Tetrahedron 68 (2012) 4846–4851

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

# A new entry of highly nucleophilic $CHBr_3$–$TiCl_4$–Mg system for the stereoselective synthesis of 1-alkenyl bromides

Yeshwant Ramchandra Bhorge, Su-Haur Chang, Cheng-Ta Chang, Tu-Hsin Yan *

*Department of Chemistry, National Chung-Hsing University, Taichung 400, Taiwan, ROC*

ARTICLE INFO

*Article history:*
Received 26 November 2011
Received in revised form 23 March 2012
Accepted 30 March 2012
Available online 6 April 2012

ABSTRACT

This $TiCl_4$–Mg promoted coupling of $CHBr_3$ with various aldehydes and ketones, especially in sterically hindered or enolizable ketones, provides a simple, practical, and stereoselective carbonyl–bromomethylenation leading primarily to (*E*)-vinyl bromides.



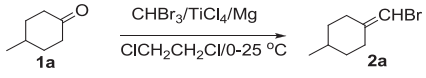
## 1. Introduction

Formation of C=C bonds by means of metallo–carbenes constitutes a particularly valuable strategy. The importance of alkenyl bromides as valuable building precursors in molecular transformations, such as Suzuki and Stille couplings has stimulated much interest in the development of new efficient methodology for their construction. Among the most direct approach to such systems involves the bromoolefination of aldehydes using (bromomethylene) triphenylphosphorane[1] and chromium–bromomethylene complexes[2] derived from a $CrCl_2$–$CHBr_3$ system. However, the basic nature of the phosphorus ylides, the low nucleophilic nature of these bromomethylene complexes,[3] and the requirement of the use of expensive $CrCl_2$ reagent to generate bromomethylene carbenoids greatly limits the general and practical utility of the method. Recently, the direct coupling of benzyl bromide with dibromomethane promoted by an excess of base (NaHMDS) constitutes a useful (*E*)-β-aryl vinyl bromide forming process.[4] The one-pot conversion of alkynes to alkenylmetals containing Al and Zr via hydro-metalation or carbometallation followed by Pd- and In-cocatalyzed cross-coupling with 1-bromo-2-iodoethylene provides a facile approach to 1-bromodienes.[5] To develop a new entry of metal-bromomethylene complexes, which are highly nucleophilic and available in bulk at a low price, we were attracted to the $TiCl_4$–Mg-mediated direct coupling of carbonyl compounds with $CHBr_3$. Earlier work in our laboratories established the feasibility of $CH_2Cl_2$–$TiCl_4$–Mg-system as a highly nucleophilic carbene complex to effect carbonyl–methylenation.[6] To expand the scope of titanium–carbenoids mediated reactions, we considered the prospect of $TiCl_4$–Mg bimetallic complex promoted bromomethylenation of ketones and aldehydes with $CHBr_3$ as a possibility. In this paper, we report that the $TiCl_4$–Mg promoted CHBr transfer reaction of $CHBr_3$ represents an extremely simple, practical, and efficient bromomethylenation of a variety of ketones and aldehydes, especially in enolizable or sterically hindered ketones.

## 2. Results and discussion

The bromomethylenation of 4-methylcyclohexanone **1a** with $CHBr_3$ was chosen to test the feasibility of the process (Table 1). Addition of a THF (0.5 mL)-$ClCH_2CH_2Cl$ solution of **1a** (1 equiv) to a mixture of $TiCl_4$ (3 equiv), magnesium powder (8 equiv), and $CHBr_3$ (1.0 equiv) in $ClCH_2CH_2Cl$ at 0 °C gave a 70% yield of the desired vinyl bromide **2a** (Table 1, entry 1). THF appears to be a good choice as an additive to effect bromomethylenation of $CHBr_3$ to the carbonyl group of **1a**. Decreasing the amount of THF causes the yield to drop to 25% with starting material remaining (entry 2). Other electron-pair-donor (EPD) additives including diethyl ether and 1,4-dioxane proved undesirable (entries 3 and

**Table 1**
Reaction conditions for bromomethylenation of ketone **1a** with $CHBr_3$[a]




| Entry | EPD additive | $TiCl_4$/Mg | Yield (%) **2a**[b] |
|---|---|---|---|
| 1 | THF (0.5 mL) | 3:8 | 70 |
| 2 | THF (0.2 mL) | 3:8 | 25 |
| 3 | $Et_2O$ (1.0) mL) | 3:8 | 0 |
| 4 | 1,4-dioxane (1.0 mL) | 3:8 | 0 |
| 5 | DME (0.5 mL) | 3:8 | ~30 |
| 6 | THF (1.0 mL) | 3:3 | ~5 |

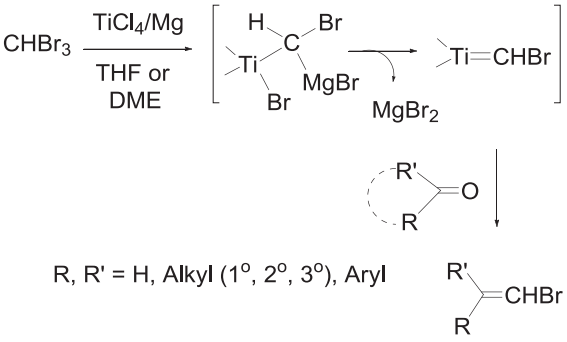
[a] The reaction was performed on a 1-mmol scale using 1.0 equiv of bromoform.
[b] Isolated yield.

* Corresponding author. E-mail address: thyan@mail.nchu.edu.tw (T.-H. Yan).

0040-4020/$ – see front matter Crown Copyright © 2012 Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2012.03.123

4). Switching the additive to DME led to a poor yield (~30%) of the desired vinyl bromid (entry 5). These results suggest that the stabilization of nanosized Ti–Mg bimetallic species is achieved by the ether solvents with high dielectric constants (e.g., THF and DME) to give an ether soluble compound. Performing the bromomethylenation by increasing the amount of THF and decreasing the amount of Mg gave unsatisfactory results (entry 6) leading to a reduction in yields of **2a** with starting material remaining.

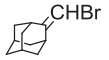
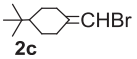
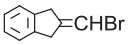
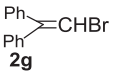
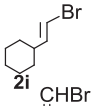
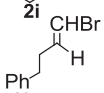
The reaction is best envisioned as involving interception of a presumed THF–$TiCl_4$ complex by the magnesium powder to give active bimetallic[Ti–Mg–Clx–THFn][6] complex followed by bromomethylene coordinated to both the titanium and magnesium to generate a presumed [Ti–CHBr–Mg–Clx–THFn] complex (Scheme 1).[7–10]




**Scheme 1.** Mg–Ti–bimetallic complexes-promoted CHBr transfer reaction of $CHBr_3$.

Having established the feasibility of the bromomethylenation, its generality with respect to the structure of the ketones was established (Table 2). The adamantanone **1b** also gave satisfactory results with $CHBr_3$–Mg–$TiCl_4$ complex (entry 1). Reaction of *t*-butylcyclohexanone **1c** with $CHBr_3$ gave a 75% yield of the bromomethylenation product **2c** using a 3 equiv of $TiCl_4$ and 14 equiv of Mg (entry 2). Notably, the reaction directly scales up; thus, vinyl bromide **2c** (entry 3) was obtained in 68% yield on a 10-mmol scale using an 18 equiv of $TiCl_4$ and 70 equiv of Mg. To further demonstrate the scope of this bromomethylene-forming methodology, the utility of this protocol was examined in the bromomethylenation of sterically demanding ketones. In contrast to Tebbe–Grubbs reagents,[11] the $CHBr_3$–Mg–$TiCl_4$ complex reacted efficiently with the 2,2-dimethylcyclohexanone **1d**. Thus, using a 3:14 $TiCl_4$–Mg ratio, a 56% yield of **2d** was obtained (entry 4). A sterically more bulky β-ketoester **1e** also proved to be a satisfactory acceptor (entry 5), in which case only addition to the keto function to give vinyl bromide **2e** (70%) is observed. In both cases, a >97:3 *E*:*Z* selectivity for vinyl bromides **2d** and **2e** was observed in the bromomethylenation of ketone. Due to the nonbasic nature of $CHBr_3$–$TiCl_4$–Mg system, highly enolizable ketone also proved to be a satisfactory trap. Thus, 2-indanone **1f** reacted effeciently with $CHBr_3$-derived bromomethylenation reagent to give the desired methylenation products **2f** (78%) (entry 6).[12] This bromomethylenation reagent is also suitable for the bromomethylenation of the less reactive aromatic ketones, such as benzophenone **1g** and 1-tetralone **1h** (entries 7,8). Thus simply reducing the amount of $TiCl_4$ by going from 3 to ~0.8 equiv, replacing THF with DME, and performing the reaction in $CH_2Cl_2$ led to smooth bromomethylenation of **1g** and **1h** at 0–25 °C. The vinyl bromides **2g** and **2h** were obtained in 67 and 74% yield, respectively. Notably, Wittig bromomethylenation of benzophenone with bromomethylene triphenylphosphorane only occurs at high temperature and gives <40% of the desired vinyl bromide.[13,14] Switching the carbonyl compound from ketone to cyclohexanecarboxaldehyde

**Table 2**
Carbonyl–bromomethylenation with $TiCl_4$/Mg/EPD/$CHBr_3$[a]

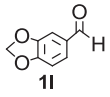
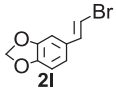
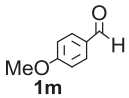
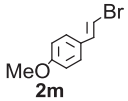
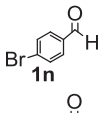
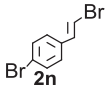
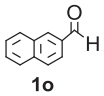
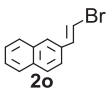
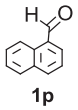
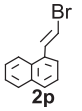
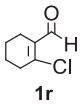
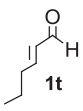
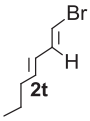
| Entry | Substrate | $TiCl_4$/Mg EPD (mL) | Product | Yield (%)[b] *E*/*Z*[c] |
|---|---|---|---|---|
| 1 |  **1b** | 3:10 THF 0.5 mL |  **2b** | 73 |
| 2 |  **1c** | 3:10 THF 0.5 mL |  **2c** | 75 |
| 3 | | 18:70[d] | | 68[d] |
| 4 |  **1d** | 3:14 THF 0.8 mL |  **2d** | 56<br>>97:3 |
| 5 |  **1e** | 3:14 THF 0.8 mL |  **2e** | 70<br>>97:3 |
| 6 |  **1f** | 3:10 THF 0.5 mL |  **2f** | 78 |
| 7 |  **1g** | 1:12 DME 3.0 mL |  **2g** | 67[e] |
| 8 |  **1h** | 0.8:10 DME 1.5 mL |  **2h** | 74[e]<br>88:12 |
| 9 |  **1i** | 2:8 THF 0.8 mL |  **2i** | 72<br>90:10 |
| 10 |  **1j** | 3:12 THF 0.5 mL |  **2j** | 58<br>58:42 |

[a] Reactions were run on a 1 mmol scale using $CHBr_3$/EPD/$ClCH_2CH_2Cl$ at 0–25 °C unless noted otherwise.
[b] Isolated yield.
[c] Determined by $^1H$ NMR spectroscopy.
[d] Reaction was run on a 10 mmol scale.
[e] Reactions were performed in $CH_2Cl_2$.

**1i** had little effect. Use of 2 equiv of $TiCl_4$ and 8 equiv of Mg proved most satisfactory, giving the corresponding (*E*)-vinyl bromide predominantly in 72% yield (entry 9). On the other hand, applying the standard reaction condition to simple aldehyde **1j** (entry 10) led to a separable 58:42 mixture of the *E*- and *Z*-vinyl bromides.

In an attempt to extend the above bromomethylenation method to aromatic aldehydes, benzaldehyde was treated with $CHBr_3$–Mg–$TiCl_4$ complex. Surprisingly, benzaldehyde failed to give gratifying results under the conditions of the bromomethylenation of saturated ketones. Most delightfully, exposure of benzaldehyd **1k** to a 0.8 equiv of $TiCl_4$ and 10 equiv of Mg in $CHBr_3$/$CH_2Cl_2$/DME led to smooth bromomethylenation to give a 78% yield of a >91:9 ratio of (*E*)- to (*Z*)-vinyl bromide (Table 3, entry 1), from which pure (*E*)-vinyl bromide **2k** can be isolated by chromatography. Changing the aromatic aldehyde to piperonal, methoxy-, or bromobenzaldehyde provided equally satisfactory results with formation of vinyl bromides **2l**, **2m**, and **2n** (Table 3, entries 2–4). In all cases, a ≥90:10 *E*:*Z* selectivity for bromomethylenation was observed. On the other hand, bromomethylenation of 1- and 2-naphthaldehydes or 2-furaldehyde can also lead to good *E*:*Z* selectivity (≥90:10) (entries 5–7). Changing the aldehydes to unsaturated aliphatic aldehydes **1r** or **1s** led to equally gratifying result with formation of the corresponding (*E*)-1-bromodienes in high stereoselectivity (entries 8,9). Bromomethylenation to simple

**Table 3**
Bromomethylenation of aldehydes with $TiCl_4$/Mg/DME/$CHBr_3$[a]

| Entry | Substrate | $TiCl_4$/Mg | Product | Yield (%)[b] *E*/*Z*[c] |
|---|---|---|---|---|
| 1 |  **1k** | 0.8:10 |  **2k** | 78<br>91:9 |
| 2 |  **1l** | 0.8:10 |  **2l** | 75<br>92:8 |
| 3 |  **1m** | 0.8:10 |  **2m** | 85<br>90:10 |
| 4 |  **1n** | 0.8:10 |  **2n** | 74<br>90:10 |
| 5 |  **1o** | 0.8:10 |  **2o** | 80<br>92:8 |
| 6 |  **1p** | 0.8:10 |  **2p** | 66<br>>95:5 |
| 7 |  **1q** | 0.8:10 |  **2q** | 68<br>90:10 |
| 8 |  **1r** | 0.8:10 |  **2r** | 76<br>>99:1 |
| 9 |  **1s** | 1:10 |  **2s** | 72[d]<br>90:10 |
| 10 |  **1t** | 3:13 |  **2t** | 52[e]<br>62:38 |

[a] Reactions were run on a 1 mmol scale using $CHBr_3$/$CH_2Cl_2$/DME at 0–25 °C unless noted otherwise.
[b] Isolated yield.
[c] Determined by $^1$H NMR spectroscopy.
[d] Reaction was stirred at 0–25 °C for 12 h.
[e] Reaction was run on a 1 mmol scale using $CHBr_3$/$ClCH_2CH_2Cl$/THF at 0–25 °C.

unsaturated aldehyde **1t** (entry 10) gave a 52 yield of a 62:38 ratio of *E*- to *Z*-vinyl bromides.

## 3. Conclusion

The successful application of the Mg–$TiCl_4$-promoted CHBr transfer to a variety of ketones and aldehydes illustrates the extraordinary reactivity of this new titanium bromomethylene complex. Not only is this $CHBr_3$–Mg–$TiCl_4$ system highly nucleophilic but it also seems selective and might become a practical bromomethylenation reagent applicable to large-scale synthesis. The utility of this new $CHBr_3$–$TiCl_4$–Mg system is exemplified by allowing rapid access to a wide range of alkenyl bromides, such as β-alkyl vinyl bromides, β-aryl vinyl bromides, and 1-bromodienes. These observations suggest that there may be a wealth of Ti–Mg intermetallic species-promoted reactions of $CHBr_3$ yet to unfold.

## 4. Experimental

### 4.1. General

Dichloromethane, dichloroethane, and DME were distilled from $P_2O_5$ prior to use. Commercially available ketones and aldehydes were used as received. Titanium tetrachloride and magnesium powder (ca. 50 mesh) were used as received. Chromatography was performed on silica gel 60 (230–400 mesh). All reactions were carried out under an atmosphere of argon. $^1$H and $^{13}$C NMR spectra were recorded on a Varian VXR-400 MHz spectrometer at ambient temperature. High-resolution mass spectra were determined on a Jeol JMS-HX 110 spectrometer.

### 4.2. General procedure for the bromomethylenation of ketones (method A): using 4-methylcyclohexanone 1a as an example

*4.2.1. 1-(Bromomethylene)-4-methylcyclohexane **2a**.* To a suspension consisting of Mg (194 mg, 8 mmol), $TiCl_4$ (3.0 mmol, 1 M in $ClCH_2CH_2Cl$, 4 mL) and $CHBr_3$ (0.087 mL), at 0 °C was added a solution 4-methylcyclohexanone **1a** (112 mg, 1 mmol) in $ClCH_2CH_2Cl$ (1 mL) and THF (0.5 mL). The black slurry was stirred for 8 h at 0–25 °C, then cooled to 0 °C, and carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The resulting mixture was stirred with 20 mL of ether and the phases were separated. After this procedure was repeated twice, the combined extracts were dried, evaporated, and purified by chromatography on silica gel (elution with hexane) to give **2a** (132 mg, 70% yield) as a colorless oil: IR (neat) 2950, 2919, 2870, 2848, 1647, 1454, 1375, 1259, 1082, 1017, 796 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 0.88 (d, *J*=3.6 Hz, 3H), 0.90–1.04 (m, 2H), 1.70–1.84 (m, 4H), 2.05 (t, *J*=4.4 Hz, 1H), 2.33 (d, *J*=14.8 Hz, 1H), 2.83 (d, *J*=16 Hz, 1H), 5.81 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 21.6, 30.4, 32.2, 34.7, 34.8, 35.9, 97.5, 144.7; high-resolution MS m/*e* calcd for $C_8H_{13}Br$ 188.0201, found 188.0198.

### 4.3. General procedure for the bromomethylenation of aldehydes (method B): using benzaldehyde 1j as an example

*4.3.1. [(E)-2-Bromovinyl]benzene **2k**.*[5] To a suspension consisting of Mg (243 mg, 10 mmol), $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 4 mL) at 0 °C was added a solution benzaldehyde **1k** (154 mg, 1 mmol), in $CH_2Cl_2$ (1 mL), $CHBr_3$ (0.3 mL), and DME (1.5 mL). The black slurry was stirred for 5 h at 0–25 °C, then cooled to 0 °C, and carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The resulting mixture was stirred with 20 mL of ether and the phases were separated. After this procedure was repeated twice, the combined extracts were dried, evaporated, gave a crude reaction mixture. *E*/*Z* analysis (400-MHz $^1$H NMR integration of the vinyl protons) of the crude adduct revealed the presence of a >91:9 ratio of *E* and *Z* isomers. Purification by flash chromatography on silica gel (elution with hexane) afforded 142 mg (78%) of **2k** as a colorless oil: $^1$H NMR ($CDCl_3$, 400 MHz) δ 6.78 (d, *J*=14.0 Hz, 1H), 7.12 (d, *J*=14.0 Hz, 1H), 7.28–7.34 (m, 5H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 106.4, 126.0, 128.2, 128.7, 135.8, 137.1; high-resolution MS m/*e* calcd for $C_8H_7Br$ 181.9731, found 181.9724.

*4.3.2. 2-(Bromomethylene)adamantane **2b**.*[15] As described above in **method A**, purification of the crude product derived from 1 mmol of **1b** by flash chromatography on silica gel (elution with hexane) afforded 165 mg (73%) of **2b** as a colorless oil: $R_f$=0.87 (Hexane): IR (neat) 2921, 2850, 1634, 1447, 1271, 1098, 949, 886, 774, 685 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 1.71–1.93 (m, 12H), 2.54 (s, 1H), 3.07 (s, 1H), 5.78 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 28.0, 34.4, 36.7, 37.8,

37.9, 39.2, 39.6, 92.8, 152.5; high-resolution MS m/*e* calcd for $C_{11}H_{15}Br$ 226.0357, found 226.0355.

*4.3.3. 1-tert-Butyl-4-(bromomethylene)cyclohexane* ***2c***.[16] As described above in **method A**, purification of the crude product derived from 1 mmol of **1c** by flash chromatography on silica gel (elution with hexane) afforded 173 mg (75%) of **2c** as a colorless oil: $R_f$=0.89 (Hexane): IR (neat) 2954, 2867, 1715, 1638, 1475, 1443, 1366, 1283, 1240, 1011, 789, 701 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.84 (s, 9H), 0.97–1.07 (m, 2H), 1.12–1.18 (m, 1H), 1.69–1.77 (m, 1H), 1.83–1.91 (m, 2H), 1.98–2.01 (m, 1H), 2.36–2.40 (m, 1H), 2.89–2.93 (m, 1H), 5.80 (t, *J*=1.6 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 27.4, 27.5, 28.5, 31.0, 32.3, 35.4, 47.9, 97.2, 145.0; high-resolution MS m/*e* calcd for $C_{11}H_{19}Br$ 230.0670, found 230.0663.

*4.3.4. (E)-2-(Bromomethylene)-1,1-dimethylcyclohexane* ***2d***. As described above in **method A**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a >97:3 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1d** by flash chromatography on silica gel (elution with hexane) afforded 113 mg (56%) of **2d** as a colorless oil: $R_f$=0.90 (Hexane) : IR (neat) 2929, 2860, 1611, 1453, 1388, 1363, 1294, 1151, 984, 830, 781, 711 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.05 (s, 6H), 1.33–1.36 (m, 2H), 1.49–1.57 (m, 3H), 2.39 (t, *J*=6.4 Hz, 2H), 5.90 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 22.2, 27.0, 27.5, 28.2, 38.5, 41.5, 98.7, 151.5; high-resolution MS m/*e* calcd for $C_9H_{15}Br$ 202.0362, found 202.0362.

*4.3.5. (E)-Methyl 2-(bromomethylene)-7,7-dimethylbicyclo[2.2.1] heptane-1-carboxylate* ***2e***. As described above in **method A**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a >97:3 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1e** by flash chromatography on silica gel (elution with hexane) afforded 191 mg (70%) of **2e** as a colorless oil: $R_f$=0.29 (Hexane): IR (neat) 2951, 2885, 1729, 1645, 1434, 1319, 1231, 1093, 793, $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.01 (d, *J*=3.6 Hz, 6H), 1.25–131 (m, 1H) 1.62–1.69 (m, 1H), 1.84–1.94 (m, 3H), 2.24–2.27 (m, 1H), 2.48 (d, *J*=13.6 Hz, 1H), 3.71 (s, 3H), 6.03 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 19.6, 20.7, 27.3, 31.5, 31.6, 38.5, 45.4, 51.4, 63.6, 98.9, 149.8, 172.3; high-resolution MS m/*e* calcd for $C_{12}H_{17}BrO_2$ 272.0412, found 272.0404.

*4.3.6. 2-(Bromomethylene)-2,3-dihydro-1H-indene* ***2f***. As described above in **method A**, purification of the crude product derived from 1 mmol of **1f** by flash chromatography on silica gel (elution with hexane) afforded 163 mg (78%) of **2f** as a colorless oil: $R_f$=0.65 (Hexane): IR (neat) 3071, 3023, 2904, 2812, 1665, 1607, 1560, 1462, 1387, 1349, 1273, 1204, 1128, 1021, 923, 864, 791, 747, 715, 595, 413 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 3.72 (d, *J*=2.4 Hz, 4H), 6.17 (t, *J*=2.0 Hz, 1H), 7.19–7.21 (m 4H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 38.9, 39.9, 99.3, 124.62, 124.68, 126.7, 126.8, 140.5, 141.2, 145.3; high-resolution MS m/*e* calcd for $C_{10}H_9Br$ 207.9888, found 207.9892.

*4.3.7. (2-Bromoethene-1,1-diyl)dibenzene* ***2g***.[17] As described above in **method B**, purification of the crude product derived from 1 mmol of **1g** by flash chromatography on silica gel (elution with hexane) afforded 173 mg (67%) of **2g** as a colorless oil: $R_f$=0.50 (Hexane): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 6.76 (s, 1H), 7.19–7.39 (m, 10H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 105.1, 127.6, 128.2, 128.4, 129.6, 139.0, 140.7, 146.8; high-resolution MS m/*e* calcd for $C_{14}H_{11}Br$ 258.0044, found 258.0038.

*4.3.8. (E)-1-(Bromomethylene)-1,2,3,4-tetrahydronaphthalene* ***2h***.[18] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of an 88:12 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1h** by flash chromatography on silica gel (elution with hexane) afforded 165 mg (74%) of **2h** as a colorless oil:$R_f$=0.80 (Hexane) : $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.82–1.86 (m, 2H), 2.61–2.64 (m, 2H), 2.74 (t, *J*=6.0 Hz, 2H), 6.71 (t, *J*=2.0 Hz, 1H), 7.10–7.19 (m, 3H), 7.45 (d, *J*=6.4 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 22.5, 29.8, 30.4, 103.5, 123.9, 126.3, 127.7, 128.8, 134.0, 137.7, 139.9; high-resolution MS m/*e* calcd for $C_{11}H_{11}Br$ 222.0044, found 222.0035.

*4.3.9. ((E)-2-Bromovinyl)cyclohexane* ***2i***.[19] As described above in **method A**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 90:10 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1i** by flash chromatography on silica gel (elution with hexane) afforded 136 mg (72%) of **2i** as a colorless oil: $R_f$=0.82 (Hexane) : IR (neat) 2932, 2856, 1726, 1649, 1582, 1447, 1164, 1036, 993, 942 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.0–1.25 (m, 5H), 1.60–1.71 (m, 5H), 1.99 (m, 1H), 5.98 (dd *J*=0.8, 13.2 Hz, 1H), 6.14 (dd, *J*=6.8, 13.2 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 25.7, 25.8, 32.2, 41.7, 103.0, 143.7; high-resolution MS m/*e* calcd for $C_8H_{13}Br$ 188.0201, found 188.0208.

*4.3.10. 1-((E)-and 1-(Z)-4-Bromobut-3-enyl)benzene* ***2j***.[20] To a suspension consisting of Mg (291 mg, 12 mmol), $TiCl_4$ (3.0 mmol, 1 M in $ClCH_2CH_2Cl$, 4 mL) and $CHBr_3$ (0.08 mL), at 0 °C was added a solution of 3-phenylpropanal (134 mg, 1 mmol) in $ClCH_2CH_2Cl$ (1 mL) and THF (0.5 mL). The black slurry was stirred for 8 h at 0–25 °C, then cooled to 0 °C, and carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The resulting mixture was stirred with 20 mL of ether and the phases were separated. After this procedure was repeated twice, the combined extracts were dried, evaporated. Diastereomer analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 58:42 ratio of *E* to *Z* isomers. Purification by chromatography on silica gel (elution with hexane) afforded a separable mixture of the *E*- and *Z*-vinyl bromides (122 mg, 58% yield). *E* isomer as a colorless oil: IR (neat) 3063, 2326, 2926, 2855, 1620, 1603, 1496, 1453, 1217, 1080, 1029, 743, 699 $cm^{-1}$, $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.31–2.37 (m, 2H), 2.69 (t, *J*=7.6 Hz, 2H), 6.04 (tt, *J*=1.6, 13.6 Hz, 1H), 6.15–6.22 (m, 1H), 7.14–7.29 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 31.3, 34.2, 108.3, 126.0, 128.3, 128.5, 133.8, 141.1; high-resolution MS m/*e* calcd for $C_{10}H_{11}Br$ 210.0044, found 210.0034. *Z* isomer as a colorless oil: IR (neat) 3027, 2925, 2657, 1621, 1603, 1495, 1453, 1305, 1288, 1077, 1029, 748, 698 $cm^{-1}$, $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.47–2.53 (m, 2H), 2.72 (t, *J*=7.1 Hz, 2H), 6.07–6.17 (m, 2H), 7.16–7.30 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 34.6, 35.0, 104.9, 126.1, 128.3, 128.4, 137.1, 140.8.

*4.3.11. 5-((E)-2-Bromovinyl)benzo[d][1,3]dioxole* ***2l***.[21] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 92:8 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1l** by flash chromatography on silica gel (elution with hexane) afforded 170 mg (75%) of **2l** as a colorless oil:$R_f$=0.45 (Hexane) : IR (neat) 3075, 2893, 1607, 1494, 1442, 1294, 1038, 931, 813, 773 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 5.94 (s, 2H), 6.58 (d, *J*=14.0 Hz, 1H), 6.72–6.73 (m, 2H), 6.79 (d, 1.2 Hz, 1H), 6.99 (d, *J*=14.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 101.2, 104.5, 105.4, 108.4, 120.9, 130.3, 136.6, 147.7, 148.1; high-resolution MS m/*e* calcd for $C_9H_7BrO_2$ 225.9629, found 225.9637.

*4.3.12. 1-((E)-2-Bromovinyl)-4-methoxybenzene* ***2m***.[5] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 90:10 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1m** by flash chromatography on silica gel

(elution with hexane) afforded 181 mg (85%) of **2m** as a colorless oil: $R_f$=0.34 (Hexane): IR (neat) 3070, 2953, 2836, 1606, 1508, 1456, 1302, 1250, 1031, 944, 834, 775, 527 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 3.79 (s, 3H), 6.60 (d, $J$=14.0 Hz, 1H), 6.82–6.85 (m, 2H), 7.03 (d, $J$=14.0 Hz, 1H), 7.20–7.22 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 55.3, 103.9, 114.2, 127.3, 128.8, 136.5, 159.7.

*4.3.13. 1-Bromo-4-((E)-2-bromovinyl)benzene* ***2n***.[22] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 90:10 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1n** by flash chromatography on silica gel (elution with hexane) afforded 193 mg (74%) of **2n** as a colorless oil: $R_f$=0.76 (Hexane): IR (neat) 3071, 2963, 1608, 1587, 1485, 1396, 1262, 1072, 1010, 930, 827, 773, 748, 499, $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 6.78 (d, $J$=14.0 Hz, 1H), 7.04 (d, $J$=14.4 Hz, 1H), 7.15(d, $J$=8.4 Hz, 2H), 7.44 (d, $J$=8.8 Hz, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$107.3, 122.2, 127.5, 131.9, 134.8, 136.0; high-resolution MS m/*e* calcd for $C_8H_6Br_2$ 259.8836, found 259.8841.

*4.3.14. (E)-2-(2-Bromovinyl)naphthalene* ***2o***.[23] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 92:8 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1o** by flash chromatography on silica gel (elution with hexane) afforded 186 mg (80%) of **2o** as a colorless oil:$R_f$=0.68 (Hexane): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 6.90 (d, $J$=13.6 Hz, 1H), 7.44–7.46 (m, 3H), 7.66 (s, 1H), 7.76–7.78 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 106.8, 122.8, 126.2, 126.3, 126.5, 127.7, 128.0, 128.5, 133.1, 133.3, 133.4, 137.2; high-resolution MS m/*e* calcd for $C_{12}H_9Br$ 231.9888, found 231.9879.

*4.3.15. (E)-1-(2-Bromovinyl)naphthalene* ***2p***.[24] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a >95:5 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1p** by flash chromatography on silica gel (elution with hexane) afforded 153 mg (66%) of **2p** as a colorless oil:$R_f$=0.60 (Hexane): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 6.77 (d, $J$=13.6 Hz, 1H), 7.42–7.53 (m, 4H), 7.80–7.85 (m, 3H), 8.03 (d, $J$=8.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 108.4, 123.7, 124.2, 125.5, 126.1, 126.4, 128.5, 128.7, 130.6, 133.60, 133.62, 135.0; high-resolution MS m/*e* calcd for $C_{12}H_9Br$ 231.9888, found 231.9882.

*4.3.16. (E)-2-(2-Bromovinyl)furan* ***2q***.[24] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 90:10 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1q** by flash chromatography on silica gel (elution with hexane) afforded 117 mg (68%) of **2q** as a colorless oil: $R_f$=0.78 (Hexane) : $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 6.23 (d, $J$=3.2 Hz, 1H), 6.35 (d, $J$=1.6 Hz, 1H), 6.70 (d, $J$=13.9 Hz, 1H), 6.87 (d, $J$=13.5 Hz, 1H),7.34 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 105.2, 108.6, 111.3, 125.4, 142.5, 151.0; high-resolution MS m/*e* calcd for $C_6H_5BrO$ 171.9524, found 171.9522.

*4.3.17. (E)-1-(2-Bromovinyl)-2-chlorocyclohex-1-ene* ***2r***. As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a >99:1 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1r** by flash chromatography on silica gel (elution with hexane) afforded 167 mg (76%) of **2r** as a colorless oil: $R_f$=0.72 (Hexane) : IR (neat) 3080, 2935, 2860, 1622, 1580, 1447, 1339, 1208, 992, 939, 822, 770, 658 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.66–1.69 (m, 4H), 2.19 (m, 2H), 2.38 (m, 2H), 6.33 (d, $J$=14.0 Hz, 1H), 7.37 (d, $J$=14.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 21.7, 23.4, 26.1, 34.5, 107.2, 128.6, 132.3, 134.9; high-resolution MS m/*e* calcd for $C_8H_{10}ClBr$ 219.9654, found 219.9659.

*4.3.18. (E)-1-(2-Bromovinyl)cyclohex-1-ene* ***2s***.[25] As described above in **method B**, *E*/*Z* analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 90:10 ratio of *E* and *Z* isomers. Purification of the crude product derived from 1 mmol of **1s** by flash chromatography on silica gel (elution with hexane) afforded 134 mg (72%) of **2s** as a colorless oil: $R_f$=0.85 (Hexane): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.55–1.65 (m, 6H), 2.05–2.06 (m, 2H), 5.74(m, 1H), 6.08 (d, $J$=13.6 Hz, 1H), 6.65 (d, $J$=14.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 22.10, 22.18, 24.1, 25.7, 102.5, 130.8, 134.6, 140.6; high-resolution MS m/*e* calcd for $C_8H_{11}Br$ 186.0044, found 186.0038.

*4.3.19. (1E,3E)-1-Bromohepta-1,3-diene* ***2t***. To a suspension consisting of Mg (315 mg, 13 mmol), $TiCl_4$ (3.0 mmol, 1 M in $ClCH_2CH_2Cl$, 4 mL) and $CHBr_3$ (0.08 mL), at 0 °C was added a solution of (*E*)-hex-2-enal (98 mg, 1 mmol) in $ClCH_2CH_2Cl$ (1 mL) and THF (0.5 mL). The black slurry was stirred for 8 h at 0–25 °C, then cooled to 0 °C, and carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The resulting mixture was stirred with 20 mL of ether and the phases were separated. After this procedure was repeated twice, the combined extracts were dried and evaporated. Diastereomer analysis (400-MHz $^1H$ NMR integration of the vinyl protons) of the crude adduct revealed the presence of a 62:38 ratio of *E* and *Z* isomers. Purification by chromatography on silica gel (elution with hexane) gave (1*E*,3*E*)- and (1*Z*,3*E*)-1-bromohepta-1,3-dienes (91 mg, 52% yield). *E* isomer as a colorless oil: IR (neat) 2959, 2929, 2872, 1641, 1621, 1583, 1460, 1378, 1260, 988, 967, 804 $cm^{-1}$, $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.87 (t, $J$=7.2 Hz, 3H), 1.35–1.43 (m, 2H), 1.98–2.08 (m, 2H), 5.65 (m, 1H), 5.94 (dd, $J$=12.0, 15.2 Hz, 1H), 6.13 (d, $J$=13.5 Hz, 1H), 6.65 (dd, $J$=10.8, 13.5 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 13.61, 22.10, 34.63, 106.0, 127.6, 136.3, 137.7; high-resolution MS m/*e* calcd for $C_7H_{11}Br$ 174.0044, found 174.0036.

## Acknowledgements

We thank the National Science Council of the Republic of China for generous support.

## Supplementary data

Copies of $^1H$ and $^{13}C$ NMR spectra for **2a**–**r**. This material is available free of charge via the internet at http://pubs.acs.org. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2012.03.123.

## References and notes

1. (a) Matsumoto, M.; Kuroda, K. *Tetrahedron Lett.* **1980**, *21*, 4021 and references therein; (b) Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173; (c) Miyano, S.; Izumi, Y.; Fujii, K.; Ohno, Y.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1197; (d) Taber, D. F.; Meagley, R. P.; Doren, D. J. *J. Org. Chem.* **1996**, *61*, 5723; (e) Hayford, A.; Kaloko, J.; El-Kazaz, J. S.; Bass, G.; Harrison, C.; Corprew, T. *Org. Lett.* **2004**, *7*, 2671.
2. (a) Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408; (b) The $CrCl_2$-promoted bromomethylenation of ketones with $CHBr_3$ led to a mixture of vinyl bromide and chloride. For problems of the $CrCl_2$-promoted carbonyl bromomethylenation, see: Trost, B. M.; Dumas, J.; Villa, M. *J. Am. Chem. Soc.* **1992**, *114*, 9836.
3. Takai, K.; Ichiguchi, T.; Hikasa, S. *Synlett* **1999**, 1268.
4. Bull, J. A.; Mousseau, J. J.; Charette, A. B. *Org. Lett.* **2008**, *10*, 8485.
5. Qian, M.; Huang, Z.; Negishi, E. *Org. Lett.* **2004**, *6*, 1531.
6. Yan, T.-H.; Tsai, C.-C.; Chien, C.-T.; Cho, C.-C.; Huang, P.-C. *Org. Lett.* **2004**, *6*, 4961.
7. (a) Yan, T.-H.; Chien, C.-T.; Tsai, C.-C.; Lin, K.-W.; Wu, Y.-H. *Org. Lett.* **2004**, *6*, 4965; (b) Lin, K.-W.; Yan, S.; Hsieh, I.-L.; Yan, T.-H. *Org. Lett.* **2006**, *8*, 2265; (c) Tsai, C.-C.; Hsieh, I.-L.; Cheng, T.-T.; Tsai, P.-K.; Lin, K.-W.; Yan, T.-H. *Org. Lett.* **2006**, *8*, 2261; (d) Lin, K.-W.; Tsai, C.-H.; Hsieh, I.-L.; Yan, T.-H. *Org. Lett.* **2008**, *10*, 1927.

8. (a) Chien, C.-T.; Tsai, C.-C.; Tsai, C.-H.; Chang, T.-Y.; Tsai, P.-K.; Wang, Y.-C.; Yan, T.-H. *J. Org. Chem.* **2006**, *71*, 4324; (b) Lin, K.-W.; Chen, C.-Y.; Chen, W.-F.; Yan, T.-H. *J. Org. Chem.* **2008**, *73*, 4759.
9. (a) Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392; (b) Hibino, J.; Okazoe, T.; Takai, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 5581.
10. (a) Takai, K.; Hotta, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1978**, *19*, 2417; (b) For a recent review on the use of titanium carbenoids to convert carbonyl compounds into alkenes, see: Hartley, R. C.; Li, J.; Main, C. A.; McKiernan, G. J. *Tetrahedron* **2007**, *63*, 4825.
11. (a) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611; (b) Pine, S. H.; Zahier, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 3270.
12. For the methylenation of highly enolizable ketones, see: Johnson, C. R.; Tait, B. D. *J. Org. Chem.* **1987**, *52*, 281.
13. Axelrad, G.; Laosooksathit, S.; Engel, R. *J. Org. Chem.* **1981**, *46*, 5200.
14. For multi-step synthesis of 1-bromo-2,2-diphenylethene, see: (a) Kauffmann, T.; Fischer, H.; Woltermann, A. *Angew. Chem., Int. Ed. Engl.* **1977**, *89*, 52; (b) Li, G.; Warner, P. M. *Tetrahedron Lett.* **1995**, *36*, 8573; (c) Lahrache, H.; Robin, S.; Rousseaou, G. *Tetrahedron Lett.* **2005**, *46*, 1635.
15. Nelsen, S. F.; Teasley, M. F.; Kapp, D. L. *J. Am. Chem. Soc.* **1986**, *108*, 5503.
16. Jiao, X.-Y.; Bentrude, W. G. *J. Org. Chem.* **2003**, *68*, 3303.
17. Annunziata, A.; Galli, C.; Gentili, P.; Guarnieri, A.; Beit-Yannai, M.; Rappoport, Z. *Eur. J. Org. Chem.* **2002**, 2136.
18. Harada, T.; Katauhira, T.; Oku, A. *J. Org. Chem.* **1992**, *57*, 5805.
19. Tikhonov, A. A. *Russ. Chem. Bull.* **2007**, *56*, 122.
20. (a) Devine, S. K. J.; Vranken, D. L. V. *Org. Lett.* **2007**, *9*, 2047; (b) Uenishi, J.; Kawahama, R.; Yonemitsu, O. *J. Org. Chem.* **1998**, *63*, 8965.
21. O'Byrne, A.; Evans, P. *Tetrahedron* **2008**, *64*, 8067.
22. Pawluc, P.; Hreczycho, G.; Szudkowska, J.; Kubicki, M.; Marciniec, B. *Org. Lett.* **2009**, *11*, 3390.
23. Kuang, C.; Senboku, H.; Tokuda, M. *Tetrahedron* **2002**, *58*, 1491.
24. Fiandanese, V.; Bottalico, D.; Marchese, G.; Punzi, A. *Tetrahedron* **2006**, *62*, 5126.
25. Hoshi, M.; Shirakawa, K. *Chem. Commun.* **2002**, 2146.