

Pd(OAc)₂-Catalyzed Isomerization of Acetates of the Baylis-Hillman Adducts

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Since the pioneering work of Baylis and Hillman¹ the 1,4-diazabicyclo[2.2.2]octane (DABCO)-catalyzed coupling of aldehydes with activated alkenes to give allylic alcohols is largely employed² and continues to stimulate research due to its immense synthetic potential. Among them, stereoselective isomerization of acetates of the Baylis-Hillman adducts catalyzed by trimethylsilyl trifluoromethanesulfonate,³ trifluoroacetic acid,⁴ benzyltrimethylammonium fluoride,⁵ DABCO⁶ and montmorillonite K10 clay⁷ has appeared in the literature. As a part of our research program aimed at the development of the Baylis-Hillman reaction, particularly for the construction of heterocycles,⁸ we decided to investigate the Pd(OAc)₂-catalyzed stereoselective isomerization of the acetates of the Baylis-Hillman adducts.

The palladium-catalyzed rearrangement of allylic esters is known and explained by the coordination of alkene to PdX₂ to give the cyclic intermediate. The intermediate can reverse the oxypalladation in either direction and the product is whichever allylic acetate has the more substituted alkene as shown in Scheme 1.⁹

Our results are summarized in the Table 1.¹⁰ In general, the yields are moderate to excellent ranging from 65 to 83%. The following procedure for converting **1** into **2** is representative: the mixture of acetate **1c** (560 mg, 2.08 mmol), triethylamine (630 mg, 6.24 mmol) and the catalyst system comprising palladium acetate (23 mg, 5 mol%) and triphenylphosphine (109 mg, 20 mol%) was stirred in acetonitrile (15 mL) under nitrogen at 80 °C. After 1 hour, the reaction mixture was diluted with brine and extracted with ether. The ethereal solution was washed twice with brine, dried and the solvent was evaporated. Flash chromatography of the residue gave 464 mg of **2c** (83% yield).

Concerning the stereoselectivity of the isomerization of representative methyl 3-acetoxy-3-aryl-2-methylenepropanoates **1a-g**, methyl 2-(acetoxymethyl)-3-arylprop-2-enotes **2a-g** were obtained in 100% (*E*)-stereoselectivity as evi-

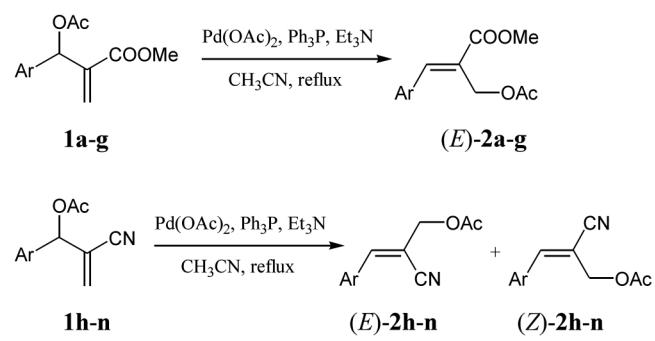
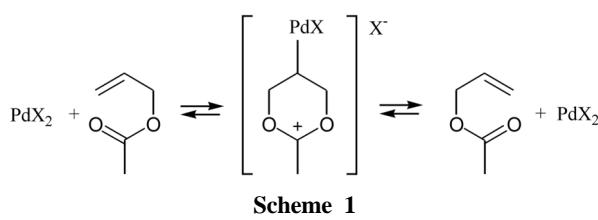
Table 1. Pd(OAc)₂-Catalyzed Isomerization of Acetates of the Baylis-Hillman Adducts

Substrate	Ar	Product	Time (h)	Yield ^a (%)
1a	C ₆ H ₅	2a ³	3	73
1b	2-ClC ₆ H ₄	2b	1	81
1c	4-ClC ₆ H ₄	2c ³	1	83
1d	2-BrC ₆ H ₄	2d	1	79
1e	2-IC ₆ H ₄	2e	1	78
1f	2-NO ₂ C ₆ H ₄	2f	2	65
1g	2-CH ₃ C ₆ H ₄	2g ³	1	80
1h	C ₆ H ₅	2h ³	2	75
1i	2-ClC ₆ H ₄	2i	1	62 (10)
1j	4-ClC ₆ H ₄	2j ³	2	76 (7)
1k	2-BrC ₆ H ₄	2k	1	65 (12)
1l	2-IC ₆ H ₄	2l	1	61 (14)
1m	2-NO ₂ C ₆ H ₄	2m	2	61 (10)
1n	2-CH ₃ C ₆ H ₄	2n ³	1	58 (12)

^aIsolated yield. Values in parentheses are those for (*Z*)-isomer.

denced by the ¹H and ¹³C NMR spectral analyses compared with those of the known compounds.³ On the other hand, 3-acetoxy-3-aryl-2-methylenepropanenitriles **1h-n** gave a mixture of (*E*)- and (*Z*)-2-(acetoxymethyl)-3-arylprop-2-enenitriles **2h-n**, and (*E*)-compounds having the aryl group *cis* to the nitrile group were obtained as major products. The assignment of the (*E*)- and (*Z*)-stereochemistry was based on the ¹H NMR and ¹³C NMR chemical shift values of the allylic methylene carbon (*e.g.* for **2i**, 64.45 vs. 59.53) in comparison with the published ones.³

A possible explanation for the reversal of stereochemical directive effects of the nitrile group with respect to the ester group is that the products are those of thermodynamic



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control in all these cases.³ That is, the more sterically demanding ester group requires a particular conformation for optimal conjugation compared to the slim cyano group with local cylindrical symmetry. Thus, the molecules **1** with ester group provide trisubstituted alkenes **2** having the aryl group *trans* to the ester group, whereas those with nitrile group produce trisubstituted alkenes **2** having the aryl group *cis* to the nitrile group exclusively (Scheme 2).

In conclusion, we have stereoselectively transformed acetates of the Baylis-Hillman adducts under the catalytic influence of Pd(OAc)₂ into thermodynamically stable trisubstituted alkenes.

Reference and Notes

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10. Spectroscopic data of new compounds **2** are as follows.
- Compound **2b**: oil; IR (neat) 1741, 1724, 1636 cm⁻¹; ¹H NMR (CDCl₃) δ 2.08 (s, 3H), 3.87 (s, 3H), 4.85 (s, 2H), 7.28-7.45 (m, 4H), 8.06 (s, 1H); ¹³C NMR (CDCl₃) δ 20.85, 52.37, 59.29, 126.81, 128.57, 129.68, 130.14, 130.52, 132.86, 134.19, 142.12, 166.65, 170.49.
- Compound **2d**: oil; IR (neat) 1740, 1724, 1638 cm⁻¹; ¹H NMR (CDCl₃) δ 2.08 (s, 3H), 3.87 (s, 3H), 4.83 (s, 2H), 7.23-7.40 (m, 3H), 7.62-7.65 (m, 1H), 7.99 (s, 1H); ¹³C NMR (CDCl₃) δ 20.87, 52.41, 59.27, 124.08, 127.40, 128.37, 130.20, 130.61, 132.83, 134.78, 144.23, 166.65, 170.49.
- Compound **2e**: mp 65-66 °C; IR (KBr) 1736, 1704, 1627 cm⁻¹; ¹H NMR (CDCl₃) δ 2.07 (s, 3H), 3.88 (s, 3H), 4.80 (s, 2H), 7.04-7.41 (m, 3H), 7.87 (s, 1H), 7.89-7.92 (m, 1H); ¹³C NMR (CDCl₃) δ 20.78, 52.36, 59.13, 99.06, 127.91, 128.15, 129.49, 130.41, 138.32, 139.15, 147.98, 166.53, 170.38.
- Compound **2f**: mp 92-94 °C; IR (KBr) 1719, 1616 cm⁻¹; ¹H NMR (CDCl₃) δ 2.02 (s, 3H), 3.88 (s, 3H), 4.73 (s, 2H), 7.34-7.71 (m, 3H), 8.20-8.22 (m, 1H), 8.23 (s, 1H); ¹³C NMR (CDCl₃) δ 20.79, 52.49, 58.99, 125.06, 128.12, 129.89, 130.59, 130.85, 133.83, 142.16, 147.34, 166.23, 170.37.
- Compound **2i**: (*E*)-isomer; oil; IR (neat) 2219, 1747, 1626 cm⁻¹; ¹H NMR (CDCl₃) δ 2.16 (s, 3H), 4.86 (s, 2H), 7.33-7.46 (m, 3H), 7.59 (s, 1H), 7.99-8.02 (m, 1H); ¹³C NMR (CDCl₃) δ 20.55, 64.45, 109.17, 116.27, 127.11, 129.05, 129.72, 130.81, 131.71, 134.31, 143.15, 169.95. (*Z*)-isomer: oil; IR (neat) 2222, 1747, 1625 cm⁻¹; ¹H NMR (CDCl₃) δ 2.15 (s, 3H), 4.77 (s, 2H), 7.23-7.49 (m, 4H), 7.60 (s, 1H); ¹³C NMR (CDCl₃) δ 20.58, 59.53, 112.39, 117.70, 126.96, 130.08, 131.07, 131.35, 131.74, 134.01, 144.99, 170.09.
- Compound **2j**: (*Z*)-isomer; oil; IR (neat) 2219, 1750, 1630 cm⁻¹; ¹H NMR (CDCl₃) δ 2.17 (s, 3H), 4.85 (s, 2H), 7.25 (d, 2H, *J* = 8.3 Hz), 7.27 (s, 1H), 7.43 (d, 2H, *J* = 8.3 Hz); ¹³C NMR (CDCl₃) δ 20.95, 59.74, 111.38, 118.44, 129.62, 130.89, 131.44, 136.95, 146.89, 170.50.
- Compound **2k**: (*E*)-isomer; oil; IR (neat) 2220, 1746, 1627 cm⁻¹; ¹H NMR (CDCl₃) δ 2.18 (s, 3H), 4.85 (s, 2H), 7.27-7.44 (m, 2H), 7.54 (s, 1H), 7.63-7.66 (m, 1H), 7.95-7.97 (m, 1H); ¹³C NMR (CDCl₃) δ 20.56, 64.32, 109.30, 116.19, 124.46, 127.72, 129.36, 131.78, 132.61, 133.01, 145.67, 169.98. (*Z*)-isomer: oil; IR (neat) 2222, 1748, 1630 cm⁻¹; ¹H NMR (CDCl₃) δ 2.14 (s, 3H), 4.75 (s, 2H), 7.22-7.38 (m, 3H), 7.54 (s, 1H), 7.64-7.67 (m, 1H); ¹³C NMR (CDCl₃) δ 20.62, 59.54, 112.21, 117.70, 123.83, 127.58, 130.16, 131.46, 132.96, 133.23, 147.16, 170.15.
- Compound **2l**: (*E*)-isomer; oil; IR (neat) 2220, 1746, 1626 cm⁻¹; ¹H NMR (CDCl₃) δ 2.18 (s, 3H), 4.85 (s, 2H), 7.09-7.14 (m, 1H), 7.38 (s, 1H), 7.42-7.47 (m, 1H), 7.86-7.93 (m, 2H); ¹³C NMR (CDCl₃) δ 20.67, 64.15, 99.94, 109.35, 116.12, 128.60, 129.11, 131.73, 136.04, 139.56, 150.15, 170.04. (*Z*)-isomer: oil; IR (neat) 2221, 1746, 1625 cm⁻¹; ¹H NMR (CDCl₃) δ 2.15 (s, 3H), 4.72 (s, 2H), 7.09-7.23 (m, 2H), 7.38-7.42 (m, 1H), 7.43 (s, 1H), 7.92-7.95 (m, 1H); ¹³C NMR (CDCl₃) δ 20.62, 59.47, 98.69, 111.86, 117.63, 128.44, 129.63, 131.24, 136.53, 139.65, 151.00, 170.15.
- Compound **2m**: (*E*)-isomer; oil; IR (neat) 2222, 1746, 1638, 1617 cm⁻¹; ¹H NMR (CDCl₃) δ 2.19 (s, 3H), 4.88 (s, 2H), 7.62-7.82 (m, 3H), 7.80 (s, 1H), 8.23-8.25 (m, 1H); ¹³C NMR (CDCl₃) δ 20.61, 63.66, 111.07, 115.69, 125.18, 128.90, 130.79, 130.96, 134.26, 143.99, 146.95, 170.01. (*Z*)-isomer: oil; IR (neat) 2224, 1746, 1638, 1617 cm⁻¹; ¹H NMR (CDCl₃) δ 2.12 (s, 3H), 4.64 (s, 2H), 7.36-7.76 (m, 3H), 7.85 (s, 1H), 8.27-8.30 (d, 1H, *J* = 7.8 Hz); ¹³C NMR (CDCl₃) δ 20.54, 59.41, 111.83, 117.31, 125.50, 128.37, 130.74, 130.86, 134.09, 145.52, 146.79, 170.06.
- Compound **2n**: (*Z*)-isomer; oil; IR (neat) 2221, 1747, 1626 cm⁻¹; ¹H NMR (CDCl₃) δ 2.14 (s, 3H), 2.31 (s, 3H), 4.77 (s, 2H), 7.08-7.35 (m, 4H), 7.59 (s, 1H); ¹³C NMR (CDCl₃) δ 19.72, 20.53, 59.55, 110.99, 118.12, 126.00, 128.62, 130.17, 130.50, 131.68, 136.91, 147.44, 170.05.