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Titanium(IV) bromide and boron(III) tribromide promoted reactions of arylaldehydes with 3-butyn-2-one, methyl propiolate and propynenitrile

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Abstract—The reactions of arylaldehydes with 3-butyn-2-one, methyl propiolate or propynenitrile in the presence of Lewis acids such as titanium(IV) bromide ($TiBr_4$) or boron(III) tribromide (BBr_3) (1.4 equiv.) can be drastically affected by the reaction temperature. When the reaction of arylaldehydes with 3-butyn-2-one was carried out at $<-20°C$, brominated compounds were obtained as the major product. However, when the reaction was carried out at room temperature (20°C), both the brominated compounds and α,β-dibrominated compounds were formed as the major products. Moreover, at 70°C in 1,2-dichloroethane, the α,β-dibrominated compounds were obtained as the sole products. On the other hand, the reactions of arylaldehydes with methyl propiolate or propynenitrile in the presence of $TiBr_4$ are very slow at room temperature (20°C). The corresponding α-brominated compounds, derived from the reactions of arylaldehydes with methyl propiolate, were obtained in low yields. While, at 70°C in 1,2-dichloroethane, β,β-dibrominated compounds were obtained from the reactions of arylaldehydes with methyl propiolate or propynenitrile in the presence of $TiBr_4$ in moderate yields. The substituent on the phenyl ring can affect the reaction rate and the *E*/*Z* ratio. In addition, with two substrate, palladium catalyzed allylic substitution and Suzuki-type coupling reaction have been examined.

1. Introduction

Research into the Baylis–Hillman reaction has made great progress since Baylis and Hillman first reported the reaction of acetaldehyde with ethyl acrylate and acrylonitrile in the presence of catalytic amounts of a strong Lewis base such as 1,4-diazabicyclo[2.2.2]octane (DABCO) in 1972.[1,2] In this area, we have reported that the combination of Lewis bases such as chalcogenides, amines or quaternary ammonium halides with the Lewis acid $TiCl_4$ can significantly speed up this reaction and give the corresponding chlorinated products and the elimination products (*Z*-olefins) at different reaction temperatures.[3,4] Moreover, very recently, the reaction of aldehydes with 3-butyn-2-one in the presence of $TiCl_4$ has been disclosed by Li and Kataoka.[5,6] This new process could afford an efficient synthetic method to the β-chloro Baylis–Hillman adducts. From the point of view of synthetic chemistry, the α-bromomethylene aldols **1** are more useful than the corresponding α-chloromethylene aldols because they can be more easily subjected to transition metal catalyzed reactions such as allylic substitution and Suzuki coupling reactions. Thus, we initially attempted the preparation of β-bromo Baylis–Hillman adducts **1** using titanium(IV) bromide ($TiBr_4$) or boron(III) tribromide (BBr_3) under the similar reaction conditions. So far, only one example using $TiBr_4$ as Lewis acid for this reaction has been examined at room temperature in these previously reported papers.[5,6] In this paper, we more carefully examined the reaction of arylaldehydes with 3-butyn-2-one in the presence of $TiBr_4$ or BBr_3 (1.4 equiv.) at different temperatures. We found that Lewis bases such as Me_2S, amines or quaternary ammonium halides did not affect the rate of this novel reaction, however, the reaction temperatures played very important roles for this reaction both on reaction products and stereoselectivities (*E*/*Z* ratio). When the reaction of arylaldehydes with 3-butyn-2-one was carried out at $<-20°C$, the brominated compounds **1** were obtained as the major product. However, when the reaction was carried out at room temperature (20°C), both **1** and α,β-dibrominated compounds **2** were formed as the major products.[7] Herein, we wish to report the details of the reactions of arylaldehydes with 3-butyn-2-one, methyl propiolate, and propynenitrile in the presence of $TiBr_4$ or BBr_3 (1.4 equiv.) at different temperatures.

2. Results and discussion

At low temperature ($<-20°C$), only α-bromomethylene aldols **1** could be obtained in moderate to high yields in the

Keywords: 3-butyn-2-one; methyl propiolate; propynenitrile; titanium(IV) bromide.

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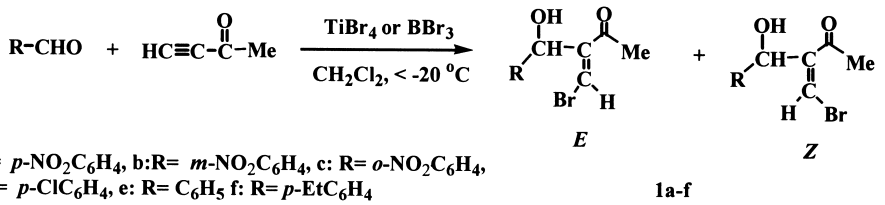


Scheme 1.

Table 1. The reaction of arylaldehydes with 3-butyn-2-one in the presence of $TiBr_4$ and BBr3 (1.4 equiv.)

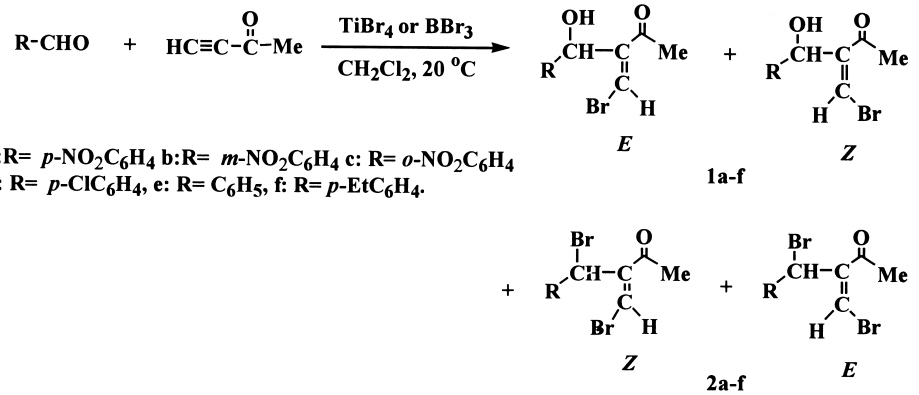
Entry	R	Lewis acid	Temperature (°C)	Time (h)	Yield[a] (%)	*E*/*Z*
1	*p*-$NO_2C_6H_4$	BBr_3	−78	40	54	19:1
2	*p*-$NO_2C_6H_4$	$TiBr_4$	−78	40	90	19:1
3	*m*-$NO_2C_6H_4$	$TiBr_4$	−78	40	61	1:1.3
4	*o*-$NO_2C_6H_4$	$TiBr_4$	−78	40	76	1:6.6
5	*p*-ClC_6H_4	$TiBr_4$	−78	72	41	19:1
6	*p*-ClC_6H_4	$TiBr_4$	−20	72	80	19:1
7	C_6H_5	$TiBr_4$	−20	72	79	19:1
8	*p*-EtC_6H_4	$TiBr_4$	−20	72	81	19:1

Aldehyde/$TiBr_4$ or BBr_3/3-butyn-2-one=1:1.4:2.
[a] Isolated yields.

presence of $TiBr_4$ or BBr_3 (1.4 equiv.) (Scheme 1). $TiBr_4$ is more effective than BBr_3 for this reaction (Table 1, entries 1 and 2). For arylaldehydes having a strong electron-withdrawing group on the phenyl ring, the reaction proceeded quickly at −78°C to give **1** in high yields (Table 1, entries 2–4). However, other arylaldehydes needed higher temperature and longer reaction time to complete the reaction (Table 1, entries 5–8). The geometry of the major isomer was determined by ^1H NMR noesy spectroscopic data and comparison of the spectral data with those of the corresponding α-chloromethylene aldols.[5,6]

At room temperature (20°C), we found that, besides α-bromomethylene aldols **1** α,β-dibrominated compounds **2** could be obtained at the same time using 1.4 equiv. of $TiBr_4$ or BBr_3 as Lewis acid (Scheme 2). As can be seen from Table 2, **2** was obtained in almost the same *E*/*Z* ratios and close yields as **1** in the presence of 1.4 equiv. of $TiBr_4$ at 20°C (Table 2, entries 1–7). In general, the α-bromomethylene aldols **1** were obtained preferentially in *E* configuration and α,β-dibrominated compounds **2** were in the *Z* configuration. The crystal structure of **2a** was disclosed by X-ray analysis (Fig. 1). But for benzaldehyde or *p*-ethylbenzaldehyde, the *E*/*Z* geometrical selectivity is low (Table 2, entries 6 and 7). The substituents on the phenyl ring can affect the *E*/*Z* geometrical selectivity.

In order to clarify the formation route of **2**, we carried out the direct reaction of **1a** (*E*/*Z*=19:1) with 1.4 equiv. of $TiBr_4$ at room temperature (Scheme 3). We found that, the corresponding **2a** was exclusively obtained in the same *E*/*Z* ratio in 10 h as in Table 1, entry 1. Based on this result, it is very clear that, product **2** is derived from **1** by the further reaction of **1** with $TiBr_4$ at room temperature (Scheme 3).



Scheme 2.

Table 2. The reaction of arylaldehydes with 3-butyn-2-one in the presence of $Tibr_4$ and BBr_3 (1.4 equiv.)

Entry	R	Lewis acid	Time (h)	Yield[a] **1** (%)	*E*/*Z*	Yield[a] **2** (%)	*E*/*Z*
1	*p*-$NO_2C_6H_4$	BBr_3	24	5	19:1	20	1:19
2	*p*-$NO_2C_6H_4$	$TiBr_4$	24	43	19:1	20	1:19
3	*m*-$NO_2C_6H_4$	$TiBr_4$	24	41	19:1	20	1:19
4	*o*-$NO_2C_6H_4$	$TiBr_4$	24	36	8:1	32	1:19
5	*p*-ClC_6H_4	$TiBr_4$	30	16	19:1	28	1:1.5
6	C_6H_5	$TiBr_4$	40	17	3:1	20	1:1.4
7	*p*-EtC_6H_4	$TiBr_4$	40	29	1:1	22	1:4

Aldehyde/$TiBr_4$/3-butyn-2-one=1:1.4:2.
[a] Isolated yields.

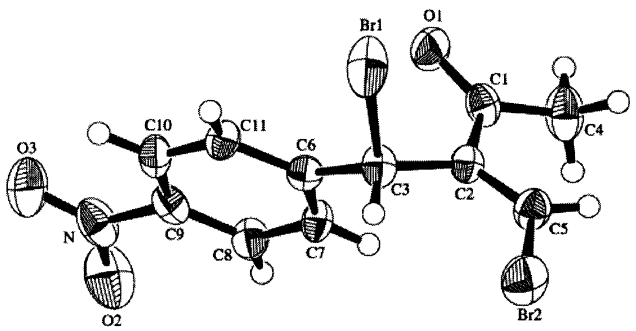
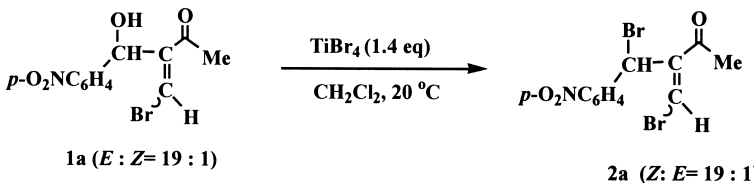


Figure 1. The crystal structure of **2a**.

We also confirmed that, using 2.5 equiv. of $TiBr_4$ at room temperature, the α,β-dibrominated compound **2** could be obtained as the major product, but in the reaction of arylaldehydes with 3-butyn-2-one in the presence of excess $TiCl_4$ at 20°C, the corresponding dichlorinated products could not be produced at all. Thus, for the formation of **2**, we believe that, at room temperature, the bromide ion at the titanium metal center can directly attack at the carbon atom bearing the activated hydroxy group to give the α,β-dibrominated compound **2** because bromide ion usually has more nucleophilicity than that of chloride ion.

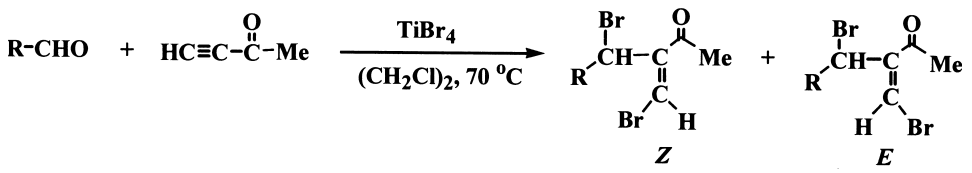
In addition, when the reaction was carried out in 1,2-dichloroethane at 70°C, α,β-dibrominated compounds **2** were exclusively obtained in moderate yields with almost the same *E*/*Z* ratios as those at room temperature (Scheme 4, Table 3). The reactions only required 8 h to completion.

On the other hand, we also examined the reaction of methyl propiolate and propynenitrile with arylaldehydes in the presence of $TiBr_4$. It was found that, these reactions are in general very slow at room temperature (20°C). The brominated products **3** were obtained in about 40% yield with a low *E*/*Z* ratio only in the reaction of nitrobenzaldehyde with methyl propiolate (Scheme 5, Table 4, entries 1–3). While, for *p*-chlorobenzaldehyde, benzaldehyde, or *p*-ethylbenzaldehyde, no reaction occurred (Table 4, entries 4–6). However, if the reaction was carried out in 1,2-dichloroethane at 70°C, we found that the β,β-dibrominated products **4** were formed predominantly along with a small amount of the corresponding compounds **3** (Scheme 6, Table 5). Under these reaction conditions, the products *E*-**4** were formed preferentially (Table 5, entries 1–7). For the reaction of arylaldehydes with propynenitrile in the presence of $TiBr_4$ in 1,2-dichloroethane at 70°C, similar results were observed and the β,β-dibrominated products **5**



1a (*E* : *Z*= 19 : 1) **2a (*Z*: *E*= 19 : 1)**

Scheme 3.



2a-f

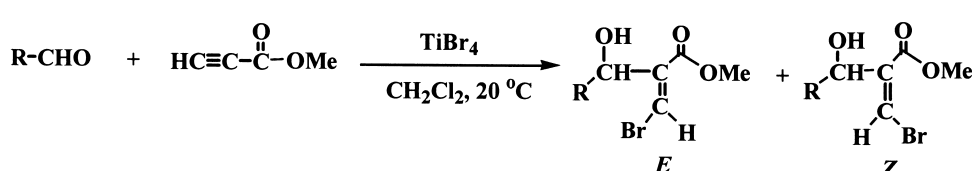
a:R= *p*-$NO_2C_6H_4$, b:R= *m*-$NO_2C_6H_4$ c: R= *o*-$NO_2C_6H_4$, d: R= *p*-ClC_6H_4, e: R= C_6H_5, f: R= *p*-EtC_6H_4.

Scheme 4.

Table 3. The reaction of arylaldehydes with 3-butyn-2-one in the presence of $TiBr_4$

Entry	R	Lewis acid	Time (h)	Yield[a] (%)	*E*/*Z*
1	*p*-$NO_2C_6H_4$	$TiBr_4$	8	70	1:19
2	*m*-$NO_2C_6H_4$	$TiBr_4$	8	43	1:19
3	*o*-$NO_2C_6H_4$	$TiBr_4$	8	72	1:19
4	*p*-ClC_6H_4	$TiBr_4$	8	68	1:1.5
5	C_6H_5	$TiBr_4$	8	50	1:1.2
6	*p*-EtC_6H_4	$TiBr_4$	8	60	1:1.7

Aldehyde/$TiBr_4$/3-butyn-2-one=1:1.4:2.
[a] Isolated yields.



a:R= *p*-$NO_2C_6H_4$, b:R= *m*-$NO_2C_6H_4$, c: R= *o*-$NO_2C_6H_4$, d: R= *p*-ClC_6H_4, e: R= C_6H_5 f: R= *p*-EtC_6H_4. **3a-f**

Scheme 5.

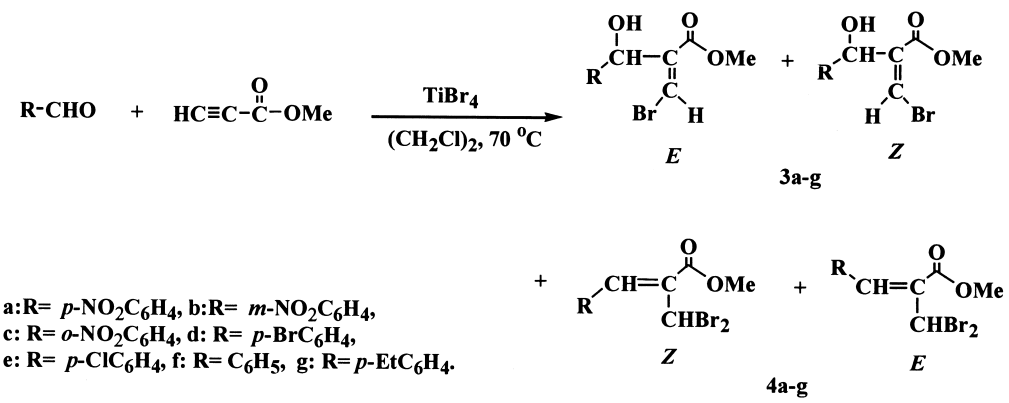
Table 4. The reaction of arylaldehydes with mythyl propiolate in the presence of $TiBr_4$

Entry	R	Lewis acid	Time (h)	Yield[a] (%)	*E*/*Z*
1	*p*-$NO_2C_6H_4$	$TiBr_4$	48	42	1:2
2	*m*-$NO_2C_6H_4$	$TiBr_4$	48	46	1:3
3	*o*-$NO_2C_6H_4$	$TiBr_4$	48	46	1:3
4	*p*-BrC_6H_4	$TiBr_4$	48	–	–
5	*p*-ClC_6H_4	$TiBr_4$	48	–	–
6	C_6H_5	$TiBr_4$	48	–	–
7	*p*-EtC_6H_4	$TiBr_4$	48	–	–

Aldehyde/$TiBr_4$/mythyl propiolate=1:1.4:2.
[a] Isolated yields.

were obtained in about 40% yield if the arylaldehydes having electron-withdrawing groups (Scheme 7, Table 6, entries 1–4). But for benzaldehyde or *p*-ethylaldehyde, no reaction occurred even at 70°C (Table 6, entries 5 and 6). The structures of **4** and **5** were established by spectral data and X-ray analyses (Figs. 2 and 3).

In order to clarify the reaction mechanism of the formation of dibrominated products, we first confirmed that **1** or **3** did not react with bromine or hydrogen bromide, which may be formed during the reaction, to give **2** or **4** in dichloromethane. Thus, the formation of **2** or **4** is only related with

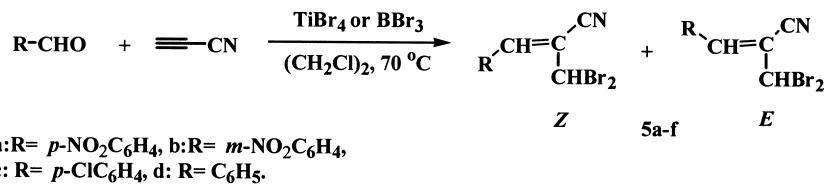


Scheme 6.

Table 5. The reaction of arylaldehydes with mythyl propiolate in the presence of $Tibr_4$

Entry	R	Lewis acid	Time (h)	Yield[a] **3** (%)	*E*/*Z*	Yield[a] **4** (%)	*E*/*Z*
1	*p*-$NO_2C_6H_4$	$TiBr_4$	14	17	19:1	56	2.5:1
2	*m*-$NO_2C_6H_4$	$TiBr_4$	24	15	19:1	52	5:1
3	*o*-$NO_2C_6H_4$	$TiBr_4$	24	Trace	–	28	2:1
4	*p*-BrC_6H_4	$TiBr_4$	24	0	–	57	2:1
5	*p*-ClC_6H_4	$TiBr_4$	24	0	–	60	1.5:1
6	C_6H_5	$TiBr_4$	24	0	–	38	2:1
7	*p*-EtC_6H_4	$TiBr_4$	24	0	–	34	3:1

Aldehyde/$TiBr_4$/mythyl propiolate=1:1.4:2.
[a] Isolated yields.



Scheme 7.

Table 6. The reaction of arylaldehydes with propynenitrile in the presence of $TiBr_4$ or BBr_3

Entry	R	Lewis acid	Time (h)	Yield[a] (%)	*E*/*Z*
1	*p*-$NO_2C_6H_4$	BBr_3	48	30	5:1
2	*p*-$NO_2C_6H_4$	$TiBr_4$	48	42	5:1
3	*m*-$NO_2C_6H_4$	$TiBr_4$	48	48	3:1
5	*p*-ClC_6H_4	$TiBr_4$	48	42	9:1
6	C_6H_5	$TiBr_4$	48	–	–
7	*p*-EtC_6H_4	$TiBr_4$	48	–	–

Aldehyde/$TiBr_4$/propynenitrile=1:1.4:2.
[a] Isolated yields.

the $TiBr_4$ or BBr_3 reagent. In Schemes 8 and 9, we tentatively proposed the reaction mechanism for the formation of α,β- and β,β-dibrominated products **2** or **4** (Schemes 8 and 9). The transition state of the six-membered ring derived from *Z*-**1** or *E*-**1** and $TiBr_4$ can only give α,β-dibrominated **2** with the corresponding *Z* or *E* configuration (Scheme 8). While, for the formation of β,β-dibrominated products **4** and **5**, we believe that, carboxyl group or nitrile group does not coordinate to the titanium metal center and the bromination takes place via another six-membered transition state shown in Scheme 9. Thus, products *E*-**4** and *E*-**5** were preferentially produced.

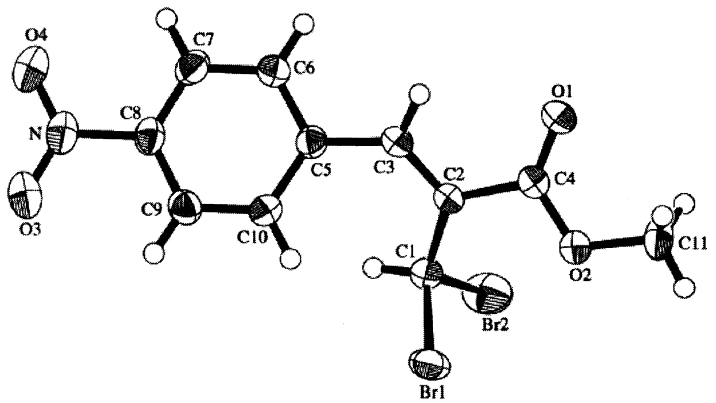


Figure 2. The crystal structure of **4a**.

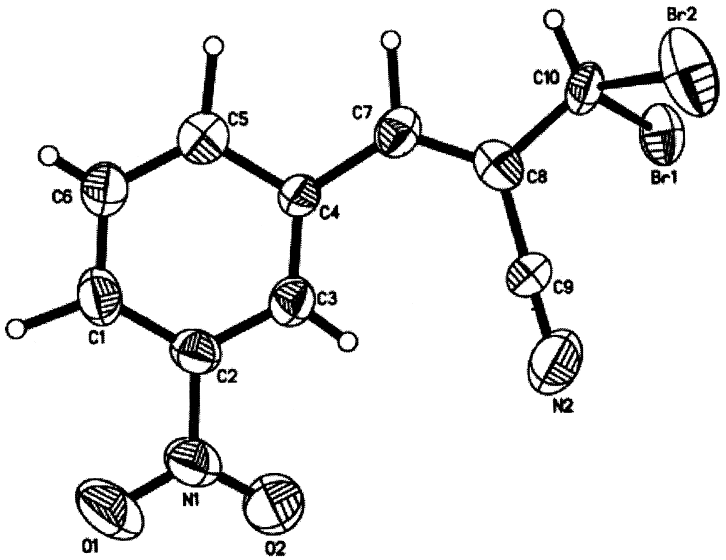
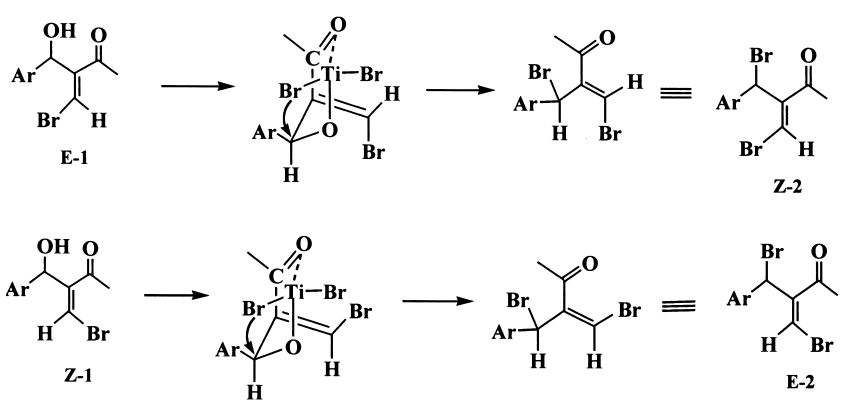


Figure 3. The crystal structure of **5**.

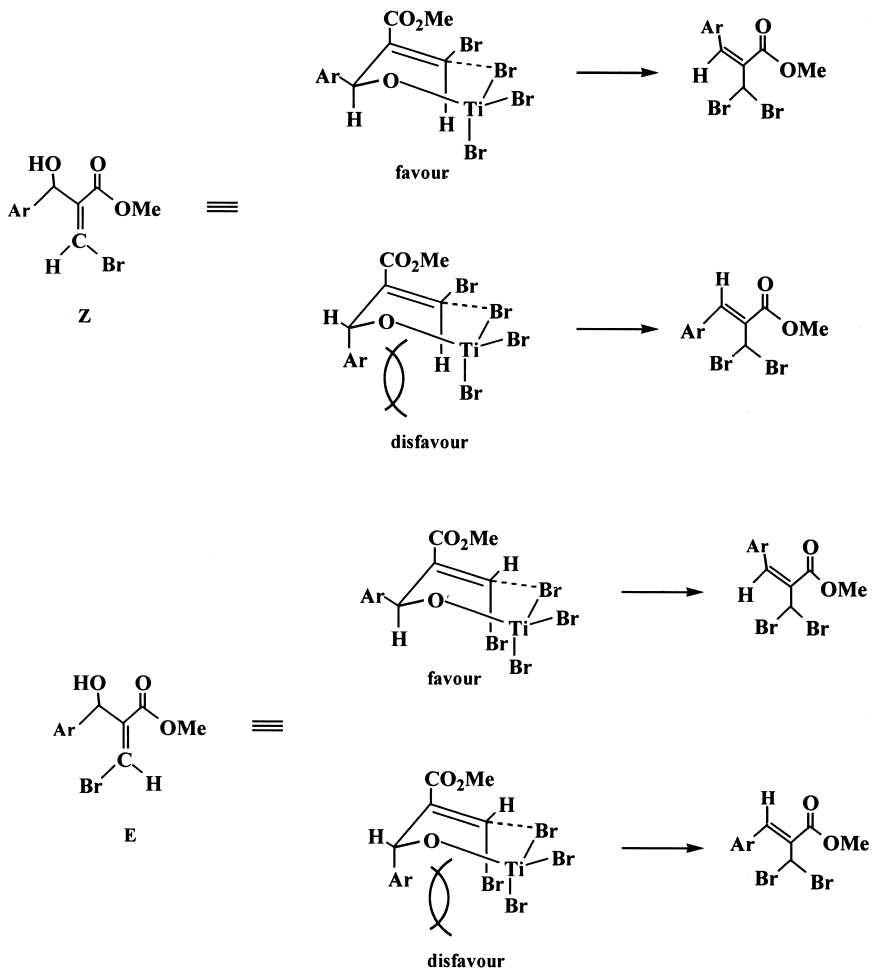
The palladium catalyzed allylic substitution and Suzuki-type coupling reactions were examined using **4a** as the substrate. It is very interesting to find that, the benzylic bromide and vinylic bromide were all replaced by the nucleophiles.[8] The optimized reaction conditions are shown in Scheme 10. The stereochemical configurations of **6** and **7** were determined by ^{1}H NMR spectral data and nosey spectroscopic analysis.

3. Conclusion

We found that the titanium(IV) bromide or boron(III) tribromide promoted Baylis–Hillman reaction of arylaldehydes with 3-butyn-2-one, methyl propiolate, or propynenitrile is not as simple as those reported before. The reaction temperature and the amount of the employed Lewis acids can drastically affect the reaction products. We first



Scheme 8.



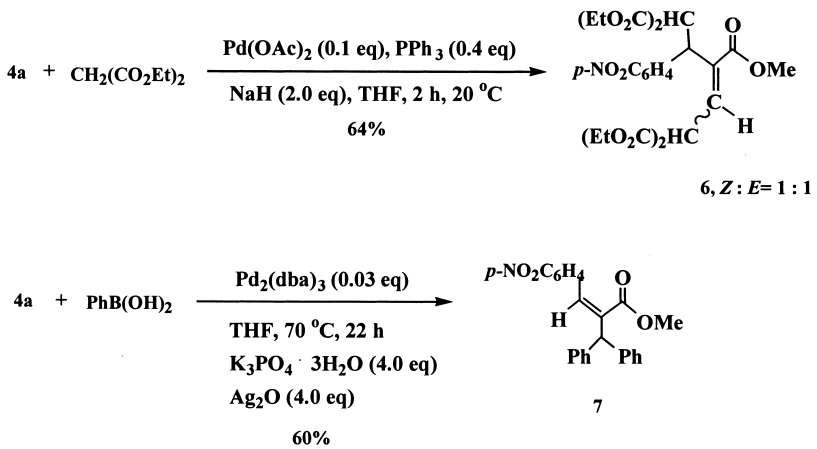
Scheme 9.

disclosed that, at room temperature (20°C), both the α-bromomethylene aldols **1** and α,β-dibrominated products **2** were formed as the major reaction products and the α,β-dibrominated products **2** could be obtained as the sole product in the presence of large excess amount of $TiBr_4$ or at 70°C in 1,2-dichloroethane. While, in the reaction of arylaldehydes with methyl propiolate, or propynenitrile at 70°C in 1,2-dichloroethane, β,β-dibrominated products **4** and **5** were formed exclusively. Efforts are underway to elucidate the mechanistic details of this reaction and to disclose its scope and limitations. Work in this direction is currently in progress.

4. Experimental

4.1. General

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Mass



Scheme 10.

spectra were recorded by EI method and HRMS was measured on a Finnigan MA+mass spectrometer. For these products having bromide, the HRMS data are obtained and calculated on Br^{79}. Organic solvents used were dried by standard methods when necessary. Commercially available reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. flash column chromatography was carried out using 300–400 mesh silica gel.

4.1.1. Typical reaction procedure of arylaldehydes with 3-butyn-2-one (at −78 or −20°C). To a solution of $TiBr_4$ (257 mg, 0.7 mmol) in freshly distilled dichloromethane (1.0 mL) was added a solution of *p*-nitrobenzaldehyde (76 mg, 0.5 mmol) in dichloromethane (1.0 mL) at −78°C. After stirring for 5 min, 3-butyn-2-one (68 mg, 1.0 mmol) was added. The reaction mixture was kept for 40 h at −78°C. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution (2 mL). After filtration, the filtrate was extracted with dichloromethane (5.0 mL×2) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give the compound **1a** (*E*-isomer isolated, 135 mg, 90%) as a yellowish solid (eluent: ethyl acetate/petroleum ether= 1:5): mp 120–121°C; IR ($CHCl_3$) ν 1666 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.35 (s, 3H, Me), 4.35 (br, 1H, OH), 6.01 (br, 1H, benzylic H), 7.56 (d, *J*=8.7 Hz, 2H, Ar H), 7.85 (s, 1H, vinyl H), 8.20 (d, *J*=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 300 (M^++1, 0.51), 220 (M^+−79, 73.49), 43 (M^+−256, 100). Anal. calcd for $C_{11}H_{10}BrNO_4$ requires C, 44.00; H, 3.33; N, 4.67%, found: C, 44.28; H, 3.43; N, 4.62%.

The compound **1b** (*Z* and *E*-mixture): 91 mg, 61%; a yellowish solid.

E-Isomer: when the reaction was carried out at room temperature, only *E*-isomer can be isolated. A yellowish solid; mp 109–111°C; IR ($CHCl_3$) ν 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.37 (s, 3H, Me), 4.41 (d, *J*=11.4 Hz, 1H, OH), 5.98 (d, *J*=11.4 Hz, 1H, benzylic H), 7.52 (dd, *J*=8.0, 7.6 Hz, 1H, Ar H), 7.75 (d, *J*=7.6 Hz, 1H, Ar H), 7.87 (s, 1H, vinyl H), 8.13 (d, *J*=8.0 Hz, 1H, Ar H), 8.21 (s, 1H, Ar H); MS (EI) *m/e* 300 (M^++1, 1.10), 220 (M^+−79, 66.03), 43 (M^+−256, 100). Anal. calcd for $C_{11}H_{10}BrNO_4$ requires C, 44.00; H, 3.33; N, 4.67%, found: C, 44.19; H, 3.44; N, 4.55%.

Z-Isomer: IR ($CHCl_3$) ν 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.46 (s, 3H, Me), 3.33 (d, *J*= 5.9 Hz, 1H, OH), 5.62 (d, *J*=5.9 Hz, 1H, benzylic H), 6.91 (s, 1H, vinyl H), 7.56 (dd, *J*=8.1, 7.9 Hz, 1H, Ar H), 7.77 (d, *J*=7.9 Hz, 1H, Ar H), 8.16 (d, *J*=8.1 Hz, 1H, Ar H), 8.25 (s, 1H, Ar H); MS (EI) *m/e* 300 (M^++1, 1.10), 220 (M^+−79, 66.03), 43 (M^+−256, 100). Anal. calcd for $C_{11}H_{10}BrNO_4$ requires C, 44.00; H, 3.33; N, 4.67%, found: C, 44.19; H, 3.44; N, 4.55%.

The compound **1c** (*Z*-isomer isolated): 99 mg, 66%; a yellowish oil; IR ($CHCl_3$) ν 1669 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.51 (s, 3H, Me), 3.91 (br, 1H, OH), 6.07 (s, 1H, benzylic H), 6.60 (s, 1H, vinyl H), 7.51 (dd, *J*=8.0, 7.41 Hz, 1H, Ar H), 7.70 (dd, *J*=7.85, 7.41 Hz, 1H, Ar H), 7.85 (d, *J*=7.85 Hz, 1H, Ar H), 8.03 (d, *J*= 8.0 Hz, 1H, Ar H); MS (EI) *m/e* 300 (M^++1, 1.18), 220 (M^+−79, 10.28), 43 (M^+−256, 57.38); HRMS calcd for $C_{11}H_{11}BrNO_4$ (M^++1) requires 299.9872, found: 299.9877.

The compound **1c** (*E*-isomer isolated): 14 mg, 10%; a yellowish solid; mp 97–98°C; IR ($CHCl_3$) ν 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.33 (s, 3H, Me), 3.91 (d, *J*=9.6 Hz, 1H, OH), 6.39 (d, *J*=9.6 Hz, 1H, benzylic H), 7.45 (m, 1H, Ar H), 7.58 (m, 2H, Ar H), 7.73 (s, 1H, vinyl H), 7.82 (d, *J*=7.65 Hz, 1H, Ar H); MS (EI) *m/e* 256 (M^+−43, 1.65), 220 (M^+−79, 2.22), 43 (M^+−256, 100); HRMS calcd for $C_{11}H_9BrNO_4$ (M^+−HBr) requires 219.0530, found: 219.0528.

The compound **1d** (*E*-isomer isolated): 115 mg, 80%; a yellowish solid; mp 71–72°C; IR ($CHCl_3$) ν 1665 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.32 (s, 3H, Me), 4.41 (d, *J*=11.2 Hz, 1H, OH), 5.88 (d, *J*=11.2 Hz, 1H, benzylic H), 7.38 (m, 4H, Ar H), 7.76 (s, 1H, vinyl H); MS (EI) *m/e* 287 (M^+−1, 1.50), 209 (M^+−79, 100), 43 (M^+−256, 71.12); HRMS calcd for $C_{11}H_{10}BrClO_2$ (M^++1) requires 287.9553, found: 287.9552.

The compound **1e** (*E*-isomer isolated): 101 mg, 79%; a yellowish oil; IR ($CHCl_3$) ν 1669 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.29 (s, 3H, Me), 4.44 (d, *J*= 11.1 Hz, 1H, OH), 5.92 (d, *J*=11.1 Hz, 1H, benzylic H), 7.32 (m, 5H, Ar H), 7.73 (s, 1H, vinylic H); MS (EI) *m/e* 254 (M^+, 0.4), 175 (M^+−79, 4.39), 131 (M^+−123, 100), 43 (M^+− 211,70.42). Anal. calcd for $C_{11}H_{11}BrO_2$ requires C, 51.79; H, 4.35%, found: C, 51.58; H, 4.53%.

The compound **1e** (*Z*-isomer): IR ($CHCl_3$) ν 1671 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.31 (s, 3H, Me), 2.98 (br, 1H, OH), 5.49 (s, 1H, benzylic H), 6.63 (s, 1H, vinyl H), 7.28 (m, 5H, Ar H); MS (EI) *m/e* 254 (M^+, 6.0), 211 (M^+−43, 5.0), 131 (M^+−123, 35.0). Anal. calcd for $C_{11}H_{11}BrO_2$ requires C, 51.79; H, 4.35%, found: C, 51.58; H, 4.53%.

The compound **1f** (*E*-isomer isolated): 115 mg, 81%, a yellowish oil; IR ($CHCl_3$) ν 1668 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.21 (t, *J*=7.4 Hz, 3H, Me), 2.30 (s, 3H, Me), 2.68 (q, 2H, *J*=7.4 Hz, CH_2), 4.41 (d, *J*= 11.1 Hz, 1H, OH), 5.98 (d, *J*=11.1 Hz, 1H, benzylic H), 7.28 (m, 4H, Ar H), 7.73 (s, 1H, vinyl H); MS (EI) *m/e* 283 (M^+, 29), 159 (M^+−124, 18), 43 (M^+−238, 100); HRMS calcd for $C_{13}H_{14}BrO$ (M^+−OH) requires 265.0227, found: 265.0216.

The compound **1f** (*Z*-isomer): a yellowish oil; IR ($CHCl_3$) ν 1666 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.25 (t, *J*=7.2 Hz, 3H, Me), 2.30 (s, 3H, Me), 2.70 (q, 2H, *J*=7.2 Hz, CH_2), 2.99 (br, 1H, OH), 5.46 (s, 1H, benzylic H), 6.61 (s, 1H, vinyl H), 7.25 (m, 4H, Ar H); MS (EI) *m/e* 283 (M^+, 0.65), 159 (M^+−124, 100), 43 (M^+−238, 71.12); HRMS calcd for $C_{13}H_{15}BrO_2$ requires 282.0255, found: 282.0259.

4.1.2. Typical reaction procedure of arylaldehydes with 3-butyn-2-one (at 70°C). To a solution of $TiBr_4$ (257 mg,

0.7 mmol) in freshly distilled 1,2-dichloroethane (1.0 mL) was added a solution of *p*-nitrobenzaldehyde (76 mg, 0.5 mmol) in 1,2-dichloroethane (1.0 mL) at room temperature. After stirring for 5 min, 3-butyn-2-one (68 mg, 1.0 mmol) was added. The reaction mixture was kept for 8 h at 70°C. The reaction was quenched by addition of a saturated aqueous $NaHCO_3$ solution (2.0 mL). After filtration, the filtrate was extracted with dichloromethane (5.0 mL×2) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give **2a** (*Z*-isomer, 126 mg, 70%) as a yellowish solid (eluent: ethyl acetate/petroleum ether=1:10): mp 122–123°C; IR ($CHCl_3$) ν 1682 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.35 (s, 3H, Me), 6.5 (s, 1H, benzylic H), 7.66 (d, J=8.7 Hz, 2H, Ar H), 7.79 (s, 1H, vinyl H), 8.16 (d, J=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 362 (M^+-1, 4.96), 282 (M^+-81, 39.6), 43 (M^+-320, 100). Anal. calcd for $C_{11}H_9Br_2NO_3$ requires C, 36.36; H, 2.48; N, 3.86%, found: C, 36.72; H, 2.67; N, 3.96%.

The compound **2b** (*Z*-isomer isolated): 78 mg, 43%, a yellowish oil; IR ($CHCl_3$) ν 1682 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.37 (s, 3H, Me), 6.50 (s, 1H, benzylic H), 7.51 (dd, J=8.1, 7.5 Hz, 1H, Ar H), 7.81 (s, 1H, vinyl H), 7.85 (d, J=7.5 Hz, 1H, Ar H), 8.13 (d, J=8.1 Hz, 1H, Ar H), 8.32 (s, 1H, Ar H); MS (EI) *m/e* 284 (M^+-79, 53.02), 203 (M^+-160, 40.57), 43 (M^+-320, 37.3); HRMS calcd for $C_{11}H_{10}Br_2NO_3$ (M^++1) requires 361.9025, found: 361.9034.

The compound **2c** (*Z*-isomer isolated): 130 mg, 72%, a yellowish oil; IR ($CHCl_3$) ν 1688 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.63 (s, 3H, Me), 6.48 (s, 1H, benzylic H), 7.62 (m, 2H, Ar H), 7.68 (s, 1H, vinyl H), 7.85 (m, 2H, Ar H); MS (EI) *m/e* 362 (M^+-1, 1.26), 203 (M^+-160, 100), 43 (M^+-320, 37.3); HRMS calcd for $C_{11}H_{10}Br_2NO_3$ (M^++1) requires 361.9028, found: 361.9034.

The compound **2d** (*E* and *Z*-mixture): 120 mg, 68%, a yellowish oil.

E-Isomer: IR ($CHCl_3$) ν 1691 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.63 (s, 1H, Me), 6.75 (s, 1H, benzylic H), 7.37 (s, 1H, vinyl H), 7.43 (m, 4H, Ar H); MS (EI) *m/e* 271 (M^+-81, 29.04), 192 (M^+-160, 1.73), 164 (M^+-188, 100); HRMS calcd for $C_{11}H_{10}Br_2ClO$ (M^++1) requires 350.8788, found: 350.8784.

Z-Isomer: IR ($CHCl_3$) ν 1691 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.33 (s, 1H, Me), 6.45 (s, 1H, benzylic H), 7.30 (m, 4H, Ar H), 7.70 (s, 1H, vinyl H); MS (EI) *m/e* 271 (M^+-81, 29.04), 192 (M^+-160, 1.73), 164 (M^+-188, 100); HRMS calcd for $C_{11}H_{10}Br_2ClO$ (M^++1) requires 350.8788, found: 350.8784.

The compound **2e** (*E* and *Z*-mixture): 79 mg, 50%, a yellowish oil.

E-Isomer: IR ($CHCl_3$) ν 1689 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.64 (s, 3H, Me), 6.78 (s, 1H, benzylic H), 7.43 (s, 1H, vinyl H), 7.51 (m, 5H, Ar H); MS (EI) *m/e* 316 (M^+, 10.0), 115 (M^+-201, 58.0), 43 (M^+-273, 100); HRMS calcd for $C_{11}H_{11}Br_2O$ requires 316.9177 (M^+-1), found: 316.9180.

Z-Isomer: IR ($CHCl_3$) ν 1689 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.31 (s, 3H, Me), 6.54 (s, 1H, benzylic H), 7.38 (m, 5H, Ar), 7.69 (s, 1H, vinyl H); MS (EI) *m/e* 316 (M^+, 10.0), 115 (M^+-201, 58.0), 43 (M^+-273, 100); HRMS calcd for $C_{11}H_{11}Br_2O$ requires 316.9177 (M^+-1), found: 316.9180.

The compound **2f** (*E* and *Z*-mixture): 103 mg, 60%, a yellowish oil.

E-Isomer: IR ($CHCl_3$) ν 1684 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.22 (t, 3H, J=7.6 Hz, Me), 2.61 (s, 3H, Me), 2.68 (q, 2H, J=7.6 Hz, CH_2), 6.84 (s, 1H, benzylic H), 7.34 (d, J=8.0 Hz, 2H, Ar), 7.45 (s, 1H, vinyl H), 7.48 (d, J=8.0 Hz, 2H, Ar H); MS (EI) *m/e* 346 (M^+, 1.21), 331 (M^+-15, 3.35), 186 (M^+-160, 46.09), 43 (M^+-303, 100); HRMS calcd for $C_{13}H_{14}Br_2O$ requires 343.9411, found: 343.9365.

Z-Isomer: IR ($CHCl_3$) ν 1684 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.28 (t, 3H, J=8.0 Hz, Me), 2.28 (s, 3H, Me), 2.65 (q, 2H, J=8.0 Hz, CH_2), 6.52 (s, 1H, benzylic H), 7.16 (d, J=8.1 Hz, 2H, Ar H), 7.41 (d, J=8.1 Hz, 2H, Ar H), 7.67 (s, 1H, vinyl H); MS (EI) *m/e* 346 (M^+, 1.21), 331 (M^+-15, 3.35), 186 (M^+-160, 46.09), 43 (M^+-303, 100); HRMS calcd for $C_{13}H_{14}Br_2O$ requires 343.9411, found: 343.9365.

4.1.3. Typical reaction procedure of arylaldehydes with methyl propiolate (at 20°C). To a solution of $TiBr_4$ (257 mg, 0.7 mmol) in freshly distilled dichloromethane (1.0 mL) was added a solution of *p*-nitrobenzaldehyde (76 mg, 0.5 mmol) in dichloromethane (1.0 mL) at room temperature. After stirring for 5 min, methyl propiolate (84 mg, 1.0 mmol) was added. The reaction mixture was kept for 48 h at 20°C. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution (2.0 mL). After filtration, the filtrate was extracted with dichloromethane (5.0 mL×2) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give the compound **3a** (*E*-isomer isolated, 22 mg, 14%) as a yellowish solid (eluent: ethyl acetate/petroleum ether=1:5): mp 105–106°C; IR ($CHCl_3$) ν 1702 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.75 (s, 3H, Me), 4.26 (d, J=11.4 Hz, 1H, OH), 6.03 (d, J=11.4 Hz, 1H, benzylic H), 7.60 (d, J=8.6 Hz, 2H, Ar H), 7.87 (s, 1H, vinyl H), 8.21 (d, J=8.6 Hz, 2H, Ar H); MS (EI) *m/e* 284 (M^+-31, 2.19), 235 (M^+-81, 23.17), 204 (M^+-122, 100). Anal. calcd for $C_{11}H_{10}BrNO_5$ requires C, 41.77; H, 3.16; N, 4.43%, found: C, 41.53; H, 3.48; N, 4.52%.

The compound **3a** (*Z*-isomer isolated): 44 mg, 28%, a yellowish oil; IR ($CHCl_3$) ν 1707 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.35 (d, J=6.2 Hz, 1H, OH), 3.76 (s, 3H, Me), 5.61 (d, J=6.2 Hz, 1H, benzylic H), 7.05 (s, 1H, vinyl H), 7.56 (d, J=8.7 Hz, 2H, Ar H), 8.22 (d, J=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 284 (M^+-31, 1.92), 235 (M^+-81, 19.78), 204 (M^+-122, 100); HRMS calcd

for $C_{11}H_{11}BrNO_5$ (M^++1) requires 315.9821, found: 315.9823.

The compound **3b** (*E*-isomer isolated): 20 mg, 13%, a yellowish oil; IR ($CHCl_3$) ν 1725 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.76 (s, 3H, Me), 4.30 (d, *J*=11.4 Hz, 1H, OH), 6.02 (d, *J*=11.4 Hz, 1H, benzylic H), 7.54 (dd, *J*=8.2, 7.6 Hz, 1H, Ar H), 7.77 (d, *J*=7.6 Hz, 1H, Ar H), 7.88 (s, 1H, vinyl H), 8.15 (d, *J*=8.2 Hz, Ar H), 8.29 (s, 1H, Ar H); MS (EI) *m/e* 316 (M^+, 0.99), 298 (M^+-18, 15.83), 204 (M^+-112, 100); HRMS calcd for $C_{11}H_{10}BrNO_5$ (M^+-H_2O) requires 296.9635, found: 296.9639.

The compound **3b** (*Z*-isomer isolated): 52 mg, 33%, a yellowish oil; IR ($CHCl_3$) ν 1701 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.39 (d, *J*=5.9 Hz, 1H, OH), 3.76 (s, 3H, Me), 5.62 (d, *J*=5.9 Hz, 1H, benzylic H), 7.08 (s, 1H, vinyl H), 7.55 (dd, *J*=8.5, 7.9 Hz, 1H, Ar H), 7.70 (d, *J*=7.9 Hz, 1H, Ar H), 8.17 (d, *J*=8.5 Hz, Ar H), 8.25 (s, 1H, Ar H); MS (EI) *m/e* 298 (M^+-18, 14.83), 266 (M^+-50, 21.00), 204 (M^+-112, 100); HRMS calcd for $C_{11}H_{10}BrNO_5$ requires 314.9751, found: 314.9749.

The compound **3c** (*Z*-isomer isolated): 19 mg, 12%, a yellowish oil; IR ($CHCl_3$ ν 1732 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.73 (s, 3H, Me), 6.16 (s, 1H, benzylic H), 7.0 (s, 1H, vinyl H), 7.50 (m, 1H, Ar H), 7.70 (m, 2H, Ar H), 7.98 (d, *J*=8.2 Hz, 1H, Ar H); MS (EI) *m/e* 284 (M^+-31, 1.22), 235 (M^+-81, 3.79), 218 (M^+-98, 94.1), 210 (M^+-106, 100); HRMS calcd for $C_{11}H_{11}BrNO_5$ (M^++1) requires 315.9821, found: 315.9825.

The compound **3c** (*E*-isomer isolated): 7 mg, 4%, a yellowish oil; IR ($CHCl_3$ ν 1731 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.78 (s, 3H, Me),3.89 (d, *J*=9.9 Hz, 1H, OH), 6.49 (d, *J*=9.9 Hz, 1H, benzylic H), 7.45 (m, 1H, Ar H), 7.59 (m, 2H, Ar H), 7.82 (s, 1H, vinyl H), 7.85 (d, *J*=8.2 Hz, 1H, Ar H); MS (EI) *m/e* 269 (M^+-46, 21.33), 218 (M^+-98, 98.64), 210 (M^+-106, 73.86); HRMS calcd for $C_{11}H_{11}BrNO_5$ (M^++1) requires 315.9821, found: 315.9828.

4.1.4. Typical reaction procedure of arylaldehydes with methyl propiolate (at 70°C). To a solution of $TiBr_4$ (257 mg, 0.7 mmol) in freshly distilled 1,2-dichloroethane (1.0 mL) was added a solution of *p*-nitrobenzaldehyde (76 mg, 0.5 mmol) in 1,2-dichloroethane (1.0 mL) at room temperature. After stirring for 5 min, methyl propiolate (84 mg, 1.0 mmol) was added. The reaction mixture was kept for 14 h at 70°C. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution (2.0 mL). After filtration, the filtrate was extracted with dichloromethane (5.0 mL×2) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give compound **4a** (*E*-isomer isolated, 76 mg, 40%) as a yellowish oil (eluent: ethyl acetate/petroleum ether=1:10). IR ($CHCl_3$) ν 1726 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.70 (s, 3H, Me), 6.47 (s, 1H, allylic H), 7.69 (d, *J*=8.7 Hz, 2H, Ar H), 7.81 (s, 1H, vinyl H), 8.16 (d, *J*=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 379 (M^+, 0.68), 348 (M^+-31, 2.59), 300 (M^+-79, 42.73), 219 (M^+-160, 38.05), 173 (M^+-206, 100); HRMS calcd for $C_{11}H_9Br_2NO_4$ requires 376.8898 (M^+), found: 376.8947.

The compound **4a** (*Z*-isomer isolated): 30 mg, 16%, a yellowish solid; mp 130–131°C. IR ($CHCl_3$) ν 1728 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.98 (s, 3H, Me), 6.62 (s, 1H, allylic H), 7.60 (d, *J*=8.6 Hz, 2H, Ar H), 7.63 (s, 1H, vinyl H), 8.36 (d, *J*=8.6 Hz, 2H, Ar H); MS (EI) *m/e* 379 (M^+, 0.59), 348 (M^+-31, 3.85), 300 (M^+-79, 46.45), 219 (M^+-160, 45.10), 173 (M^+-206, 100). Anal. calcd for $C_{11}H_9Br_2NO_4$ requires C, 34.83; H, 2.37; N, 3.69%, found: C, 34.96; H, 2.43; N, 3.69%.

The compound **4b** (*E*-isomer isolated): 84 mg, 44%, a yellowish oil; IR ($CHCl_3$) ν 1725 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.73 (s, 3H, Me), 6.49 (s, 1H, allylic H), 7.53 (dd, *J*=4.0, 7.0 Hz, 1H, Ar H), 7.83 (s, 1H, vinyl H), 7.89 (d, *J*=7.0 Hz, 1H, Ar H), 8.13 (d, *J*=4.0 Hz, 1H, Ar H), 8.40 (s, 1H, Ar H); MS (EI) *m/e* 348 (M^+-31, 2.63), 300 (M^+-79, 59.91), 219 (M^+-160, 60.06), 188 (M^+-191, 64.16); HRMS calcd for $C_{10}H_6Br_2NO_3$ (M^+−OMe) requires 345.8715, found: 345.8757.

The compound **4b** (*Z*-isomer isolated): 15 mg, 8%, a yellowish solid; mp 125–126°C. IR ($CHCl_3$) ν 1729 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) 3.97 (s, 3H, Me), 6.65 (s, 1H, allylic H), 7.64 (s, 1H, vinyl H), 7.70 (dd, *J*=7.7, 8.2 Hz, 1H, Ar H), 7.80 (d, *J*=7.7 Hz, 1H, Ar H), 8.31 (d, *J*=8.2 Hz, 1H, Ar H), 8.36 (s, 1H, Ar H); MS (EI) *m/e* 348 (M^+-31, 2.55), 300 (M^+-79, 51.98), 219 (M^+-160, 64.45), 188 (M^+-191, 58.30); HRMS calcd for $C_{11}H_9Br_2NO_4$ (M^+−OMe) requires 345.8715, found: 345.8706.

The compound **4c** (*E*-isomer isolated): 36 mg, 19%, a yellowish oil; IR ($CHCl_3$) ν 1701 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.95 (s, 3H, Me), 6.42 (s, 1H, allylic H), 7.57 (d, *J*=7.6 Hz, 1H, Ar H), 7.65 (m, 1H, Ar H), 7.81 (m, 1H, Ar H),7.92 (s, 1H, vinyl H), 8.21 (d, *J*=9.1 Hz, 1H, Ar H); MS (EI) *m/e* 379 (M^+, 4.53), 348 (M^+-31, 5.71), 300 (M^+-79, 10.68), 219 (M^+-160, 41.32), 187 (M^+-192, 100); HRMS calcd for $C_{10}H_6Br_2NO_3$ (M^+−OMe) requires 345.8715, found: 345.8708.

The compound **4c** (*Z*-isomer isolated): 17 mg, 9%, a yellowish oil; IR ($CHCl_3$) ν 1726 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.58 (s, 3H, Me), 6.72 (s, 1H, allylic H), 7.28 (d, *J*=9.6 Hz, 1H, Ar H), 7.53 (m, 1H, Ar H), 7.63 (m, 1H, Ar H), 8.05 (s, 1H, vinyl H), 8.24 (d, *J*=8.2 Hz, 1H, Ar H); MS (EI) *m/e* 379 (M^+, 1.57), 300 (M^+-79, 6.77), 219 (M^+-160, 31.79), 187 (M^+-192, 100); HRMS calcd for $C_{11}H_9Br_2NO_4$ requires 376.8898 (M^+), found: 376.8925.

The compound **4d** (*E*-isomer isolated): 78 mg, 38%, a yellowish oil; IR ($CHCl_3$) ν 1728 cm^{-1} (C═O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.73 (s, 3H, Me), 6.39 (s, 1H, allylic H), 7.41–7.39 (m, 4H, Ar H), 7.75 (s, 1H, vinyl H); MS (EI) *m/e* 412 (M^+, 0.90), 333 (M^+-79, 2.59), 253 (M^+-160, 100); HRMS calcd for $C_{11}H_9Br_3O_2$ requires 409.8153, found: 409.8152.

The compound **4d** (*Z*-isomer isolated): 39 mg, 19%, a yellowish oil; IR ($CHCl_3$) ν 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.94 (s, 3H, Me), 6.70 (s, 1H, allylic H), 7.31 (d, J=8.4 Hz, 2H, Ar H), 7.52 (s, 1H, vinyl H), 7.63 (d, J=8.4 Hz, 2H, Ar H); MS (EI) *m/e* 412 (M^+, 0.83), 333 (M^+-79, 49.59), 253 (M^+-160, 99.63); HRMS calcd for $C_{11}H_9Br_3O_2$ requires 409.8153, found: 409.8157.

The compound **4e** (*E*-isomer isolated): 64 mg, 35%, a yellowish oil; IR ($CHCl_3$) ν 1728 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.61 (s, 3H, Me), 6.30 (s, 1H, allylic H), 7.16 (d, J=8.4 Hz, 2H, Ar H), 7.36 (d, J=8.4 Hz, 2H, Ar H), 7.63 (s, 1H, vinyl H); MS (EI) *m/e* 337 (M^+-31, 1.75), 289 (M^+-79, 49.99), 207 (M^+-158, 100); HRMS calcd for $C_{10}H_6ClBr_2O$ (M^+-OMe) requires 334.8473, found: 334.8493.

The compound **4e** (*Z*-isomer isolated): 46 mg, 25%, a yellowish oil; IR ($CHCl_3$) ν 1728 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.83 (s, 3H, Me), 6.60 (s, 1H, allylic H), 7.27 (d, J=8.4 Hz, 2H, Ar H), 7.36 (d, J=8.4 Hz, 2H, Ar H), 7.43 (s, 1H, vinyl H); MS (EI) *m/e* 368 (M^+, 1.22), 289 (M^+-79, 41.76), 207 (M^+-158, 100); HRMS calcd for $C_{10}H_6ClBr_2O$ (M^+-OMe) requires 334.8473, found: 334.8451.

The compound **4f** (*Z*-isomer isolated): 23 mg, 14%, a yellowish oil; IR ($CHCl_3$) ν 1730 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.94 (s, 3H, Me), 6.45 (s, 1H, allylic H), 7.25–7.51 (m, 5H, Ar H), 7.63 (s, 1H, vinyl H); MS (EI) *m/e* 334 (M^+, 6.40), 255 (M^+-79, 54.50), 173 (M^+-160, 100); HRMS calcd for $C_{11}H_{10}Br_2O_2$ requires 331.9048 (M^+), found: 331.9086.

The compound **4f** (*E*-isomer isolated): 40 mg, 24%, a yellowish oil; IR ($CHCl_3$) ν 1715 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.89 (s, 3H, Me), 5.68 (s, 1H, allylic H), 7.30–7.52 (m, 5H, Ar H), 7.60 (s, 1H, vinyl H); MS (EI) *m/e* 334 (M^+, 0.72), 254 (M^+-79, 23.18), 173 (M^+-160, 100); HRMS calcd for $C_{11}H_9BrO_2$ (M^+-HBr) requires 251.9784, found: 251.9779.

The compound **4g** (*E* and *Z*-isomer isolated): 61 mg, 34%, a yellowish oil.

E-Isomer: IR ($CHCl_3$) ν 1711 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.27 (m, 3H, Me), 2.60 (m, 2H, CH_2), 3.88 (s, 3H, Me), 5.64 (s, 1H, allylic H), 7.36 (d, J=7.8 Hz, 2H, Ar H), 7.53 (d, J=7.8 Hz, 2H, Ar H), 7.66 (s, 1H, vinyl H); MS (EI) *m/e* 282 (M^+-79, 21.50), 251 (M^+-110, 2.83, 201 (M^+-160, 100); HRMS calcd for $C_{13}H_{13}BrO_2$ (M^+-HBr) requires 280.0097, found: 280.0093.

Z-Isomer: IR ($CHCl_3$) ν 1711 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.27 (m, 3H, Me), 2.60 (m, 2H, CH_2), 3.88 (s, 3H, Me), 5.65 (s, 1H, allylic H), 7.47 (s, 1H, vinyl H), 7.16–7.27 (m, 4H, Ar H); MS (EI) *m/e* 282 (M^+-79, 21.50), 251 (M^+-110, 2.83, 201 (M^+-160, 100); HRMS calcd for $C_{13}H_{13}BrO_2$ (M^+-HBr) requires 280.0097, found: 280.0093.

4.1.5. Typical reaction procedure of arylaldehydes with propynenitrile (at 70°C). To a solution of $TiBr_4$ (257 mg, 0.7 mmol) in freshly distilled 1,2-dichloroethane (1.0 mL) was added a solution of *p*-nitrobenzaldehyde (76 mg, 0.5 mmol) in 1,2-dichloroethane (2.0 mL) at room temperature. After stirring for 5 min, propynenitrile (51 mg, 1.0 mmol) was added. The reaction mixture was kept for 48 h at 70°C. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ (2.0 mL). After filtration, the filtrate was extracted with dichloromethane (5.0 mL×2) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give the compound **5a** (*E* and *Z*-mixture, 73 mg, 42%) as a yellowish oil (eluent: ethyl acetate/petroleum ether=1:10).

Z-Isomer: IR ($CHCl_3$) ν 2230, 2304 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 5.74 (s, 1H, allylic H), 7.43 (s, 1H, vinyl H), 7.71 (d, J=8.8 Hz, 2H, Ar H), 8.28 (d, J=8.8 Hz, 2H, Ar H); MS (EI) *m/e* 347 (M^++1, 10.83), 267 (M^+-79, 37.66), 221 (M^+-125, 36.00), 140 (M^+-206, 100); HRMS calcd for $C_{10}H_6Br_2N_2O_2$ requires 343.8796 (M^+), found: 343.8752.

E-Isomer: IR ($CHCl_3$) ν 2230, 2304 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 6.35 (s, 1H, allylic H), 7.34 (s, 1H, vinyl H), 8.0 (d, J=11.0 Hz, 2H, Ar H), 8.31 (d, J=11.0 Hz, 2H, Ar H); MS (EI) *m/e* 347 (M^++1, 10.83), 267 (M^+-79, 37.66), 221 (M^+-125, 36.00), 140 (M^+-206, 100); HRMS calcd for $C_{10}H_6Br_2N_2O_2$ requires 343.8796 (M^+), found: 343.8752.

The compound **5b** (*Z*-isomer isolated): 21 mg, 12%, a yellowish oil; IR ($CHCl_3$) ν 2331 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 5.72 (s, 1H, allylic H), 7.42 (s, 1H, vinyl H), 7.65 (dd, J=7.9, 8.1 Hz, 1H, Ar H), 7.91 (d, J=8.1 Hz, 1H, Ar H), 8.28 (d, J=7.9 Hz, 1H, Ar H), 8.33 (s, 1H, Ar H); MS (EI) *m/e* 347 (M^++1, 9.20), 267 (M^+-79, 39.40), 221 (M^+-125, 22.06), 186 (M^+-160, 47.20), 140 (M^+-206, 100); HRMS calcd for $C_{10}H_6Br_2N_2O_2$ requires 343.8796 (M^+), found: 343.8823.

The compound **5b** (*E*-isomer isolated): 62 mg, 36%, a yellowish solid; mp 132–133°C; IR ($CHCl_3$) ν 2304 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 6.33 (s, 1H, allylic H), 7.32 (s, 1H, vinyl H), 7.71 (dd, J=7.8, 8.0 Hz, 1H, Ar H), 8.30 (d, J=7.8 Hz, 1H, Ar H), 8.36 (d, J=8.0 Hz, 1H, Ar H), 8.53 (s, 1H, Ar H); MS (EI) *m/e* 346 (M^+, 0.83), 267 (M^+-79, 54.47), 221 (M^+-125, 13.47), 186 (M^+-160, 33.11), 140 (M^+-206, 100); HRMS calcd for $C_{10}H_6BrN_2O_2$ (M^+-Br) requires 264.9612, found: 264.9611.

The compound **5c** (*E* and *Z*-mixture): 71 mg, 42%, a yellowish oil.

Z-Isomer: IR ($CHCl_3$) ν 2226, 2304 cm^{-1} (CN); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 5.62 (s, 1H, allylic H), 7.28 (s, 1H, vinyl H), 7.35 (d, J=8.7 Hz, 2H, Ar H), 7.42 (d, J=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 336 (M^++1, 10.27), 256 (M^+-79, 90.73), 174 (M^+-160, 100); HRMS calcd for $C_{11}H_6Br_2ClN$ requires 332.8555, found: 332.8540.

E-Isomer: IR ($CHCl_3$) ν 2226, 2304 cm^{-1} (CN); ^1H NMR

($CDCl_3$, TMS, 300 MHz) δ 6.33 (s, 1H, allylic H), 7.18 (s, 1H, vinyl H), 7.44 (d, J=9.2 Hz, 2H, Ar H), 7.77 (d, J=9.2 Hz, 2H, Ar H); MS (EI) *m/e* 336 (M^++1, 10.27), 256 (M^+−79, 90.73), 174 (M^+−160, 100); HRMS calcd for $C_{11}H_6Br_2ClN$ requires 332.8555, found: 332.8540.

4.1.6. Typical procedure for the reaction of 4a with $NaCH(CO_2Et)_2$. A solution of sodium dimethyl malonate in THF (4.0 mL of a 0.175 M solution, 0.7 mmol) prepared from the reaction of dimethyl malonate (0.7 mmol) with sodium hydride (0.7 mmol) was added to a mixture of **4a** (123 mg, 0.33 mmol), triphenylphophine (10.5 mg, 0.04 mmol), and palladium acetate (2.2 mg, 0.01 mmol) under argon atmosphere at room temperature. After the mixture was stirred for 10 h at rt, the reaction was quenched by addition of saturated $NaHCO_3$ solution (5 mL). The layers were separated and the aqueous phase was extracted with ether. The combined organic phases were dried over $MgSO_4$. The solvents were removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give the compound **6***E* (57 mg, 32%) and the compound **6***Z* (57 mg, 32%) as a yellowish oil, respectively.

The compound **6***E*: IR ($CHCl_3$) ν 1749, 1731, 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.1–1.4 (m, 12H, 4Me), 3.65 (s, 3H, Me), 4.05–4.13 (m, 4H, $2CH_2$), 4.18–4.28 (m, 4H, $2CH_2$), 4.78–4.89 (m, 3H), 7.08 (d, J=10.7 Hz, 1H, vinyl H), 7.53 (d, J=8.7 Hz, 2H, Ar H), 8.10 (d, J=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 538 (M^++1, 13.70), 506 (M^+−31, 57.25), 491 (M^+−46, 100), 492 (M^+−45, 32.14); HRMS calcd for $C_{25}H_{31}NO_{12}$ requires 537.1846, found: 537.1863.

The compound **6***Z*: IR ($CHCl_3$) ν 1732 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.1–1.6 (m, 12H, 4Me), 3.67 (s, 3H, Me), 3.9–4.02 (m, 4H, $2CH_2$), 4.12–4.24 (m, 4H, $2CH_2$), 4.26 (d, J=12.2 Hz, 1H), 4.77 (d, J=12.2 Hz, benzylic H), 5.02 (d, J=9.1 Hz, allylic H), 6.53 (d, J=9.1 Hz, vinyl H), 7.47 (d, J=8.7 Hz, 2H, Ar H), 8.13 (d, J=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 538 (M^++1, 26.76), 506 (M^+−31, 100), 491 (M^+−46, 35.38), 492 (M^+−45, 50.53); HRMS calcd for $C_{25}H_{31}NO_{12}$ requires 537.1846, found: 537.1855.

4.1.7. Typical procedure for the reaction of 4a with $PhB(OH)_2$. To a solution of **4a** (100 mg, 0.26 mmol), $PhB(OH)_2$ (106 mg, 0.86 mmol), Ag_2O (231 mg, 1.0 mmol), and $K_3PO_4{\cdot}H_2O$ (266 mg, 1.0 mmol) in THF (2.0 mL) was added $Pd(dba)_3$ (5 mg, 0.009 mmol) under argon atmosphere. The reaction mixture was stirred for 22 h under reflux, then cooled to room temperature. The reaction mixture was extracted with CH_2Cl_2 (10 mL×2), washed with brine (10 mL), and dried over $MgSO_4$. The solvents were removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give **7** (60 mg, 60%) as a yellowish oil. IR ($CHCl_3$) ν 1719 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.49 (s, 3H, Me), 5.50 (s, benzylic H), 6.35 (s, vinyl H), 7.20–7.45 (m, 12H, Ar H), 8.16 (d, J=8.7 Hz, 2H, Ar H); MS (EI) *m/e* 373 (M^+, 53.94), 342 (M^+−31, 18.84), 314 (M^+−59, 15.25), 296 (M^+−77, 31.56); HRMS calcd for $C_{23}H_{19}NO_4$ requires 373.1314, found: 373.1316.

4.2. Crystallography

A suitable single crystal was mounted at the top of a glass capillary. Data were collected on a Rigaku AFC7R diffractometer with graphite-monochromated Mo Kα radiation λ=0.71069 Å using the $\omega-2\theta$ technique at 20°C. The data were collected for Lorentz polarization effects. The structure was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically by full-matrix least squares. All hydrogen atoms were included in calculated position. All calculations were performed using the TEXSAN crystallographic software package. Their crystal structures have been deposited at the Cambridge Crystallographic Data Center and have been allocated the deposition numbers: CCDC 172325 for **2a**, CCDC 172326 for **4a**, and CCDC 172327 for **5**.

Crystal data of **2a**: empirical formula, $C_{11}H_9O_3NBr_2$; formula weight, 363.29; crystal color, habit, colorless, prismatic; crystal dimensions, 0.20×0.20×0.30 mm^3; crystal system, orthorhombic; lattice type, primitive; lattice parameters, a=13.988(4) Å, b=17.119(6) Å, c=10.524(4) Å, V=2520(1) $Å^3$; space group: *Pbca*(#61); Z_{value}=8; D_{calc}=1.018 g/cm^3; F_{000}=792.00; μ(Mo Kα)=16.44 cm^{-1}; residuals: R; Rw=0.045; 0.046.

Crystal data of **4a**: empirical formula, $C_{11}H_9O_4NBr_2$; formula weight, 379.00; crystal color, habit, colorless, prismatic; crystal dimensions, 0.20×0.20×0.30 mm^3; crystal system, triclinic; lattice type, primitive; lattice parameters, a=10.566(3) Å, b=11.427(6) Å, c=5.764(4) Å, α=92.27(3)°, β=102.09(2)°, γ=71.23(3)°, V=644.0(4) $Å^3$; space group: $P1$(#2); Z_{value}=2; D_{calc}=1.954 g/cm^3; F_{000}=368.00; μ(Mo Kα)=63.17 cm^{-1}; residuals: R; Rw=0.032; 0.039.

Crystal data of **5**: empirical formula, $C_{10}H_6O_2N_2Br_2$; formula weight, 345.99; crystal color, habit, colorless, prismatic; crystal dimensions, 0.20×0.20×0.30 mm^3; crystal system, monoclinic; lattice type, primitive; lattice parameters, a=8.4790(18) Å, b=19.671(4) Å, c=7.1537(15) Å, α=90.0°, β=100.529(4)°, γ=90.0(0)°, V=1173.1(4) $Å^3$; space group: $P2(1)/c$; Z_{value}=4; D_{calc}=1.959 g/cm^3; F_{000}=664.00; residuals: R; Rw=0.096; 0.113.

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