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Efficient Radical Coupling of Organobromides
Using Dimanganese Decacarbonyl

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Abstract: Wurtz–type radical coupling of a variety of allylic and benzylic bromides was observed on irradiation with dimanganese decacarbonyl in excellent yield (77-99%). Efficient cross–coupling of two different bromides was also readily achieved.

The coupling of organohalides using sodium metal, a so–called Wurtz reaction, has found relatively little application in synthesis. This is primarily due to side reactions and the harsh reductive conditions employed. Alternative and milder organometallic reagents have since been developed with a view to overcoming these problems. Examples include $Ni(CO)_4$,[1] SmI_2,[2] R_2NLi/CuI,[3] $CrCl_2/DMF$,[4] Te^{2-},[5] VCl_3 or $CrCl_3/LiAlH_4$,[6] $TiCl_3$ or $TiCl_4/LiAlH_4$,[7] Mg/BH_3,[8] Cu[9] or $Mn/CuCl_2$.[10] One common approach is to prepare Grignard or organolithiums and then react these with alkyl halides. The majority of these

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reactions involve metal–halogen exchange to give an intermediate organometallic which reacts with a second molecule of the organohalide. This often necessitates the need for low–temperatures/anhydrous reaction conditions and the high reactivity of these intermediates can lead to side reactions with a number of common functional groups *e.g.* acids and esters. As a consequence, we aimed to develop an efficient, quick and mild method of coupling which could be applied to a wide variety of functionalised organohalides.

The method involves irradiation of the organohalide in the presence of dimanganese decacarbonyl (Mn$_2$CO$_{10}$).[11] This was expected[12] to proceed *via* halogen atom abstraction by the manganese pentacarbonyl radical (produced on photolytic cleavage of the Mn–Mn bond) to give a carbon–centred radical which could then undergo coupling. Initial investigations centred on photolysis of benzyl bromide (1 eq) and Mn$_2$(CO)$_{10}$ (0.5 eq) in dichloromethane at r.t. to give bibenzyl (Scheme 1). After 2 h, all the starting material had reacted (as evidenced by t.l.c.) and a orange–yellow precipitate of manganese pentacarbonyl bromide was formed. The ^{1}H NMR spectrum of the crude mixture (after filtration) showed clean formation of bibenzyl and purification using column chromatography afforded the desired product in 99% yield. Complete removal of byproduct BrMn(CO)$_5$ (which can trail down a silica column) could be achieved using a work–up procedure involving reaction of the crude mixture with DBU. This method has been found to aid removal of tin byproducts[13] and reaction of DBU with BrMn(CO)$_5$ was found to result in ligand exchange[14] (rather than bromide displacement as observed for R$_3$SnBr) giving a complex which is retained at the head of the column (along with any excess DBU). It was not necessary to dry the dichloromethane and the best yields of bibenzyl were obtained for reactions carried out under an atmosphere of nitrogen (which prevented oxidation of the manganese). Reaction of benzyl chloride under the same conditions was found to be much slower and after 4 h bibenzyl was isolated in only 15% yield.
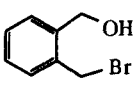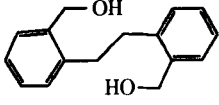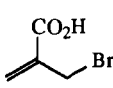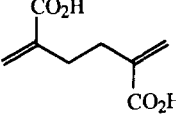
$$Ph\diagup\!\!\!\diagdown Br \xrightarrow[\text{CH}_2\text{Cl}_2,\ hv]{\text{Mn}_2^{\cdot}(\text{CO})_{10}} Ph\diagdown\!\!\!\diagup\!\!\!\diagdown Ph \quad 99\%$$
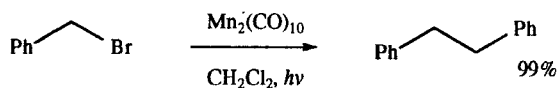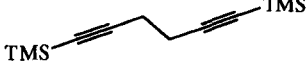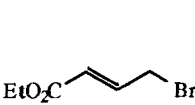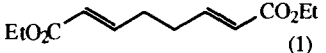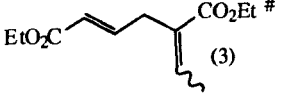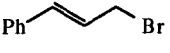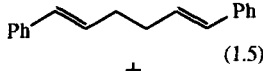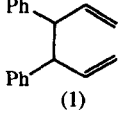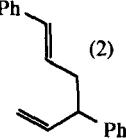
SCHEME 1

TABLE 1

¶Product ratios (determined from the ^{1}H NMR spectrum) are shown in brackets.
#Formed by isomerisation of the 2,6–heptadienoate on DBU workup.

Bromide	Product(s)¶	Yield (%)
		88
		92
		86
		71[15]
		83

This method was found to work well using a variety of substrates containing a number of functional groups (Table 1). This included alcohols, esters and acids which would be more difficult to couple using anionic/basic reaction conditions. It was found that allylic radicals, which could couple in more than one position, reacted predominantly at the least hindered position.

TABLE 2

‡The molar ratio of starting materials are shown in brackets.
¶Product ratios (determined from the ^{1}H NMR spectrum) are shown in brackets.
∞Yield based on the bromide present in one equivalent.

Bromides‡	Product(s)¶	Yield (%)∞
		70
		61
		73
		77

Cross–coupling of two different bromides was also investigated, a reaction which could give rise to both homo– and cross–coupled products. It was found that by using one of the bromides in two–fold excess, synthetically useful yields of cross–coupled products could be obtained as shown in Table 2.[16]

Terpenes can also be prepared using this approach (Scheme 2). Coupling two C–5 allylic bromides[17] gave an inseparable mixture of C–10 dienes in 68%

SCHEME 2
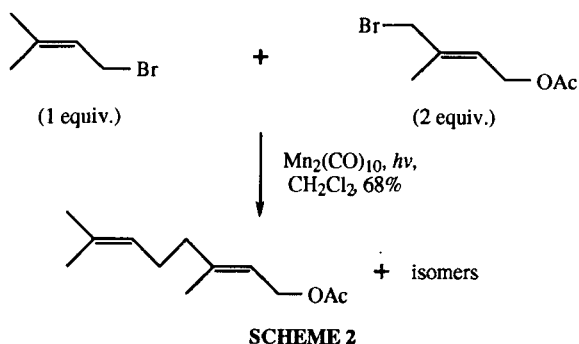
yield. GCMS showed the presence of all 6 possible isomers (in the ratio 1:1.1:2.1:4.9:5.0:8.9), the major isomer of which was geranyl acetate.

This method represents a quick, easy and efficient approach to coupling allylic and benzylic bromides. The cost of $Mn_2(CO)_{10}$ may prohibit large scale synthesis but for small scale preparations this approach has a number of advantages over existing methods.

Experimental

Typical Procedure for Homo–coupling.

1,2–Bis[2–(hydroxymethyl)phenyl]ethane.

To a stirred solution of (2–bromomethylphenyl)methanol (0.29 g, 1.45 mmol) in degassed dichloromethane (10 cm^3) was added dimanganese decacarbonyl (0.29 g, 0.73 mmol) and the solution was irradiated (ICL 302 UV xenon lamp, 300 W) under an atmosphere of nitrogen for typically 2 h. After photolysis, 1,8–diazabicyclo[5.4.0]undec–7–ene (DBU) (0.44 g, 2.90 mmol) was added dropwise and after 1 h, the dark coloured solution was adsorbed onto silica. Column chromatography (diethyl ether) afforded 1,2–bis[2–(hydroxymethyl)phenyl]ethane[18,19] (0.31 g, 88%) as a pale yellow solid; R_f 0.4 (diethyl ether); m.p. 151–153°C; υ_{max} (CHCl$_3$) 3693 (m), 2926 (s), 1602 (m), 1001 (br, w) and 758 (s) cm^{-1}; δ_H (270 MHz, CDCl$_3$) 7.39-7.16 (8H, m, aromatics), 4.81 (4H, s, 2 x C$\underline{H}_2$OH), 3.02 (4H, s, C$\underline{H}_2$–C$\underline{H}_2$), 1.64 (2H, br s, 2 x CH$_2$O$\underline{H}$); δ_C (67.5 MHz, CDCl$_3$) 141.4 ($\underline{C}$CH$_2$OH), 132.3 ($\underline{C}$CH$_2$), 129.1, 128.3, 127.9, 126.4 ($\underline{C}$H=C), 63.5 ($\underline{C}$H$_2$OH) and 34.8 ($\underline{C}$H$_2$CH$_2$); *m/z* (CI, NH$_3$) 260 (M+NH$_4^+$, 100%), 242 (30), 224 (90), 212 (32) and 207 (23); Found: M+NH$_4^+$, 260.1648. $C_{16}H_{18}O_2$ requires for M+NH$_4^+$, 260.1651.

Typical Procedures for Cross–Coupling.

Methyl 6–trimethylsilyl–2–methylidene–5–hexynoate.

To a stirred solution of methyl (2–bromomethyl)propenoate (0.17 g, 0.97 mmol) and 3–bromo–1–(trimethylsilyl)prop–1–yne (0.38 g, 1.95 mmol) in degassed dichloromethane (20 cm^3) was added dimanganese decacarbonyl (0.57 g, 1.46 mmol). The solution was irradiated (ICL 302 UV xenon lamp, 300 W) under an atmosphere of nitrogen for 3 h after which 1,8–diazabicyclo[5.4.0]undec–7–ene (DBU) (0.89 g, 5.85 mmol) was added dropwise. After 1 h, the crude product was adsorbed onto silica and column chromatography (10:1, petroleum ether–diethyl ether) afforded the title product (0.11 g, 61 %) as a colourless oil; R_f 0.4 (10:1, petroleum ether–diethyl ether); υ_{max} (CHCl$_3$) 2957 (s), 2173 (m), 1722 (s), 1632 (m), 1440 (m), 1251 (m), 1203 (m) and 846 (s) cm^{-1}; δ_H (270 MHz, CDCl$_3$) 6.10 (1H, s, C=C$\underline{H}$), 5.51 (1H, s, C=C$\underline{H}$), 3.61 (3H, s, CO$_2$C$\underline{H}_3$), 2.41–2.22 (4H, m, C$\underline{H}_2$C$\underline{H}_2$), 0.00 (9H, s, 3 x SiC$\underline{H}_3$); δ_C (67.5 MHz, CDCl$_3$) 167.7 ($\underline{C}$O$_2$), 138.1 ($\underline{C}$=CH$_2$), 127.3 (C=$\underline{C}$H$_2$), 106.0, 90.0 (C≡$\underline{C}$Si and CH$_2\underline{C}$≡C), 52.2 ($\underline{C}$H$_3$OCO), 31.8, 18.9 ($\underline{C}$H$_2\underline{C}$H$_2$) and 2.2 (3xSi$\underline{C}$H$_3$); *m/z* (CI, NH$_3$) 228 (M+NH$_4^+$, 100%), 211 (M+H$^+$, 95), 195 (8), 106 (9) and 90 (13); Found: M+NH$_4^+$, 228.1416. C$_{11}$H$_{18}$O$_2$Si requires for M+NH$_4^+$, 228.1420.

Methyl 6–methyl–2–methylidene–5–heptenoate and methyl
4,4–dimethyl–2–methylidene–5–hexenoate.

To a stirred solution of methyl (2–bromomethyl)propenoate (0.17 g, 0.97 mmol) and 1–bromo–3–methyl–2–butene (0.29 g, 1.95 mmol) in degassed dichloromethane (20 cm^3) was added dimanganese decacarbonyl (0.57 g, 1.46 mmol). The solution was irradiated (ICL 302 UV xenon lamp, 300 W) under an atmosphere of nitrogen for 5 h after which 1,8–diazabicyclo[5.4.0]undec–7–ene (DBU) (0.89 g, 5.85 mmol) was added dropwise. After 1 h, the crude product was adsorbed onto silica and column chromatography (10:1, petroleum ether–diethyl ether) afforded methyl 6–methyl–2–methylidene–5–heptenoate and methyl 4,4–dimethyl–2–methylidene–5–hexenoate (0.12 g, 73 %) as an inseparable mixture in a ratio of 9.5:1 (from the ^{1}H NMR spectrum).

Methyl 6–methyl–2–methylidene–5–heptenoate. R_f 0.5 (10:1, petroleum ether–diethyl ether); υ_{max} (CHCl$_3$) 2953 (m), 1713 (s), 1631 (w), 1440 (m), 1308 (w), 1200 (s) and 947 (w) cm^{-1}; δ_H (270 MHz, CDCl$_3$) 6.15 (1H, s, C=C$\underline{H}$), 5.53 (1H, s, C=C$\underline{H}$), 5.15–5.06 (1H, m, C=C$\underline{H}$), 3.78 (3H, s, CO$_2$C$\underline{H}_3$), 2.45 (2H, t, *J*

7.5 Hz, C$\underline{H}_2$CH$_2$), 2.18 (2H, br q, J 7.5 Hz, CH$_2$C$\underline{H}_2$), 1.73 (3H, s, C=CC$\underline{H}_3$), 1.61 (3H, s, C=CC$\underline{H}_3$); δ_C (67.5 MHz, CDCl$_3$) 167.8 ($\underline{C}$O$_2$), 140.3 ($\underline{C}$=CH$_2$), 132.4 (C=$\underline{C}$CH$_3$), 124.9 (C=$\underline{C}$H$_2$), 123.4 (C=$\underline{C}$H), 51.8 ($\underline{C}$H$_3$OCO), 32.1, 27.0 ($\underline{C}$H$_2\underline{C}$H$_2$), 25.7 (C=C$\underline{C}$H$_3$), 17.7 (C=C$\underline{C}$H$_3$); m/z (CI, NH$_3$) 186 (M+NH$_4^+$, 20%), 169 (M+H$^+$, 70), 137 (15) and 109 (10); Found: M+H$^+$, 169.1231. C$_{10}$H$_{16}$O$_2$ requires for M+H$^+$, 169.1230.

Methyl 4,4–dimethyl–2–methylidene–5–hexenoate. The presence of this was indicated by NMR spectroscopy; δ_H (270 MHz, CDCl$_3$) 5.77 (1H, dd, J 16 and 8 Hz, C$\underline{H}$=CH$_2$), 4.90–4.80 (2H, m, CH=C$\underline{H}_2$) and 0.95 (6H, s, 2xCC$\underline{H}_3$); δ_C (67.5 MHz, CDCl$_3$) 110.7 (C=$\underline{C}$H$_2$) and 26.3 (2xC$\underline{C}$H$_3$).

Acknowledgements.

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      frequency. This is consistent with reduced back–bonding due to the CO
      ligands.

15.   Reaction in THF has been reported to give a lower (33%) yield of coupled
      products as a 1.8:1 mixture of isomers. Masters, A.P. and Sorensen, T.S.
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      derived from bromides present in two–fold excess, although these were
      not isolated.

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