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# Geminal Dialkylation, Alkylative Reduction and Olefination of Aliphatic Aldehydes. Reaction of *gem*-Bistriflates with Higher Order Dialkylcyanocuprates.

**A. García Martínez,[a*] J. Osío Barcina,[a] B. Ruiz Díez,[a] L. R. Subramanian[b]**

[a]Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Complutense, Ciudad Universitaria, E-28040 Madrid, Spain

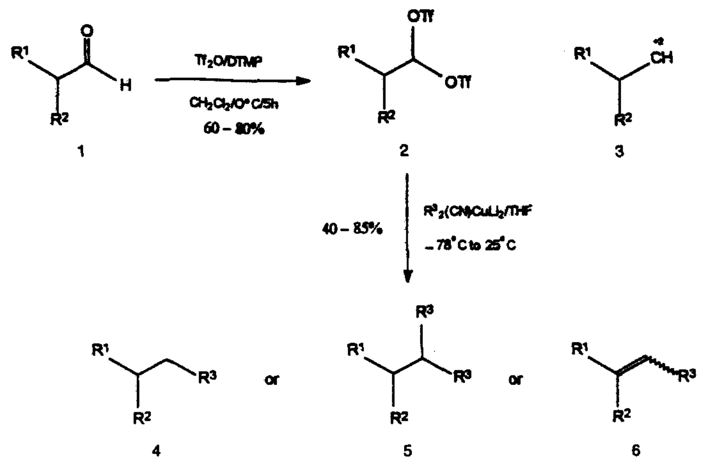
[b]Institut für Organische Chemie, Lehrstuhl für Organische Chemie II, Auf der Morgenstelle 18, D-72076 Tübingen, Germany

*Abstract:* *gem*-Dialkylation or alkylative reduction of $\alpha$-unbranched aliphatic aldehydes **1** is advantageously achieved by reaction of the corresponding *gem*-bistriflates **2** with di-*n*-alkylcyanocuprates or di-*sec*- and di-*tert*-alkylcyanocuprates respectively. The reaction of $\alpha$-branched *gem*-bistriflates **2** with dialkylcyanocuprates in the presence of boron trifluoride affords the olefins **6** in good yield.

The *gem*-bistriflates **2** are easily obtained in good yields as primary products in the reaction of aliphatic aldehydes **1** with triflic anhydride ($Tf_2O$).[1,2] The chemistry of these compounds is important because they can be considered as synthetic equivalents of the dications **3** (Scheme 1). In search of new methods for the formation of carbon framework, we present here the reaction of *gem*-bistriflates **2** with organocuprates. Lithium dialkylcuprates couple with vinyl triflates, however, they do not react with aryl triflates.[3] Coupling reactions of higher order dialkylcyanocuprates[4] with both vinyl[5] and aryl triflates,[6] but not with alkyl triflates, have been reported.

We have found that the reaction of lithium dialkylcuprates with **2** affords always complicated mixtures of products. Fortunately, the reaction with higher order dialkylcyanocuprates $R_2^3(CN)CuLi_2$ in tetrahydrofuran furnishes single products in good yields, whose structure is very much dependent on the steric hindrance of the radicals $R^1$-$R^3$ (Scheme 1 and Table).

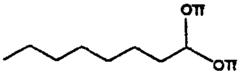
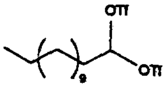
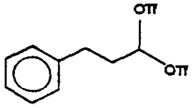
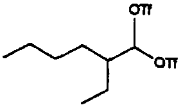
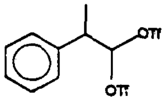
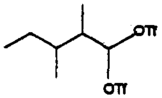
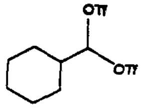
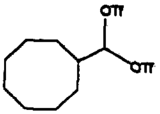
Thus, the reaction of $\alpha$-unbranched *gem*-bistriflates **2** ($R^2$= H) with primary cyanocuprates ($R^3$= $CH_3$, *n*-Bu) yields the corresponding *gem*-dialkylated products **5a-d**. When $R^3$ is secondary ($R^3$= *s*-Bu) or tertiary ($R^3$= *t*-Bu) the reaction leads to the alkylative reduction products **4e, f**. In the case of $\alpha$-branched **2** ($R^1$, $R^2 \neq$ H), the reaction takes place only when $R^3$= $CH_3$ yielding the olefins **6g, k, m, q**. However, under addition of $Et_2O.BF_3$[6] the reaction succeeds also with secondary and tertiary radicals ($R^3$= *s*-Bu, *t*-Bu) affording




| 4-6 | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| a | $n$-$C_6H_{13}$ | H | $CH_3$ |
| b | $n$-$C_{11}H_{23}$ | H | $CH_3$ |
| c | $C_6H_5$-$CH_2$ | H | $CH_3$ |
| d | $C_6H_5$-$CH_2$ | H | $n$-Bu |
| e | $C_6H_5$-$CH_2$ | H | $s$-Bu |
| f | $C_6H_5$-$CH_2$ | H | $t$-Bu |
| g | $C_4H_9$ | $C_2H_5$ | $CH_3$ |
| h | $C_4H_9$ | $C_2H_5$ | $n$-Bu |
| i | $C_4H_9$ | $C_2H_5$ | $s$-Bu |
| j | $C_4H_9$ | $C_2H_5$ | $t$-Bu |
| k | $C_6H_5$ | $CH_3$ | $CH_3$ |
| l | $CH_3$-$CH_2$-CH-$CH_3$ | $CH_3$ | $t$-Bu |
| m | -$(CH_2)_5$- | | $CH_3$ |
| n | -$(CH_2)_5$- | | $n$-Bu |
| o | -$(CH_2)_5$- | | $s$-Bu |
| p | -$(CH_2)_5$- | | $t$-Bu |
| q | -$(CH_2)_7$- | | $CH_3$ |

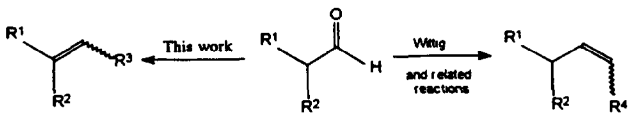
Scheme 1

**Table**. Reaction of *gem*-Bistriflates **2** with Higher Order Dialkylcyanocuprates.

| **2** | Product | Yield (%)[a] |
|---|---|---|
|  | **5a** | 60 |
|  | **5b** | 50 |
|  | **5c** | 70 |
| | **5d** | 40 |
| | **4e** | 56 |
| | **4f** | 44 |
|  | **6g** | 80 (*Z*/*E*= 55/45)[b] |
| | **6h** | 52 (*Z*/*E*= 55/45)[b] |
| | **6i** | 71 (*Z*/*E*= 55/45)[b] |
| | **6j** | 60 (*Z*/*E*= 52/48)[b] |
|  | **6k** | 50 (*Z*/*E*= 74/26)[b] |
|  | **6l** | 55 (*Z*/*E*= 60/40)[b] |
|  | **6m** | 85 |
| | **6n** | 50 |
| | **6o** | 77 |
| | **6p** | 40 |
|  | **6q** | 60 |

[a]Yield of isolated product. [b]Calculated by GC. The configurations were determinated by $^{13}$C-NMR.

the corresponding olefins **6h-j**, **l**, **n-p**. It is noteworthy that, although in some examples (**6g-6j**) the *Z*/*E* ratios are close to 50:50, the Z-isomers were obtained predominantly in every case (see Table) and also that this procedure leads to olefins which are positional isomers of those obtained with the Wittig and related reactions[7] from the same aldehydes (Scheme 2).




Scheme 2

In summary, the reaction of α-unbranched *gem*-bistriflates **2** with higher order dialkylcyanocuprates is an efficient alternative to the *gem*-dialkylation of α-unbranched aldehydes *via* the corresponding *gem*-dihalides.[8] The reaction of α-branched *gem*-bistriflates **2** constitutes a new method for the regioselective olefination of the corresponding aldehydes, which is suitable for the preparation of highly hindered alkenes. Studies on the mechanism and the influence of promoters to increase the stereoselectivity of the process are in progress.

## EXPERIMENTAL

Starting materials and solvents were used as received from commercial suppliers. Tetrahydrofuran (THF) was distilled from sodium/benzophenone and $LiAlH_4$ under argon atmosphere. $^1H$-NMR and $^{13}C$-NMR spectra were recorded on a Bruker-AC 250 MHz spectrometer in $CDCl_3$ and chemical shifts are expresed in ppm. IR spectra were recorded on a Perkin-Elmer 781 spectrometer. Mass spectra were recorded on a Varian-MAT 711 instrument.

**General procedure for the preparation of *gem*-bistriflates.** The *gem*-bistriflates **2** were prepared according to a procedure previously described by us,[1] by reaction of the corresponding aldehyde (25 mmol) with trifluoromethanosulphonic anhydride ($Tf_2O$) (27 mmol) in $CH_2Cl_2$ (100 ml) at 0°C. Yield 60-85%.

**General procedure for the reaction of *gem*-bistriflates 2 with higher order lithium dialkylcyanocuprates.** To a suspension of CuCN (4 mmol) in 50 ml of THF at -78°C under argon was added the corresponding alkyllithium (8 mmol) dropwise with stirring. The mixture was allowed to warm to 0°C for 10 min and cooled to -78°C. A solution of the *gem*-bistriflate **2** (1 mmol) in THF (10 ml) was added slowly. After stirring for

12 h the reaction mixture was hydrolyzed with a 10% solution of $NH_4OH$ in saturated $NH_4Cl$ (100 ml). The resulting mixture was filtered through Celite, extracted with pentane (3 x 25 ml) and dried over magnesium sulphate. The solvent was removed by distillation and the reaction products were purified by column chromatography (silica gel, *n*-pentane). When the reaction was carried out with α-branched *gem*-bistriflates **2**, 4 mmol of boron trifluoride etherate were added to the solution of the dialkylcyanocuprate just before the addition of the triflate.

**Data of 5a:**[8] Yield: 60%. IR (film): $\nu$= 2970, 2930, 1470, 1380, 1370 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): δ= 1.56-1.42 (m, 1H), 1.24 (m, 12H), 0.86 (t, 3H), 0.84 (d, 6H) ppm; $^{13}C$-NMR ($CDCl_3$): δ= 39.0, 31.9, 29.8, 29.3, 27.9, 27.3, 22.6, 22.6, 14.0 ppm.

**Data of 5b:** Yield: 50%. IR ($CCl_4$): $\nu$= 2970, 2930, 2860, 1470, 1390, 1370 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): δ= 1.42-1.56 (m, 1H), 1.24 (m, 22H), 0.86 (t, 3H), 0.84 (d, 6H) ppm; $^{13}C$-NMR ($CDCl_3$): δ= 39.1, 32.0, 30.0, 29.7, 29.4, 28.0, 27.5, 22.8, 22.7, 14.2 ppm; MS m/e (%B): 212 ($M^+$, 9), 169 (12), 113 (14), 99 (19), 71 (52), 57 (100), 43 (98).

**Data of 5c:**[8] Yield: 70%. IR ($CCl_4$): $\nu$= 3020, 2970, 2870, 1600, 1500, 1450, 1390, 1370, 750, 700 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): δ= 7.43 (m, 5H), 2.75 (t, 2H), 1.8-1.6 (m, 3H), 1.08 (d, 6H) ppm; $^{13}C$-NMR ($CDCl_3$): δ= 143.2, 128.4, 128.3, 125.6, 41.66, 34.6, 22.6, 28.4 ppm.

**Data of 5d:**[8] Yield: 40%. IR ($CCl_4$): $\nu$= 3020, 2970, 2930, 2870, 1600, 1490, 1460, 1380 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): δ= 7.3-7.1 (m, 5H), 2.6-2.5 (t, 2H), 1.6-1.5 (m, 1H), 1.3-1.2 (m, 14H), 0.89 (m, 6H) ppm; $^{13}C$-NMR ($CDCl_3$): δ= 143.4, 128.4, 128.3, 125.6, 37.2, 35.8, 33.2, 28.9, 23.2, 14.3 ppm.

**Data of 4e:**[8] Yield: 56%. IR ($CCl_4$): $\nu$= 3020, 2970, 2930, 2870, 1600, 1500, 1450, 1375, 730, 700 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): δ= 7.28-7.06 (m, 5H), 2.6 (t, 2H), 1.7-1.6 (m, 2H), 1.3 (m, 3H), 1.2-1.1 (m, 2H), 0.8 (m, 6H) ppm; $^{13}C$-NMR ($CDCl_3$): δ= 142.9, 128.3, 128.2, 125.5, 36.4, 34.2, 29.2, 28.8, 19.0, 11.5 ppm.

**Data of 4f:**[8] Yield: 44%. IR ($CCl_4$): $\nu$= 3020, 2970, 2870, 1600, 1500, 1450, 1390, 1360, 1250, 900 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): δ= 7.3-7.1 (m, 5H), 2.55 (t, 2H), 1.7-1.5 (m, 2H), 1.2 (m, 2H), 0.85 (s, 9H) ppm; $^{13}C$-NMR ($CDCl_3$): δ= 143.1, 128.5, 128.3, 125.7, 44.1, 37.0, 30.4, 29.7, 26.8 ppm.

**Data of *Z/E*-6g:**[9] Yield: 80%. IR (film): $\nu$= 2970, 2930, 1670, 1460, 1380, 910, 830, 750 $cm^{-1}$; $^1H$-NMR ($CDCl_3$): δ= 5.2-5.1 (q, 1H), 2.15-1.8 (m, 4H), 1.6-1.5 (d, 3H), 1.3-1.2 (m, 5H), 0.9-0.8 (m, 5H) ppm; $^{13}C$-NMR ($CDCl_3$): δ= 142.1, 117.5 (*E*), 116.9 (*Z*), 36.5, 30.6, 30.5, 29.7, 29.6, 22.9, 22.7, 22.6, 14.1, 14.0, 13.2, 13.0, 12.9, 12.8 ppm; MS m/e (%B): 126 ($M^+$, 9), 84 (25), 69 (51), 56 (20), 55 (100), 43 (13), 41 (58).

**Data of *Z/E*-6h:**[10] Yield: 52%. IR (film): $\nu$= 2990, 2930, 2870, 1660, 1455, 1380, 1010, 850, 730 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 5.1 (q, 1H), 2.0 (m, 6H), 1.3-1.2 (m, 7H), 0.9-0.7 (m, 10H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 141.1, 141.1, 124.1 (*E*), 123.4 (*Z*), 36.3, 32.5, 32.0, 30.8, 30.5, 29.9, 29.6, 29.4, 27.4, 27.3, 23.0, 22.9, 22.7, 22.6, 22.5, 22.4, 14.1, 14.0, 13.2, 12.9 ppm; MS m/e (%B): 168 ($M^+$, 12), 111 (6), 97 (19), 83 (37), 69 (100), 55 (85), 41 (62).

**Data of *Z/E*-6i:** Yield: 71%. IR (film): $\nu$= 2980, 2970, 2890, 1660, 1460, 1380, 890 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 6.4 (d, 1H), 2.3-2.2 (m, 1H), 2.1 (m, 4H), 1.4-1.2 (m, 10H), 0.8-1 (m, 8H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 135.1, 130.6 (*E*), 130.3 (*Z*), 34.2, 30.2, 29.8, 29.3, 27.2, 24.3, 22.5, 22.4, 22.3, 20.6, 14.1, 13.8, 12.1, 11.9 ppm; MS m/e (%B): 168 ($M^+$, 11), 139 (19), 111 (17), 97 (17), 83 (82), 69 (71), 55 (100), 41 (54).

**Data of *Z/E*-6j:**[10] Yield: 60%. IR (film): $\nu$= 2970, 2940, 2870, 1650, 1460, 1360, 910, 840 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 5.1 (s, 1H), 2.1 (q, 2H), 1.9 (q, 2H), 1.5-1.4 (m, 5H), 1.1 (s, 9H), 0.8-0.7 (m, 5H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 140.7, 140.4, 134.5 (*E*), 133.6 (*Z*), 37.2, 34.2, 31.7, 31.6, 31.1, 31.0, 30.7, 30.3, 23.3, 23.1, 22.5, 22.4, 14.2, 14.1, 13.5, 13.4 ppm; MS m/e (%B): 168 ($M^+$, 8), 139 (7), 111 (23), 97 (25), 83 (51), 69 (100), 55 (66), 41 (56).

**Data of *Z/E*-6k:**[11] Yield: 50%. IR (film): $\nu$= 3020, 2970, 2920, 2870, 1600, 1500, 1450, 1380, 1040, 910, 820, 760, 700 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 7.4-7.2 (m, 5H), 5.6 (q, 1H), 2.1 (dq, 3H), 1.6 (dq, 3H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 141.9 (*Z*), 136.8 (*E*), 128.5, 127.7, 126.4, 121.7, 25.5 (*Z*), 22.3 (*E*), 14.9 (*Z*), 14.0 (*E*) ppm; MS m/e (%B): 132 ($M^+$, 64), 117 (29), 91 (39), 77 (16), 65 (21), 51 (28).

**Data of *Z/E*-6l:** Yield: 55%. IR (film): $\nu$= 2970, 2940, 1650, 1460, 1360, 910, 740 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 5.15 (s, 1H), 1.9-1.7 (m, 1H), 1.6-1.5 (s, 3H), 1.4-1.2 (m, 2H), 1.0 (s, 9H), 0.8-0.6 (m, 6H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 139.3, 135.7 (*E*), 134.7 (*Z*), 46.2, 35.8, 32.3, 31.9, 31.2, 27.7, 27.6, 22.5, 19.7, 19.1, 18.7, 12.8, 12.3, 12.1 ppm; MS m/e (%B): 154 ($M^+$, 10), 125 (6), 97 (56), 83 (62), 69 (100), 55 (82), 41 (64).

**Data of 6m:**[12] Yield: 85%. IR (film): $\nu$= 2940, 2870, 1645, 1450, 1387, 1010, 900, 820 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 5.20 (qd, 1H), 1.9 (m, 4H), 1.40 (d, 3H), 1.39-1.35 (m, 6H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$=

140.2, 115.1, 37.2, 28.5, 28.1, 27.5, 26.9, 12.6 ppm; MS m/e (%B): 110 ($M^+$, 23), 95 (14), 82 (22), 81 (100), 69 (22), 67 (64), 41 (45).

**Data of 6n:**[13] Yield: 50%. IR (film): $\nu$= 2970, 2920, 1650, 1470, 1385, 1345, 1200, 1090, 1050 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 5.1-5.0 (t, 1H), 2.1-1.9 (m, 6H), 1.6-1.5 (m, 6H), 1.2 (m, 4H), 0.9-0.8 (t, 3H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 139.5, 121.4, 37.2, 32.4, 28.7, 28.6, 27.8, 26.9, 26.7, 22.9, 14.0 ppm; MS m/e (%B): 152 ($M^+$, 13), 109 (29), 96 (29), 81 (53), 67 (100), 55 (26), 41 (34).

**Data of 6o:** Yield: 77%. IR (film): $\nu$= 2960, 2860, 1665, 1450, 1370, 790 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 4.8 (d, 1H), 2.3 (m, 1H), 2.2-2.0 (m, 4H), 1.5 (m, 6H), 1.3-1.1 (m, 2H), 1.0-0.8 (m, 6H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 138.3, 128.1, 37.4, 33.5, 30.7, 29.2, 28.9, 28.1, 26.9, 21.5, 12.1 ppm; MS m/e (%B): 152 ($M^+$, 17), 123 (81), 95 (12), 81 (100), 67 (80), 41 (44), 28 (78), 17 (82).

**Data of 6p:**[13,14] Yield: 40%. IR (film): $\nu$= 2970, 2930, 1655, 1450, 1370, 1205, 840 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 5.1 (s, 1H), 2.2. (s, 2H), 1.95 (s, 2H), 1.5 (m, 6H), 1.1 (s, 9H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 139.4, 131.9, 38.7, 31.6, 29.9, 29.8, 29.1, 27.8, 27.3 ppm; MS m/e (%B): 152 ($M^+$, 16), 137 (25), 109 (30), 95 (19), 81 (43), 69 (100), 55 (29), 41 (47).

**Data of 6q:**[12] Yield: 60%. IR (film): $\nu$= 2930, 2870, 1640, 1470, 1450 $cm^{-1}$; $^1$H-NMR ($CDCl_3$): $\delta$= 5.3-5.2 (qd, 1H), 2.2-2.1 (m, 7H), 1.6-1.5 (m, 10H) ppm; $^{13}$C-NMR ($CDCl_3$): $\delta$= 141.5, 118.7, 37.7, 28.5, 27.3, 27.1, 26.6, 26.5, 26.0, 25.9 ppm; MS m/e (%B): 138 ($M^+$, 92), 123 (11), 110 (96), 109 (96), 95 (67), 82 (98), 67 (100).

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