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COMPLETE REVERSAL OF REGIOCHEMISTRY IN CYCLIC ACYLPALLADATION. NOVEL SYNTHESIS OF QUINONES.[1]

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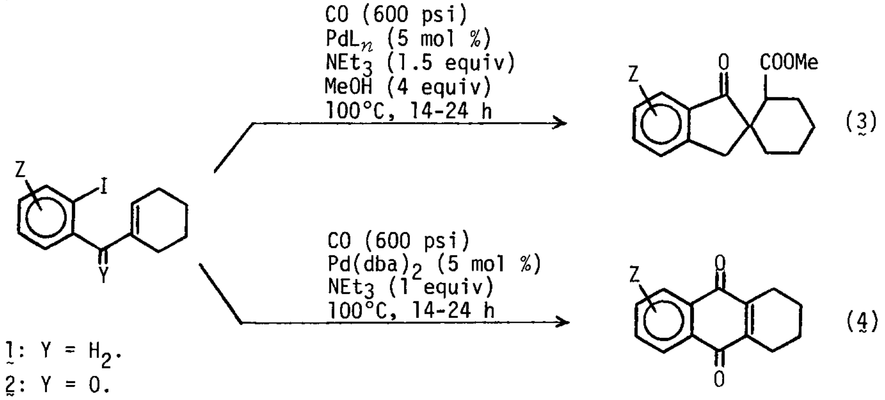
SUMMARY: Treatment of *o*-iodoaryl alkenyl ketones with CO (600 psi) in CH_3CN in the presence of 5 mol % of $Pd(dba)_2$ and 1 equiv of NEt_3 can give bicyclic and polycyclic quinones in high yields via acylpalladation in an "endo" mode, which appears to be totally regiospecific.

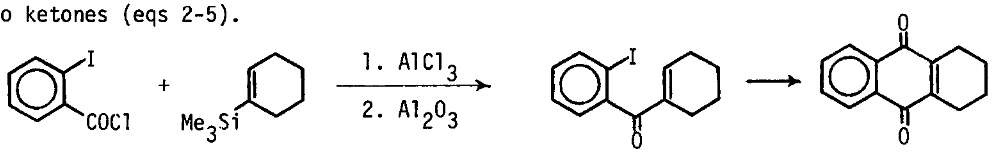
We recently reported a Pd-catalyzed regiospecific cyclic acylpalladation reaction proceeding exclusively in an "exo" mode,[3] e.g., 1→3 in eq 1. In view of the significance of strictly regiospecific synthesis of bicyclic and polycyclic quinones,[4] we hoped to be able to reverse the regiochemistry of acylpalladation. We now report that the use of ketones 2 and Pd complexes which do not contain phosphines, e.g., $Pd(dba)_2$, where dba = dibenzylideneacetone, completely reverses the regiochemistry of cyclic acylpalladation from "exo" to "endo", thereby providing a potentially regioselective synthesis of bicyclic and polycyclic quinones, e.g., 2→4 in eq 1. Some addition reactions of acylmetallates with α,β-unsaturated carbonyl compounds are known.[5] However no cyclic versions of these reactions have been reported.



(1)

1: Y = H_2.
2: Y = O.
Z = substituent.

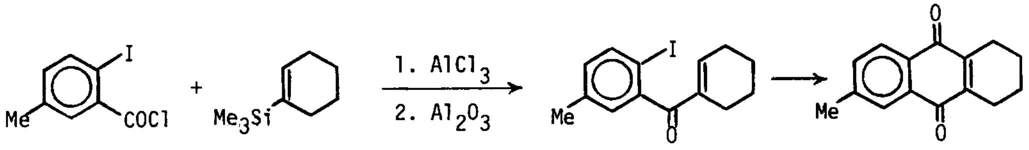
The following synthesis of 2,6-dimethyl-5,7,8-trihydro-9,10-anthraquinone (5) is representative. To a glass vial containing a magnetic stirring bar were sequentially added *o*-iodo-*m*-tolyl 4-methylcyclohexen-1-yl ketone (0.36 g, 1.0 mmol) in benzene (2 mL) and CH_3CN (2 mL), triethylamine (0.11 g, 1.0 mmol), and $Pd(dba)_2$ (0.029 g, 0.05 mmol). The vial was placed in a stainless steal autoclave.[6] The autoclave was charged with CO (600 psi) and heated to 100°C for 24 h with stirring. The reaction mixture was poured into a mixture of water and ether. After the usual extractive workup, chromatography (silica gel, 50% CH_2Cl_2 in hexane) provided 0.19 g (81% yield) of 5: mp 115-118°C; IR (Nujol) 1650 (s), 1580 (s), cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) 1.08 (d, J = 6 Hz, 3 H), 1.7-2.9 (m with a peak at 2.43, 10 H), 7.3-7.5 (m, 1 H), 7.7-7.9 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) 21.49, 21.70, 23.34, 27.51, 29.39, 31.29, 126.25 (2 carbons), 129.92, 132.00, 133.82 (2 carbons), 144.06 (2 carbons), 184.36, 184.72. High Resolution MS Calcd for $C_{16}H_{16}O_2$: 240.1151. Found: 240.1158. In this manner 4a, 4b, 5, and 6 were prepared in the yields indicated in parentheses from the corresponding iodo ketones (eqs 2-5).



(2)

2a

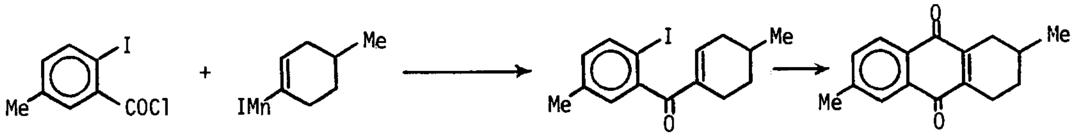
4a[7] (93%)



(3)

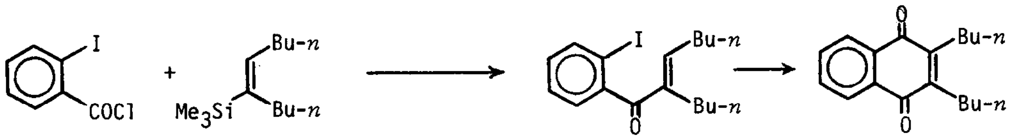
2b

4b[7] (92%)



(4)

5 (81%)

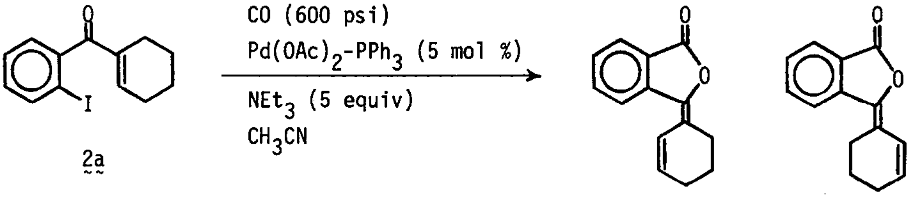


(5)

6 (95%)

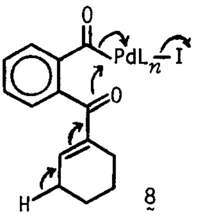
The starting compounds have been prepared by the reactions of *o*-iodoaroyl chlorides with either alkenylsilanes in the presence of $AlCl_3$[8] or alkenylmanganese iodides.[9] All of the products obtained above are homogeneous, and there was no indication for the formation of any other monomeric products by GLC and spectroscopic examinations. Since only one regioisomer is formed in the synthesis of 5, the acylpalladation reaction appears to be strictly regiospecific, although this point needs to be further clarified.

To observe a satisfactory acylpalladation reaction proceeding in a "endo" mode, it was necessary to avoid the following side reactions. The use of Pd-PPh_3 complexes as catalysts did not produce the desired quinones. Thus, for example, the reaction of 2a with CO (600 psi) in the presence of $Pd(OAc)_2$-PPh_3 (5 mol %) and NEt_3 (5 equiv) led to the formation of a ca. 1:1 mixture of 7a and 7b in 58% combined yield. It is likely that 7 was formed via NEt_3-induced cyclization of 8.



2a 7a 7b (6)

A recent study of the stoichiometric intramolecular addition of $ROOCPdL_n$ to alkenes and alkynes shows that 1.5 equiv of PPh_3 retards the reaction rate by a factor of 10 to 50.[10] A similar retardatory effect of PPh_3 on the acylpalladation step with 2a would provide a plausible explanation for the formation of 7. In the case of a β,β-disubstituted enone 9, even the reaction carried out under the conditions generally satisfactory for the preparation of quinones led to the formation of 10 in 68% yield.



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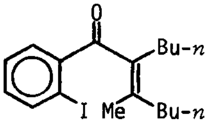

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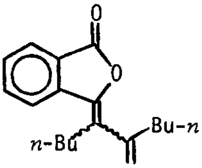

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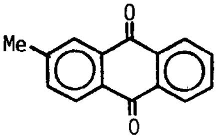

11

It also appears important to avoid an excess of NEt_3. When the amount of NEt_3 was increased from 1 to 3 equiv in the conversion of 2b into 4b (eq 1), a ca. 1:1 mixture of 4b and 11 was obtained in 79% combined yield. One limitation which has not been overcome is that the present reaction has failed to give quinone products in any detectable yields in cases where the starting enones are either α- or β-monosubstituted. This point is under current investigation.

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REFERENCES AND NOTES

(1) Metal-Promoted Cyclization. 13. Part 12: Negishi, E.; Zhang, Y.; Cederbaum, F. E.; Webb, M. B. *J. Am. Chem. Soc.,* submitted.

(2) Graduate Research Fellow supported by the IBM Corporation.

(3) Tour, J. M.; Negishi, E. *J. Am. Chem. Soc.* 1985, *107*, 8289.

(4) For example, recent methods for the synthesis of anthraquinones have been reviewed. Kelly, T. R., Ed. *Tetrahedron* 1984, *40*, 4537.

(5) (a) Corey, E. J.; Hegedus, L. S. *J. Am. Chem. Soc.* 1969, *91*, 4926. (b) Hegedus, L. S.; Perry, R. J. *J. Org. Chem.* 1985, *50*, 4955. (c) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* 1986, *27*, 1473.

(6) A 45-mL autoclave purchased from Parr Instrument Co., Moline, Ill, was used.

(7) Ditsent, V. E. *Zhur. Obshchei Khim.* 1959, *29*, 1370.

(8) Fleming, I.; Pearce, A. *J. Chem. Soc., Chem. Commun.* 1975, 633.

(9) Friour, G.; Cahiez, G.; Normant, J. F. *Synthesis* 1984, 37.

(10) Samsel, E. G.; Norton, J. R. *J. Am. Chem. Soc.* 1984, *106*, 5505.

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