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Rhodium-catalyzed alkylation of terephthaldialdimine with terminal alkenes via C–H bond activation

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Abstract—Terephthaldialdimine **1a** reacted with alkenes to give 2,6-dialkylated products selectively in moderate to high isolated yields. In the case of terephthaldialdimine **1b** having a substituent at site 2 in the phenyl ring, the alkylation takes place selectively at site 6 in the phenyl ring. In this alkylation, a *meta*-substituent affected the reactivity significantly because of the steric hindrance.
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Transition metal catalyzed C–C bond formations involving the C–H bond activations have recently attracted much attention, because this method for the functionalization of unreactive C–H bonds is an efficient and economical strategy in organic synthesis.[1] By using the C–H bond activation, alkylation and alkenylation of the aromatic ring through the coupling reaction with alkenes and alkynes have been reported by us[2] and other groups.[3–11] The alkylation of benzaldimines with alkenes is well documented.[2h,k,3f,5c] The alkylation of bisaldimines with alkenes, however, has not been reported until now. So the reactivity, regioselectivity, and effect of substituents of this alkylation are under the veil. Moreover, dialkylated terephthaldicarboxaldehydes are served as good monomers for semiconducting polymers.[12] In order to achieve this alkylation, terephtaldialdimine **1a** is chosen as a substrate for this alkylation. Terephthaldialdimine **1a** has four sites for alkylation, so it has possibilities to give five alkylated products; one mono-, two di-(sites 2,5 and sites 2,6), one tri-, and one tetra-alkylated product. First of all, to know the reactivity, **1a** reacted with 3,3-dimethyl-1-butene **2a** (5 equiv) in the presence of a rhodium catalyst (5 mol %), $[RhCl(coe)_2]_2/Cy_3P$ in toluene at 140 °C for 24 h to give 2,6-dialkylated product **4a** and 2-monoalkylated product **3a** together with trace amount of 2,5-dialkylated product **5a** in 51% isolated yield after hydrolysis and chromatographic isolation (**3a**:**4a**:**5a** = 16:83:1)[13] as shown in Scheme 1. Surprisingly, this alkylation gave the 2,6-dialkylated product **4a** as a major product. On the other hand, the sterically more stable 2,5-dialkylated product **5a**, which is furthest from each group, gave ~1% yield. Moreover, other alkylated products, tri- and tetra-alkylated zproducts could not be found in the reaction mixture. When 10 equiv of **2a** was used under the same reaction conditions, this reaction gave higher isolated yield (77%, **3a**:**4a**:**5a** = 10:88:2). When 8 mol % of the catalyst and 10 equiv of **2a** were used, the isolated yield increased up to 97% (**3a**:**4a**:**5a** = 8:88:4). Another rhodium catalyst, Wilkinson's catalyst gave the corresponding products in low yield (Table 1, run 3). Ruthenium catalysts such as $Ru_3(CO)_{12}$ (4 mol %, **2a**, 2 equiv) and $RuH_2(CO)(PPh_3)_3$ (6 mol %, **2a**, 2 equiv) were inactive.

From the above results, it showed that even though it has two coordinating sites, this alkylation took place at one side selectively.

The results of this alkylation with several terminal alkenes are listed in Table 1. Terminal alkenes such as 1-butene **2b**, 1-pentene **2c**, and 1-hexene **2d** also gave 2,6-dialkylated products as major products in 55%, 62%, and 53% isolated yields, respectively (runs 6, 8, and 9 in Table 1).[13] Another alkene, 3-methyl-1-butene **2e** works well to give high yields (92%, **3e**:**4e**:**5e** = 7:90:3, run 10 in Table 1).[13]

Keywords: Alkylation; C–C bond formation; C–H activation; Rhodium catalyst; Bisaldimine.
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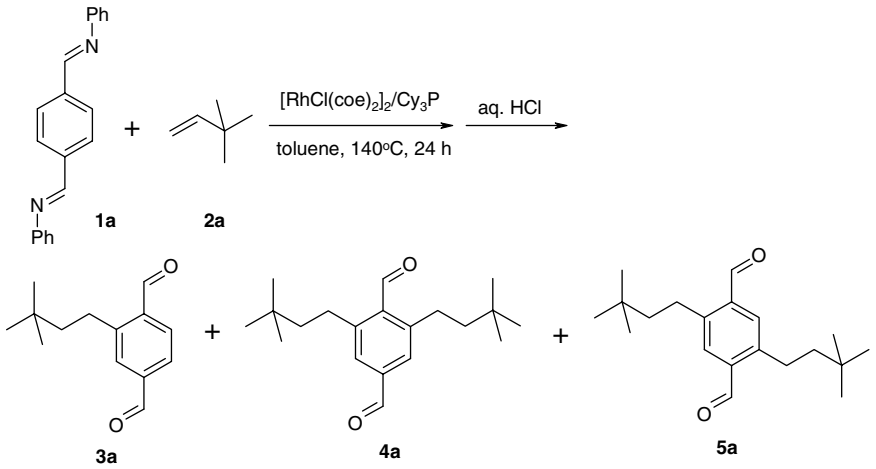
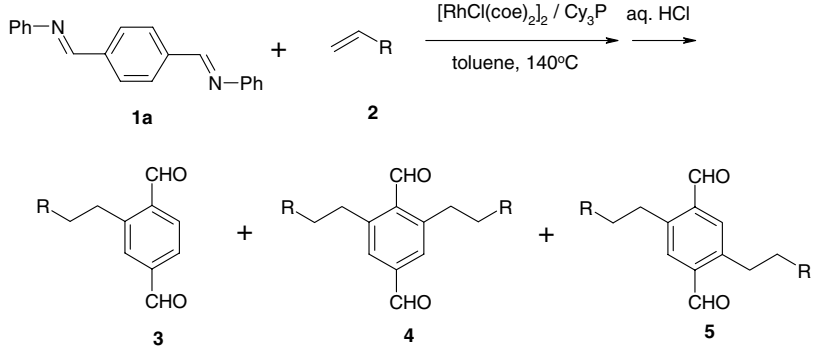


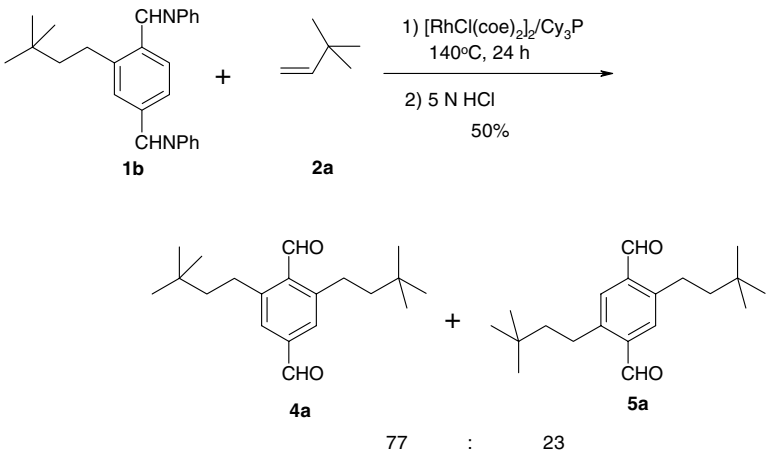
Scheme 1.

Table 1. The results of alkylation of terephthaldialdimine **1a** with alkenes[a]

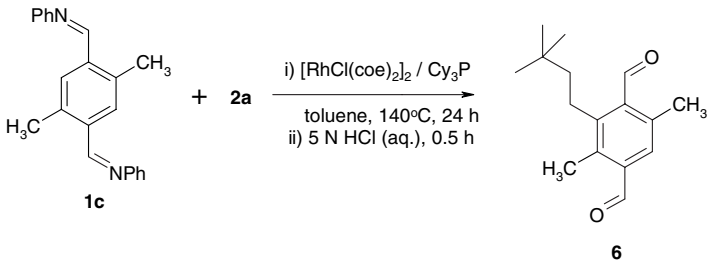


Run	Substrate	Alkene (equiv)	Catalyst (mol%)	Yield (%)[b]	Ratio of **3**:**4**:**5**[c]
1	**1a**	**2a** (5)	5	51	**3a**:**4a**:**5a** = 16:83:1
2	**1a**	**2a** (10)	5	77	**3a**:**4a**:**5a** = 10:88:2
3[d]	**1a**	**2a** (10)	10	18	**3a**:**4a**:**5a** = 74:26:0
4	**1a**	**2a** (10)	8	97	**3a**:**4a**:**5a** = 8:88:4
5	**1a**	1-Butene **2b** (10)	5	45	**3b**:**4b**:**5b** = 18:82:0
6	**1a**	**2b** (10)	8	55	**3b**:**4b**:**5b** = 16:84:0
7	**1a**	1-Pentene **2c** (10)	5	31	**3c**:**4c**:**5c** = 38:62:0
8	**1a**	1-Pentene **2c** (10)	8	62	**3c**:**4c**:**5c** = 10:90:0
9	**1a**	1-Hexene **2d** (10)	8	53	**3d**:**4d**:**5d** = 9:89:2
10	**1a**	3-Methyl-1-butene **2e** (10)	8	92	**3e**:**4e**:**5e** = 7:90:3

[a] **1a**:[RhCl(coe)$_2$]$_2$:Cy$_3$P:**2a** = 1:0.08:0.48, toluene (2 mL), 140 °C, 24 h.
[b] Isolated yields.
[c] The ratios were determined by ^{1}H NMR and/or GC.
[d] 10 mol % of Wilkinson's catalyst was used.

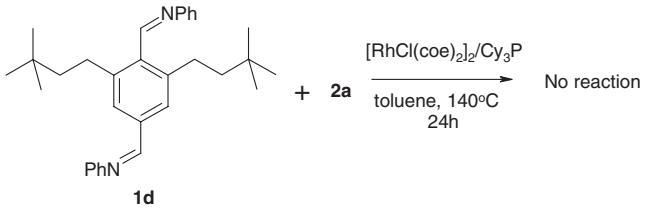


Scheme 2.



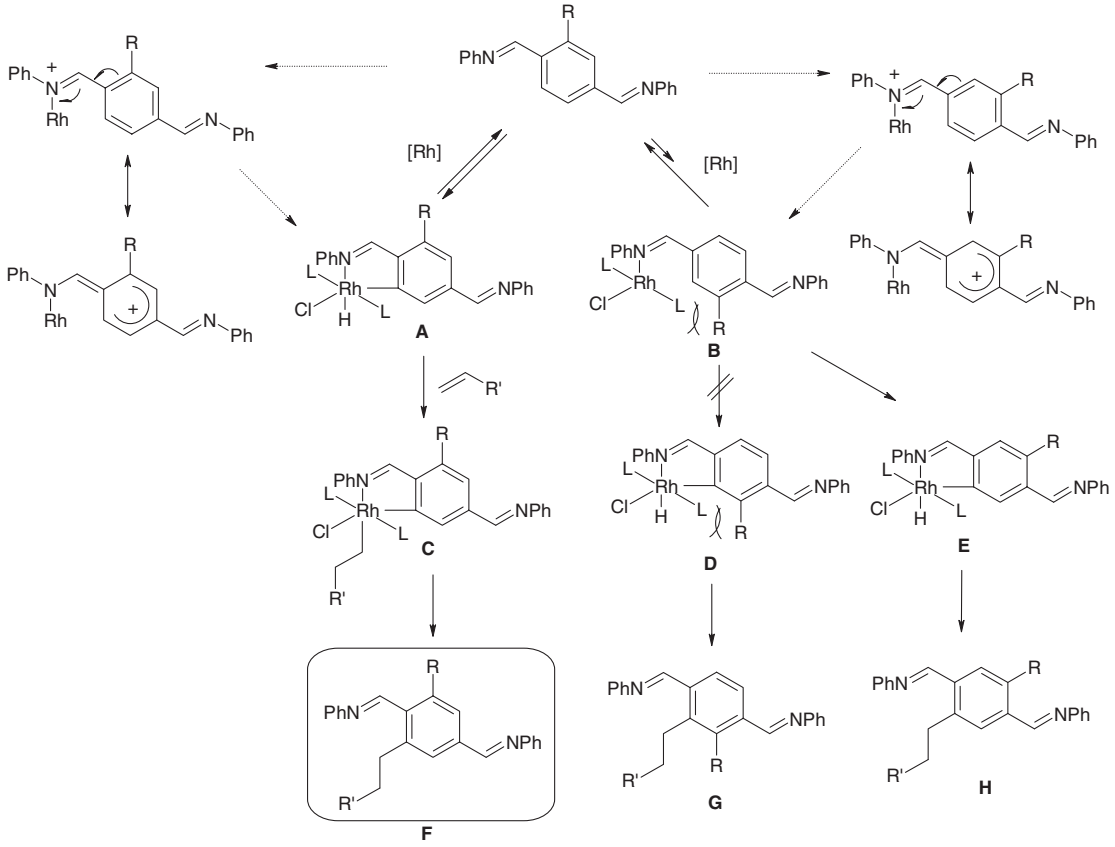
Scheme 3.

To know the effect of the substituent in a substrate, substrate **1b** having one alkyl group at site 2 reacted with **2a** under the same reaction conditions. Interestingly, this alkylation gave **4a** as a major product in 50% yield by reason of steric hindrance (**4a**:**5a** = 77:23) as shown in Scheme 2. Unexpectedly, the alkylation took place at the side of aldimine having *ortho*-substituent largely. This result implied that when rhodium metal approached the nitrogen of aldimine for coordination, alkyl group disturbed the coordination of aldimine, which was sterically free rather than the opposite side. Therefore, the aldimine fixed by an alkyl group coordinated more easily to rhodium metal for this alkylation. This is a very interesting result.



Scheme 4.

To know the effect of substituents once more, another substrate **1c** having two methyl groups at sites 2 and 5 reacted with **2a** under the similar reaction conditions. This alkylation gave mono alkylated product **6** in 11% isolated yield as shown in Scheme 3. This reaction was affected largely by substituents and the yield of alkylation was very low. Unlike **1b**, each of methyl groups in **1c** locates on *meta*-position of the aldimine



Scheme 5.

for coordination. This result showed that a substituent at *meta*-position to the coordinated aldimine affected the reactivity of this alkylation.

To prove this *meta*-substituent effect, substrate **1d** having two big alkyl groups at sites 2 and 6 was applied to this alkylation. This substrate has two alkyl groups at only *meta*-position to the aldimine for the coordination. Substrate **1d** did not react with **2a** completely under the same reaction conditions as shown in Scheme 4. Consequently, it showed that *meta*-substituents to the aldimine group for the coordination affected to this alkylation extensively.

The exact mechanism is unclear at this time. However, we deduced the proposed mechanism from the above results. The mechanism of this alkylation is proposed to be similar to that previously reported, except *meta*-substitutent effect as shown in Scheme 5. When rhodium metal coordinates to the nitrogen of two different types of aldimines, the choice of aldimine by rhodium metal can be affected by the steric and electronic effects. In the case of the coordination of the rhodium metal to the nitrogen of the aldimine having *ortho*-alkyl group, the alkyl group, as an electron-donating group, stabilizes the intermediate. But, the one at the opposite side cannot receive help from the alkyl group. Moreover, *meta*-substitutent disturbs the approach of rhodium metal to the nitrogen of aldimine because of the steric hindrance between a substituent and a ligand like **B**. So the rhodium metal favors the nitrogen of the aldimine having *ortho*-alkyl group rather than the one at the other side to give the intermediate **A**. And then, the insertion of alkene into the Rh–H bond in **A** gives the linear alkyl rhodium intermediate **C** according to the anti-Markovnikov rule. The intermediate **C** gives the alkylated product **F** by reductive elimination. The intermediate **B** formed with difficult gives **H** as a minor product.

In conclusion, we have found that terephthaldialdimine **1a** reacted with alkenes to give 2,6-dialkylated products selectively in moderate to high isolated yields. In the case of terephthaldialdimine **1b** having a substituent at site 2 in the phenyl ring, the alkylation takes place selectively at site 6 in the phenyl ring. In this alkylation, a *meta*-substituent affected the reactivity significantly because of the steric hindrance.

References and notes

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13. Selected analytical data. Compound **4a**: ^{1}H NMR (600 MHz, $CDCl_3$) 10.59 (s, 1H, 1-C*H*O), 10.02 (s, 1H, 4-C*H*O), 7.58 (s, 2H, 3,5-Hs in Ar), 2.91–2.94 (m, 4H, α-CH_2 to Ar), 1.46–1.50 (m, 4H, β-CH_2 to Ar), 0.99 (s, 18H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) 193.36, 192.01, 146.92, 138.42, 136.90, 129.51, 46.89, 30.86, 29.19, 28.78; IR (KBr, neat, cm^{-1}) 2954 (s), 2905 (m), 2867 (m), 1696 (vs, C=O), 1571 (w), 1466 (m), 1365 (m), 1247 (w), 1186 (m), 876 (w), 809 (w), 755 (w); MS (*m*/*z*)

302 (8, M^+), 247 (6), 246 (38), 245 (40), 229 (21), 176 (12), 175 (11), 157 (10), 145 (11), 129 (13), 128 (13), 117 (15), 115 (23), 103 (11), 91 (20), 77 (12), 59 (17), 57 (100), 55 (10); HRMS found: 302.2243 (calcd for $C_{20}H_{30}O_2$ 302.2246). Compound **5a**: ^{1}H NMR (600 MHz, $CDCl_3$) 10.35 (s, 2H, C*H*O), 7.72 (s, 2H, 3,6-Hs in Ar), 2.99–3.03 (m, 4H, α-CH_2 to Ar), 1.46–1.50 (m, 4H, β-CH_2 to Ar), 1.00 (s, 18H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) 191.52, 144.00, 136.80, 133.04, 47.21, 30.88, 29.19, 27.30. Compound **3a**: ^{1}H NMR (300 MHz, $CDCl_3$) 10.35 (s, 1H, 1-C*H*O), 10.06 (s, 1H, 4-C*H*O), 7.97 (d, 1H, $J = 7.8$ Hz, 6-H in Ar), 7.82 (dd, 1H, $J = 7.8$ Hz, 1.5 Hz, 5-H in Ar), 7.77 (d, 1H, $J = 1.5$ Hz, 3-H in Ar), 3.03–3.10 (m, 2H, α-CH_2 to Ar), 1.01–1.54 (m, 2H, β-CH_2 to Ar), 1.02 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 191.58, 191.14, 147.06, 139.21, 137.28, 131.76, 131.33, 127.24, 47.18, 31.00, 29.27, 27.95; IR (KBr, neat, cm^{-1}) 2954 (m), 2865 (w), 1695 (vs, C=O), 1572 (w), 1466 (w), 1365 (w), 1191 (w), 809 (w), 790 (w); MS (*m*/*z*) 218 (M^+). Compound **4b**: ^{1}H NMR (300 MHz, $CDCl_3$) 10.59 (s, 1H, 1-C*H*O), 10.00 (s, 1H, 4-C*H*O), 7.58 (s, 2H, 3,5-Hs in Ar), 2.95 (t, 4H, $J = 7.8$ Hz, α-CH_2 to Ar), 1.50–1.63 (m, 4H, β-CH_2 to Ar), 1.41 (sextet, 4H, $J = 8.1$ Hz, γ-CH_2 to Ar), 0.94 (t, 6H, $J = 7.2$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 193.39, 191.82, 146.01, 137.96, 136.75, 129.41, 34.39, 33.11, 22.73, 13.96; IR (KBr, neat, cm^{-1}) 2958 (m), 2930 (m), 2872 (m), 1695 (vs, C=O), 1571 (w), 1456 (w), 1183 (m), 813 (w); MS (*m*/*z*) 246 (M^+). Compound **4c**: ^{1}H NMR (300 MHz, $CDCl_3$) 10.58 (s, 1H, 1-C*H*O), 10.00 (s, 1H, 4-C*H*O), 7.58 (s, 2H, 3,5-Hs in Ar), 2.91–2.97 (m, 4H, α-CH_2 to Ar), 1.52–1.64 (m, 4H, β-CH_2 to Ar), 1.30–1.39 (8H, γ,δ-CH_2 to Ar), 0.87–0.93 (6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 193.43, 191.89, 146.09, 137.98, 136.63, 129.44, 33.39, 32.01, 31.80, 22.54, 14.10; IR (KBr, neat, cm^{-1}) 2956 (m), 2929 (m), 2858 (m), 1695 (vs, C=O), 1571 (w), 1457 (w), 1380 (w), 1182 (w), 799 (w); MS (*m*/*z*) 274 (M^+). Compound **4d**: ^{1}H NMR (300 MHz, $CDCl_3$) 10.58 (s, 1H, 1-C*H*O), 10.00 (s, 1H, 4-C*H*O), 7.58 (s, 2H, 3,5-Hs in Ar), 2.94 (t, 4H, $J = 8.1$Hz, α-CH_2 to Ar), 1.61 (quintet, 4H, $J = 7.8$ Hz, β-CH_2 to Ar), 1.27–1.41 (12H, CH_2), 0.88 (t, 6H, $J = 6.6$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 193.38, 191.82, 146.06, 137.99, 136.76, 129.40, 33.42, 32.26, 31.62, 29.30, 22.62, 14.13; IR (KBr, neat, cm^{-1}) 2956 (m), 2928 (s), 2856 (m), 1696 (vs, C=O), 1571 (w), 1457 (w), 1380 (w), 1185 (w); MS (*m*/*z*) 302 (M^+). Compound **4e**: ^{1}H NMR (300 MHz, $CDCl_3$) 10.58 (s, 1H, 1-C*H*O), 9.99 (s, 1H, 4-C*H*O), 7.58 (s, 2H, 3,5-Hs in Ar), 2.91–2.98 (m, 4H, α-CH_2 to Ar), 1.67 (septet, 2H, J 6.6 Hz, C*H*Me_2), 1.47–1.56 (m, 4H, β-CH_2 to Ar), 0.97 (d, 12H, J 6.6 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 193.14, 191.67, 146.28, 138.08, 136.59, 129.25, 41.51, 31.31, 28.28, 22.45; IR (KBr, neat, cm^{-1}) 2956 (s), 2870 (m), 1696 (vs, C=O), 1571 (w), 1467 (m), 1383 (m), 1367 (m), 1183 (m), 879 (w), 806 (w), 757 (w); MS (*m*/*z*) 274 (M^+).