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ALLYLIC GEMINAL DIACETATES. UNUSUAL CARBONYL SUBSTITUTES VIA METAL CATALYZED REACTIONS

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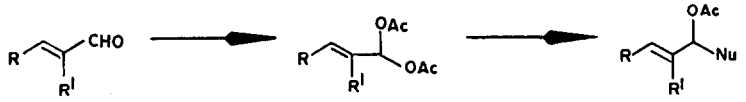
Summary. Palladium catalysis facilitates replacement of an acetoxy group of an allylic geminal diacetate by stabilized nucleophiles.

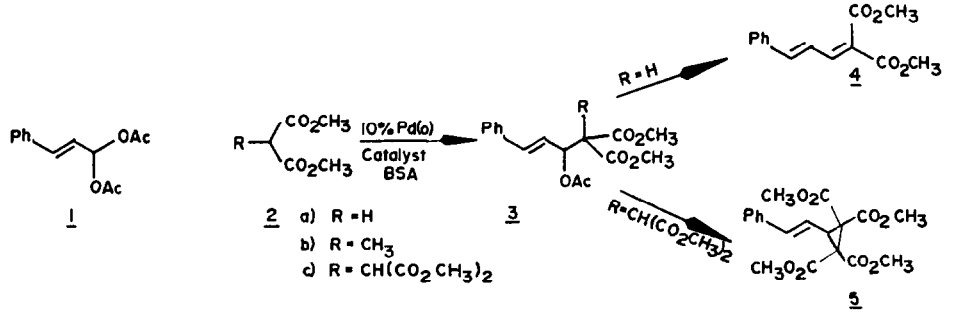
While carbonyl groups condense smoothly with reactive anions, stabilized anions add reversibly and the equilibrium frequently lies towards the starting materials. The availability of allylic geminal diacetates from carbonyl compounds[1] suggested the feasibility of effecting an irreversible



(1)

addition based upon the notion that a low valent metal[2] could selectively catalyze the replacement of one (or both) allylic acetate(s) according to eq. 1. A recent report suggesting that the anion of malonic ester cannot be used in a palladium catalyzed allylic alkylation of such allylic geminal acetates[3] prompts our disclosing our independent results.

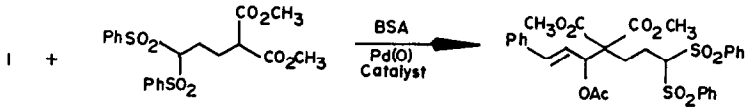
The geminal diacetate from cinnamaldehyde 1[2] was employed as a model system. The Pd(0) catalyst (10 mol%) was conveniently generated *in situ* from palladium acetate using 1-hexene as the reductant in the presence of 5 eq. of triphenylphosphine. Refluxing a THF solution of 1 and 2a using BSA[4] as base in the presence of 10% Pd(0) catalyst led directly to 4 in 93%



(2)

yield, presumably through the intermediacy of 3a. By employing a methylated malonate 2b to preclude elimination, 3b[5] was isolated in 85% yield. By using 2.5 mol% $(dba)_3Pd_2 \cdot CHCl_3$ and dppe[4] as catalyst, the alkylated product 3b was obtained in 91% after 3h at 42° instead of 18h at reflux.

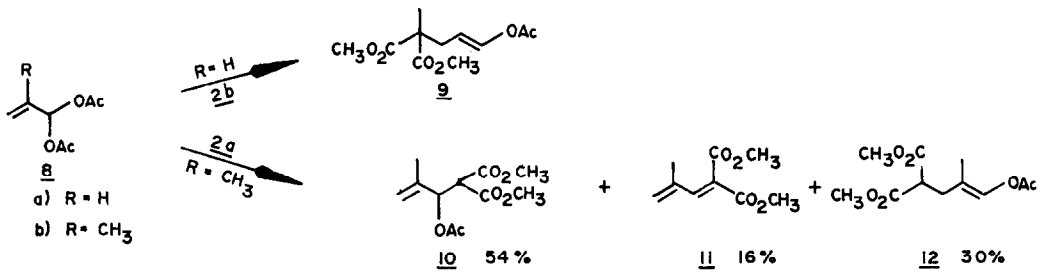
The fact that an allylic acetate remains in the product suggested the possibility of a second palladium catalyzed alkylation reaction. However, using 2 eq. of 2b still only produced 3b in 90% yield. On the other hand, subjecting the initial alkylation product 3c derived from the dimalonate 2c[6] and 1 to 5 mol% of a $(dppe)_2Pd$ catalyst generated in situ as above in dioxane at 70-85° gave a 65% yield of the cyclopropane 5[5] in addition to 35% recovery of starting material. Using these latter conditions, 1 and 2c gave the cyclopropane 5 directly in 70% yield (100% based upon recovered starting material). Interestingly, alkylation of 1 with the bifunctional



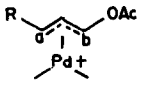
6 7

alkylating conjunctive reagent 6 led chemoselectively to attack alpha to the esters rather than the sulfone to give 7.[5]

With the geminal acetate from acrolein 8a, alkylation with dimethyl methylmalonate occurred at the less substituted carbon to give 9 (70% yield) rather than alpha to oxygen as with 1. On the other hand,



decreasing the steric hindrance of the attacking nucleophile reorients attack back to the carbon bearing oxygen (10 + 11 : 12 70:30, 90% yield). These results indicate an electronic bias to attack the intermediate 13 at site "b" when steric factors do not dominate. This electronic bias contrasts with that found for alkylations proceeding through 14 which has an electronic bias for nucleophiles to attack distal to the oxygen substituent (i.e. at site "a").[7] Such a reactivity pattern directly mirrors the effect of oxygen substituents on the reactivity of alkyl halides.



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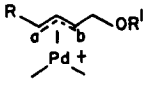

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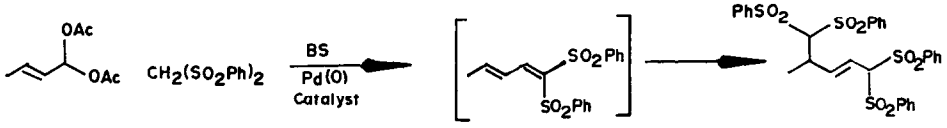
bis-(Phenylsulfonyl)methane also served as a nucleophile in these alkylations using the standard conditions as shown in eq. 3. As in the case of dimethyl malonate, the initial product eliminates the elements of



(3)

15 16

acetic acid under the reaction conditions to give 15. However, the fact that this bis-sulfone is an excellent Michael donor leads to the product of Michael addition to 15, i.e. 16, as the observed one (57%).

Control experiments established the inability of these weak nucleophiles to condense with the carbonyl group of the conjugated aldehydes. Thus, these geminal diacetates serve as "activated" forms of the carbonyl group. The previously reported failure except for anions derived from acylmalonates is not consistent with our results. At present we have no explanation for the discrepancy.

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4. BSA = O,N-bis(trimethylsilyl)acetamide. dppe = 1,2-bis(diphenylphosphine) ethane.

5. 3b Kugelrohr distillation at 170-5°@ 0.5 mm Hg. ^{1}H Nmr ($CDCl_3$): δ 7.38-7.24, m, 5H; 6.66, d, J = 14.8 Hz, 1H; 6.19, dd, J = 14.8, 7.2 Hz, 1H; 6.11, d, J = 7.2 Hz, 1H; 4.26-4.15, m, 4H; 2.07, s, 3H; 1.53, s, 3H; 1.28-1.21, m, 6H.
^{13}C Nmr: δ 168.8, 168.5, 135.6, 134.4, 128.0, 127.6, 126.2, 122.5, 74.5, 61.3, 57.6, 20.7, 15.8, 13.8. Ir (CH_2Cl_2): 1740 cm^{-1}.
5: Mp 118° (ether). ^{1}H Nmr: δ 7.42-7.21, m, 5H; 6.83, d, J = 16 Hz, 1H; 6.35, dd, J = 16, 10 Hz, 1H; 3.80, s, 12H; 3.26, d, J = 10 Hz, 1H.
^{13}C Nmr: δ 165.8, 164.1, 136.1, 128.1, 127.5, 126.1, 119.3, 53.2, 52.9, 45.0, 39.2. Ir ($CHCl_3$): 1730 cm^{-1}.
7: ^{1}H Nmr: δ 7.98-7.88, m, 4H; 7.71-7.26, m, 11H; 6.66, d, J = 15.3 Hz, 1H; 6.19, dd, J = 15.3, 8 Hz, 1H; 6.03, d, J = 8 Hz, 1H; 4.37, m, 1H; 3.73, s, 3H; 3.72, s, 3H; 2.36, m, 4H; 2.06, s, 3H.
IR ($CHCl_3$): 1740 cm^{-1}.
9: ^{1}H Nmr: δ 7.10, d, J = 12.4 Hz, 1H; 5.32, dt, J = 12.4, 8.1 Hz, 1H; 3.73, s, 6H; 2.55, d, J = 8.1 Hz, 2H; 2.10, s, 3H; 1.40, s, 3H.
^{13}C Nmr: δ 171.3, 167.0, 137.7, 108.2, 53.5, 52.1, 33.6, 20.3, 19.6
Ir ($CHCl_3$): 1760-1735, 1675 cm^{-1}.
16: ^{1}H Nmr: δ 8.00-7.49, m, 20H; 6.19, dd, J = 15.8 Hz, 1H; 5.55, ddd, J = 15, 10.5, 1 Hz, 1H; 4.90, d, J = 10.5 Hz, 1H; 4.40, d, J = 1.5 Hz, 1H; 3.32, m, 1H; 1.20, d, J = 7 Hz, 3H.
Ir ($CHCl_3$): 1580, 1320, 1140 cm^{-1}.

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