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New synthesis of *t*-butyl arylpropiolates using diazo(trimethylsilyl)methylmagnesium bromide

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ABSTRACT

Diazo(trimethylsilyl)methylmagnesium bromide smoothly reacted with *t*-butyl aryl(oxo)acetates to afford the corresponding arylpropiolates via alkylidenecarbene intermediates. In this reaction system, the magnesium bromide salt of trimethylsilyldiazomethane was significantly efficient compared to the lithium one, commonly known as a reagent for the conversion of aldehydes and aryl ketones into acetylenes.

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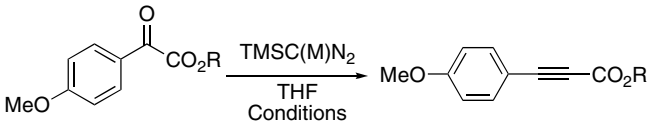
Arylpropiolates have attracted attention as useful intermediates in organic synthesis,[1] and have been generally prepared by modified Wittig methodology using acid chlorides and triphenylphosphoranylidene acetates followed by flash vacuum pyrolysis,[2] Corey–Fuchs homologation[3] of aryl aldehydes followed by treatment of the resulting aryl acetylides with chloroformates, cross-coupling reactions of aryl iodides with propiolates (modified Sonogashira reaction),[4] or reaction of aldehydes with Ph_3P and Br_3CCO_2Et.[5]

Quite recently, we have reported a convenient preparation of arylpropiolates from aryl aldehydes using lithium trimethylsilyldiazomethane ($TMSC(Li)N_2$) in one-pot process, which involves the homologation of aldehydes to aryl acetylenes[6] via alkylidenecarbene intermediates, followed by ethoxycarbonylation of the resulting acetylenes with ethyl chloro(or cyano)formate.[7] As an extension of this work, we now wish to describe a new and convenient synthesis of arylpropiolates from aryl(oxo)acetates via alkylidenecarbene intermediates.

Initially, the examination of reaction conditions using (*p*-methoxyphenyl)(oxo)acetates was carried out as shown in Table 1.[8,9] Similarly to the preparation of arylacetylenes from aryl ketones,[6] upon treatment of **1** with $TMSC(Li)N_2$ in THF at −78 °C followed by heating under reflux conditions, **1** was converted to the desired (*p*-methoxyphenyl)propiolate **2**, but the yield was very low (entry 1). In this reaction, there is a possibility that the reaction of $TMSC(Li)N_2$ with an ester moiety of **1** competes with that with a ketone moiety. Therefore, the ethyl ester of **1** was replaced by more bulky *tert*-butyl ester **3a**. As a result, the use of **3a** as a substrate led to a slight increase in the yield of the corresponding acethylene **4a** (entry 2). Interestingly, by changing the counter cation of $TMSC(Li)N_2$ from Li to MgBr,[10] the reaction efficiency was

Table 1
Examination of reaction conditions



1 and **3a** → **2** and **4a**

Entry	Substrate	$TMSC(M)N_2$	Conditions	Yield (%)
1	**1** (R = Et)	$TMSC(Li)N_2$ (1.2 equiv)	−78 °C, 1 h→reflux, 3 h	11 (**2**)
2	**3a** (R = Bu^t)	$TMSC(Li)N_2$ (1.2 equiv)	−78 °C, 1 h→reflux, 3 h	20 (**4a**)
3	**3a**	$TMSC(MgBr)N_2$ (1.5 equiv)	−78 °C, 1.5 h→reflux, 1 h	54 (**4a**)
4	**3a**	$TMSC(MgBr)N_2$ (1.5 equiv)	−78 °C, 3 h→reflux, 1 h	56 (**4a**)
5	**3a**	$TMSC(MgBr)N_2$ (1.5 equiv)	−78 °C, 3 h→reflux, 2 h	64 (**4a**)
6	**3a**	$TMSC(MgBr)N_2$ (1.5 equiv)	−78 °C, 3 h→reflux, 3 h	60 (**4a**)

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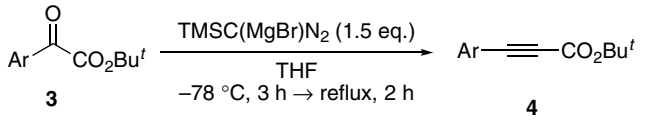
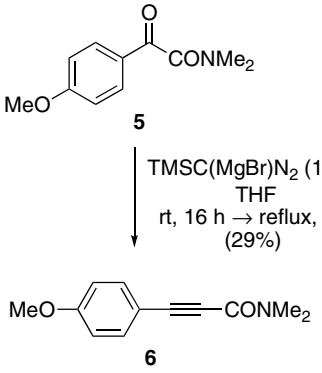
Table 2
Examination of reaction conditions



3 4

Entry	Ar	Substrate	Yield (%)
1[a]	*p*-(MeO)Ph	**3a**	64 (**4a**)
2	Ph	**3b**	58 (**4b**)
3	*p*-ClPh	**3c**	52 (**4c**)
4	*o*-MePh	**3d**	58 (**4d**)
5	2-Naphthyl	**3e**	61 (**4e**)
6	2-Pyridyl	**3f**	16 (**4f**)
7	3-Pyridyl	**3g**	27 (**4g**)
8	2-Furyl	**3h**	52 (**4h**)
9	2-Thienyl	**3i**	54 (**4i**)
10	2-Benzo[*b*]thienyl	**3j**	42 (**4j**)

[a] Shown in entry 5 of Table 1.



Scheme 1.

dramatically improved and **4a** was obtained in 54–64% yields (entries 3–6).

Next, using the optimized reaction conditions (entry 5 in Table 1), the reactions with various *t*-butyl aryl(oxo)acetates were examined (Table 2).[8,9] Analogously to **3a**, TMSC(MgBr)N_2 smoothly reacted with *t*-butyl aryl(oxo)acetates such as phenyl (**3b**), *p*-chlorophenyl (**3c**), *o*-tolyl (**3d**), or 2-naphthyl (**3e**) ones to afford the corresponding arylpropiolates **4b–e** in 52–61% yields (entries 1–5). Substituents on the benzene ring of **3** did not significantly affect the yield of **4**. Pyridyl derivatives **3f** and **3g** also underwent the reaction giving desired **4f** and **4g**, but the yields were 16% and 27%, respectively (entries 6 and 7). The low yields of **4f** and **4g** were probably due to poor migration ability of the electron-deficient pyridine ring. The reactions with **3h–j** bearing five-membered heteroacromatics also proceeded to give the corresponding propiolates **4h–j** in moderate yields (entries 7–9). In addition, the reaction was applicable to the synthesis of arylpropiolamide **6** from aryl(oxo)acetamide **5**, though prolonged reaction time was required and the yield was low (Scheme 1).[9,11]

In conclusion, the present method makes possible the easy conversion of aryl(oxo)acetates, readily prepared from arylmetals (arylmagnesium bromide or aryllithium) and oxalate derivatives,[12–14] to arylpropiolates and will provide an added flexibility in the synthesis of arylpropiolates.

Acknowledgement

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8. *General procedure:* $MgBr_2$ (1.0 M in ether and toluene (1:1) solution, 0.75 ml, 0.75 mmol) was added dropwise to a solution of TMSC(Li)N_2, prepared from $TMSCHN_2$ (1.80 M in hexane solution, 0.42 ml, 075 mmol) and *n*-BuLi (1.60 M in hexane solution, 0.47 ml, 0.75 mmol) in THF (4.0 ml), at −78 °C under an argon atmosphere and the mixture was stirred at −78 °C for 0.5 h. After addition of a solution of the *t*-butyl aryl(oxo)acetate **3** (0.5 mmol) in THF (1.0 ml) at −78 °C, the reaction mixture was stirred at −78 °C for 3 h and then refluxed for 2 h. After being quenched with satd NH_4Cl aq at 0 °C, the mixture was extracted with ethyl acetate (three times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (BW-820 MH) to give the *t*-butyl arylpropiolate **4**.
9. *Selected data for* **2**, **4a–j** *and* **6**: Compound **2a**, Ref. 15. Compound **4a**, ^{1}H NMR ($CDCl_3$) δ: 1.54 (s, 9H), 3.83 (s, 3H), 6.87 (d, J = 8.9 Hz, 2H), 7.52 (d, J = 8.9 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ: 28.1, 55.3, 81.4, 83.1, 84.5, 111.7, 114.1, 134.6, 153.2, 161.0. IR (neat) ν: 2205, 1699 cm^{-1}. Compound **4b**, Ref. 16. Compound **4c**, ^{1}H NMR ($CDCl_3$) δ: 1.54 (s, 9H), 7.33 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ: 28.2, 82.4, 82.8, 83.7, 118.5, 128.9, 133.9, 136.6, 152.8. IR (neat) ν: 2212, 1709 cm^{-1}. Compound **4d**, ^{1}H NMR ($CDCl_3$) δ: 1.55 (s, 9H), 2.48 (s, 3H), 7.12–7.25 (m, 2H), 7.31 (dt, J = 1.5, 7.5 Hz, 1H), 7.52 (dd, J = 1.3, 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 20.7, 28.1, 82.8, 83.3, 85.7, 119.7, 125.6, 129.6, 130.1, 133.1, 141.9, 153.1. IR (neat) ν: 2206, 1701 cm^{-1}. Compound **4e**, ^{1}H NMR ($CDCl_3$) δ: 1.57 (s, 9H), 7.49–7.58 (m, 2H), 7.77–7.85 (m, 4H), 8.13 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.2, 82.2, 83.5, 84.2, 117.1, 126.8, 127.6, 127.7, 128.0, 128.2, 128.2, 132.5, 133.6, 133.8, 153.0. IR (nujol) ν: 2216, 1703 cm^{-1}. Compound **4f**, ^{1}H NMR ($CDCl_3$) δ: 1.53 (s, 9H), 1.32 (ddd, J = 1.2, 4.8, 7.7 Hz, 1H), 7.56 (td, J = 1.2, 7.7 Hz, 1H), 7.69 (dt, J = 1.8, 7.7 Hz, 1H), 8.63 (ddd, J = 1.2, 1.8, 4.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.1, 80.6, 81.6, 83.9, 124.2, 128.2, 136.1, 140.8, 150.3, 152.3. IR (neat) ν: 2220, 1713 cm^{-1}. Compound **4g**, ^{1}H NMR ($CDCl_3$) δ: 1.54 (s, 9H), 7.30 (ddd, J = 1.0, 4.9, 7.9 Hz, 1H), 7.84 (ddd, J = 1.6, 2.1, 7.9 Hz, 1H), 8.62 (dd, J = 1.6, 4.9 Hz, 1H), 8.78 (dd, J = 1.0, 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.1, 80.0, 84.0, 84.9, 117.3, 123.0, 139.6, 150.2, 152.4, 153.0. IR (neat) ν: 2216, 1713 cm^{-1}. Compound **4h**, ^{1}H NMR ($CDCl_3$) δ: 1.53 (s, 9H), 6.44 (dd, J = 1.8, 3.5 Hz, 1H), 6.88 (dd, J = 0.8,3.5 Hz, 1H), 7.48 (dd, J = 0.8, 1.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.2, 74.1, 83.9, 86.9, 111.4, 120.3, 134.8, 145.7, 152.6. IR (neat) ν: 2210, 1705 cm^{-1}. Compound **4i**, ^{1}H NMR ($CDCl_3$) δ: 1.54 (s, 9H), 7.03 (dd, J = 3.6, 5.1 Hz, 1H), 7.42 (dd, J = 1.2, 5.1 Hz, 1H), 7.45 (dd, J = 1.2, 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.2, 77.7, 83.6, 86.1, 119.8, 127.3, 130.5, 135.9, 152.8. IR (neat) ν: 2208, 1703 cm^{-1}. Compound **4j**, ^{1}H NMR ($CDCl_3$) δ: 1.56 (s, 9H), 7.35–7.43 (m, 2H), 7.75–7.81 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 28.1, 77.6, 83.9, 87.0, 119.6, 122.0, 124.4, 124.9, 126.5, 133.0, 138.3, 141.1, 152.5. IR (neat) ν: 2210, 1703 cm^{-1}. Compound **6**, ^{1}H NMR ($CDCl_3$) δ: 3.02 (s, 3H), 3.28 (s, 3H), 3.83 (s, 3H), 6.87 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ: 34.2, 38.5, 55.4, 80.8, 90.7, 112.4, 114.1, 134.0, 154.8, 160.8. IR (neat) ν: 2206, 1628 cm^{-1}.
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13. *Synthesis of* **3a**: A solution of 4-methoxyphenylmagnesium bromide, prepared from 1-bromo-4-methoxybenzene (1.87 g, 10 mmol) and magnesium turnings (225 mg, 10.5 mmol) in THF (10 ml), was added dropwise to *tert*-butyl ethyl oxalate (1.92 g, 11 mmol) in THF (10 ml) at −78 °C under an argon atmosphere and the mixture was stirred at −78 °C for 2 h. After being quenched with satd NH_4Cl aq at −78 °C, the mixture was extracted with ethyl acetate (three times). The organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (BW-820 MH, hexane–ethyl acetate = 50:1) to give **3a** (1.94 g, 82%) as a colorless oil.
14. *Selected data for* **1**, **3a–j** *and* **5**: Compound **1**, Ref. 17. Compound **3a**, Ref. 18. Compound **3b**, Ref. 18. Compound **3c**, Ref. 18. Compound **3d**, ^{1}H NMR ($CDCl_3$) δ: 1.62 (s, 9H), 2.61 (s, 3H), 7.24–7.36 (m, 2H), 7.46 (dt, J = 1.1, 7.4 Hz, 1H), 7.68 (dd, J = 1.1, 7.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 21.6, 28.0, 84.3, 125.7, 131.0, 132.0, 132.2, 133.3, 141.1, 164.1, 188.9. IR (neat) ν: 1728, 1682 cm^{-1}. Compound **3e**,

Ref. 17. Compound **3f**, ^{1}H NMR ($CDCl_3$) δ: 1.62 (s, 9H), 7.49 (ddd, J = 1.1, 4.8, 7.8 Hz, 1H), 7.86 (dt, J = 1.6, 7.8 Hz, 1H), 8.06 (td, J = 1.1, 7.8 Hz, 1H), 8.72 (ddd, J = 1.1, 1.6, 4.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.3, 84.7, 123.2, 127.7, 136.9, 149.6, 150.6, 164.6, 187.2. IR (neat) ν: 1736, 1711 cm^{-1}. Compound **3g**, ^{1}H NMR ($CDCl_3$) δ: 1.64 (s, 9H), 7.46 (ddd, J = 0.8, 4.9, 8.0 Hz, 1H), 8.30 (ddd, J = 1.8, 2.2, 8.0 Hz, 1H), 8.84 (dd, J = 1.8, 4.9 Hz, 1H), 9.20 (dd, J = 0.8, 2.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.1, 85.4, 123.6, 128.5, 136.9, 151.3, 154.4, 162.0, 185.1. IR (neat) ν: 1728, 1693 cm^{-1}. Compound **3h**, Ref. 16. Compound **3i**, ^{1}H NMR ($CDCl_3$) δ: 1.61 (s, 9H), 7.16 (dd, J = 4.0, 4.9 Hz, 1H), 7.16 (dd, J = 1.2, 4.9 Hz, 1H), 8.02 (dd, J = 1.2, 4.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.0, 84.8, 128.4, 136.5, 136.7, 139.1, 161.1, 177.4. IR (neat) ν: 1728, 1666 cm^{-1}. Compound **3j**, ^{1}H NMR ($CDCl_3$) δ: 1.64 (s, 9H), 7.41 (ddd, J = 1.0, 7.1, 7.9 Hz, 1H), 7.49 (ddd, J = 1.2, 7.1, 8.2 Hz, 1H), 7.85–7.89 (m, 1H), 7.92 (dd, J = 1.2, 7.9 Hz, 1H), 8.31 (d, J = 0.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ: 28.0, 85.0, 122.8, 125.2, 126.6, 128.3, 134.4, 138.7, 138.8, 143.5, 160.9, 179.1. IR (nujol) ν: 1736, 1651 cm^{-1}. **5**, Ref. 19.

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