 g, 2 mmol) and CuCN (176 mg, 2 mmol) at 5–10 °C for 18 h to yield (*Z*)-**6d** and (*E*)-**6d** (335 mg, 71%, *Z*:*E* = 3:4). (*Z*)-**6d**: ^1H NMR (300 MHz, CDCl_3) δ 1.08 (d, $J = 6.6$ Hz, 3 H), 2.12–2.19 (m, 5 H, embodied a singlet at 2.14 due to the methyl group), 2.69 (doublet of sextet, $J = 9.6, 6.6$ Hz, 1 H), 5.00 (d, $J = 10.2$ Hz, 1 H), 5.05 (d, $J = 17.2$ Hz, 1 H), 5.74 (d, $J = 9.6$ Hz, 1 H), 5.83 (ddt, $J = 17.2, 10.2, 7.2$ Hz, 1 H), 7.39–7.46 (m, 2 H), 7.56 (dd, $J = 8.4, 1.5$ Hz, 1 H), 7.74–7.81 (m, 3 H); ^{13}C NMR (80 MHz, CDCl_3) δ 16.1, 20.5, 33.3, 41.8, 115.8, 124.0, 124.5, 125.4, 126.0, 127.4, 127.5, 128.0, 132.4, 133.3, 133.5, 135.0, 137.1, 141.1; IR (neat, cm^{-1}) 3055, 2958, 2921, 1639, 1503, 1452, 1381, 911, 851, 814, 745; MS (70 eV) m/z (rel intensity) 236 (16), 195 (100), 165 (48), 153 (22), 128 (6), 115 (6), 77 (3), 65(3); HRMS calcd for $\text{C}_{18}\text{H}_{20}$ m/z 236.1565, found m/z 236.1568. (*E*)-**6d**: ^1H NMR (300 MHz, CDCl_3) δ 0.96 (d, $J = 6.6$ Hz, 3 H), 1.96–2.09 (m, 2 H), 2.10 (d, $J = 1.2$ Hz, 3 H), 2.37 (doublet of sextet, $J = 10.2, 6.6$ Hz, 1 H), 4.94–5.00 (m, 2 H), 5.35 (dd, $J = 10.2, 1.2$ Hz, 1 H), 5.71 (ddt, $J = 17.0, 10.0, 7.0$ Hz, 1 H), 7.33 (dd, $J = 8.4, 1.5$ Hz, 1 H), 7.46 (m, 2 H), 7.64 (s, 1 H), 7.80–7.85 (m, 3 H); ^{13}C NMR (80 MHz, CDCl_3) δ 20.9, 25.8, 33.0, 41.9, 115.5, 125.4, 125.9, 126.1, 126.7, 127.5, 127.6, 127.9, 132.2, 133.3, 133.8, 135.1, 137.2, 140.1;

IR (neat, cm^{-1}) 3055, 2961, 2922, 1639, 1503, 1436, 1373, 910, 856, 818, 747; MS (70 eV) m/z (rel intensity) 236 (13), 195 (100), 165 (42), 153 (31), 128 (7), 115 (8), 77 (5), 65 (4); HRMS calcd for $\text{C}_{18}\text{H}_{20}$ m/z 236.1565, found m/z 236.1568.

5-(1-Tetralenylidene)-4-methyl-1-pentene (6e). In a manner similar to that described above, a benzene (20 mL) solution of dithioacetal **5e** (444 mg, 2 mmol) was treated with **4** (6.00 mmol) in the presence of $\text{NiCl}_2(\text{PPh}_3)_2$ (1.31 g, 2.00 mmol) and CuCN (176 mg, 2.00 mmol) for 18 h to afford a mixture of (*Z*)-**6e** and (*E*)-**6e** (309 mg, 73%, *Z*:*E* = 3:4). (*Z*)-**6e**: ^1H NMR (300 MHz, CDCl_3) δ 1.04 (d, $J = 6.6$ Hz, 3 H), 1.82–1.91 (m, 2 H), 2.02–2.16 (m, 2 H), 2.32–2.37 (m, 2 H), 2.69–2.87 (m, 3 H), 4.90–5.00 (m, 2 H), 5.17 (d, $J = 10.5$ Hz, 1 H), 5.72 (ddt, $J = 17.2, 10.0, 7.2$ Hz, 1 H), 7.13 (m, 3 H), 7.30 (m, 1 H); ^{13}C NMR (80 MHz, CDCl_3) δ 21.0, 24.4, 29.6, 32.4, 34.5, 42.3, 115.6, 125.0, 126.7, 127.7, 128.4, 132.4, 134.4, 136.4, 137.0, 138.7; IR (neat) 3069, 2950, 2927, 2865, 1639, 1483, 1452, 911, 761 cm^{-1} ; MS (70 eV) m/z (rel intensity) 212 (17), 184 (5), 171 (100), 155 (6), 129 (55), 115 (22), 91 (11), 77 (5), 55 (19); HRMS calcd for $\text{C}_{16}\text{H}_{20}$ m/z 212.1565, found m/z 212.1560. (*E*)-**6e**: ^1H NMR (300 MHz, CDCl_3) δ 1.02 (d, $J = 6.6$ Hz, 3 H), 1.76–1.85 (m, 2 H), 2.08–2.13 (m, 2 H), 2.46–2.51 (m, 2 H), 2.64 (doublet of sextet, $J = 9.6, 6.6$ Hz, 1 H), 2.76 (t, $J = 6.3$ Hz, 1 H), 4.93–5.04 (m, 2 H), 5.71–5.83 (m, 2 H), 7.09 (m, 3 H), 7.55 (m, 1 H); ^{13}C NMR (80 MHz, CDCl_3) δ 20.5, 23.4, 26.6, 30.5, 32.5, 41.8, 115.7, 123.7, 125.9, 126.4, 128.8, 130.2, 133.0, 136.4, 137.2, 137.3; IR (neat) 3065, 3016, 2956, 2925, 2864, 1483, 1454, 1439, 911, 754 cm^{-1} ; MS (70 eV) m/z (rel intensity) 212 (21), 195 (3), 171 (100), 153 (6), 129 (47), 115 (19), 91 (7), 77 (4), 55 (17); HRMS calcd for $\text{C}_{16}\text{H}_{20}$ m/z 212.1565, found m/z 212.1558.

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