$Pd(OAc)_2$-Catalyzed Isomerization of Acetates of the Baylis-Hillman Adducts

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Since the pioneering work of Baylis and Hillman[1] the 1,4-diazabicyclo[2.2.2]octane (DABCO)-catalyzed coupling of aldehydes with activated alkenes to give allylic alcohols is largely employed[2] 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] DABCO[6] and montmorillonite K10 clay[7] 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 PdX_2 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).

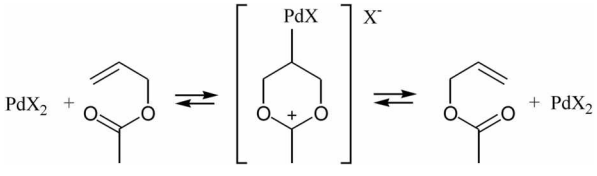
Concerning the stereoselectivity of the isomerzation of representative methyl 3-acetoxy-3-aryl-2-methylenepropanoates **1a-g**, methyl 2-(acetoxymethyl)-3-arylprop-2-enoates **2a-g** were obtained in 100% (*E*)-stereoselectivity as evidenced by the ^1H and ^{13}C NMR spectral analyses compared with those of the known compounds.[3] On the other hand, 3-acetoxy-3-aryl-2-methylenepropanenitriles **1h-n** gave a mixture of (2*E*)- and (2*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 ^{13}C 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

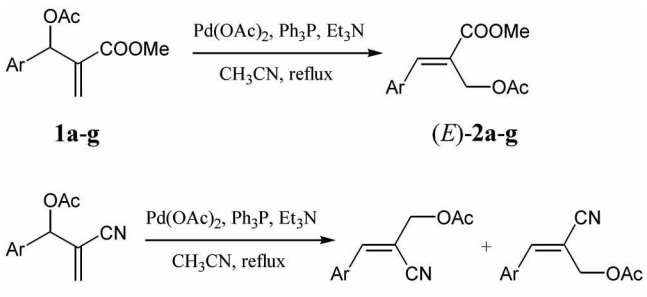
Table 1. $Pd(OAc)_2$-Catalyzed Isomerization of Acetates of the Baylis-Hillman Adducts

Substrate	Ar		Product	Time (h)	Yield[a] (%)
1a	C_6H_5	COOMe	**2a**[3]	3	73
1b	2-ClC_6H_4	COOMe	**2b**	1	81
1c	4-ClC_6H_4	COOMe	**2c**[3]	1	83
1d	2-BrC_6H_4	COOMe	**2d**	1	79
1e	2-IC_6H_4	COOMe	**2e**	1	78
1f	2-$NO_2C_6H_4$	COOMe	**2f**	2	65
1g	2-$CH_3C_6H_4$	COOMe	**2g**[3]	1	80
1h	C_6H_5	CN	**2h**[3]	2	75
1i	2-ClC_6H_4	CN	**2i**	1	62 (10)
1j	4-ClC_6H_4	CN	**2j**[3]	2	76 (7)
1k	2-BrC_6H_4	CN	**2k**	1	65 (12)
1l	2-IC_6H_4	CN	**2l**	1	61 (14)
1m	2-$NO_2C_6H_4$	CN	**2m**	2	61 (10)
1n	2-$CH_3C_6H_4$	CN	**2n**[3]	1	58 (12)

[a]Isolated yield. Values in parentheses are those for (*Z*)-isomer.



Scheme 1



Scheme 2

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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.

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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 ($CDCl_3$) δ 2.08 (s, 3H), 3.87 (s, 3H), 4.85 (s, 2H), 7.28-7.45 (m, 4H), 8.06 (s, 1H); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) δ 2.15 (s, 3H), 4.77 (s, 2H), 7.23-7.49 (m, 4H), 7.60 (s, 1H); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 ($CDCl_3$) δ 2.14 (s, 3H), 2.31 (s, 3H), 4.77 (s, 2H), 7.08-7.35 (m, 4H), 7.59 (s, 1H); ^{13}C NMR ($CDCl_3$) 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.