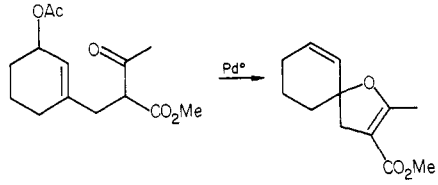
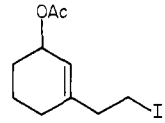
systems was unsuccessful. Utilization of a variety of Lewis acid and protic acid catalysts in conjunction with a number of palladium complexes also met with failure.

The spirofuran 12[10] was prepared in quantitative yield by treatment of the methyl acetoacetate monoanion alkylation product of 9 under the usual cyclization conditions.[11]



12

Attempted use of the homoallylic iodoacetate 13 in the



13

methyl acetoacetate dianion reaction resulted largely in the formation of the conjugated diene. As a result, a new route to the β-keto ester precursor of a spiro[5.5]undecene system was developed as shown in Scheme III. Pyridinium chlorochromate oxidation[21] of the previously prepared enone alcohol 14[8] yielded the aldehyde 15[10] (63%). Specific reduction of 15 to the allylic alcohol–aldehyde 16[10] was accomplished by the use of the $CeCl_3$–$NaBH_4$ reagent.[22] Preparation of the π-allyl precursor 17[10] was completed by pivalation (40%), Reformatsky reaction on the aldehyde with ethyl bromoacetate (85%), and Collins oxidation[23] (58%). Treatment of the sodium hydride generated anion of 17 with 10 mol % of $Pd(PPh_3)_4$ in toluene at 120 °C in a sealed tube (14 h) yielded only the C-alkylated β-keto ester 18[10] (67%). Use of the $Pd(diphos)_2$ catalyst in THF under similar conditions gave directly the decarboxylated spirocyclic ketone 19.[10] The more forcing conditions required for cyclization (relative to 10 → 11) are presumably due to the lower propensity of the pivalate (vs. acetate) to undergo oxidative addition and/or the inherent slower rate of six- relative to five-membered ring formation. Subjection of 10 to comparable reaction conditions did not provide C-alkylated material.

Pearson[1] has noted similar behavior in the iron diene catalyzed spirocyclization of β-keto esters, which he rationalized on the basis of Baldwin's rules (i.e., five O-alkylates, six C-alkylates). We believe that the inherent degree of reversibility in the cyclization (six membered ≫ five membered) is a more likely explanation.[24]

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(19) Trost, B. M.; Jungheim, L.; Runge, T. *J. Am. Chem. Soc.* **1980**, *102*, 2840.
(20) Tsuji, J.; Kobayashi, Y.; Kataoka, H.; Takahashi, T. *Tetrahedron Lett.* **1980**, 1475.
(21) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(22) Luche, J.; Gemal, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 5848.
(23) Smith, A. B.; Levenberg, P. A.; Jerris, P. J.; Scarborough, R. M.; Wovkulich, P. M.; *J. Am. Chem. Soc.* **1981**, *103*, 1501.
(24) We have noted in several other spirocycles the greater tendency of the six-membered ring analogues to open at the spiro center.
(25) White, J. D.; Ruppert, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 1808.

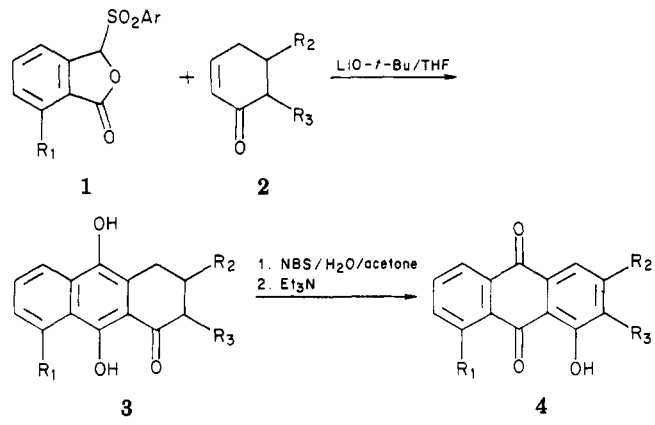
Novel Oxidative Transformation: Regiospecific Preparation of Naturally Occurring 1-Hydroxyanthraquinones

Summary: A brief reaction sequence for synthesis of the naturally occurring anthraquinones 1-hydroxyanthraquinone (**4a**), 1-hydroxy-2-methylanthraquinone (**4b**), pachybasin (**4c**), chrysophanol (**5a**), and rhein (**5c**) has been developed.

Sir: We have found that treatment of 9,10-dihydroxy-1,2,3,4-tetrahydroanthracen-1-ones (**3**) with *N*-bromosuccinimide (NBS) in acetone–water followed by quenching with triethylamine results in oxidative transformation to 1-hydroxyanthraquinones (**4**) in good yield. This finding has been employed to develop a general reaction sequence for preparation of the naturally occurring 1-hydroxyanthraquinones **4a–c**, chrysophanol (**5a**), and rhein (**5c**).

The intermediate tetrahydroanthracenones **3** were prepared by using the annelation methodology we developed earlier for regiospecific synthesis of polycyclic aromatic systems possessing a 1,4-dihydroxy aromatic fragment and an electron-withdrawing group at the 2-position.[1-3] Analogous condensations of the anion[4] of sulfones 1[1,5] with

Scheme I[a]



[a] a, $R_1 = R_2 = R_3 = H$; b, $R_1 = R_2 = H$, $R_3 = CH_3$; c, $R_1 = R_3 = H$, $R_2 = CH_3$; d, $R_1 = OCH_3$, $R_2 = CH_3$, $R_3 = H$; e, $R_1 = OCH_3$, $R_2 = CO_2CH_3$, $R_3 = H$.

(1) Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1978**, *43*, 178.
(2) For the use of this reaction in natural products synthesis and related studies, see: Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1980**, *45*, 3061. Hauser, F. M.; Combs, D. W. *Ibid.* 4071. Hauser, F. M.; Prasanna, S. *Ibid.* **1979**, *44*, 2596. Hauser, F. M.; Prasanna, S. *J. Am. Chem. Soc.* **1981**, *103*, 6378. Russell, R. A.; Warrener, R. N. *J. Chem. Soc., Chem. Commun.* **1981**, 108.
(3) For related ring annelations see: Kraus, G. A.; Sugimoto, H. *Tetrahedron Lett.* **1978**, 2263. Wildeman, J.; Bergen, P. C.; Pluim, H.; Rouwette, P.; VanLeusen, A. M. *Ibid.* **1978**, 2213.
(4) Lithium *tert*-butoxide, used as a base in the reaction, was obtained by adding *n*-butyllithium (3.02 equiv) to a solution of *tert*-butanol (3.2 equiv) in dry THF at 0 °C.
(5) Hauser, F. M.; Rhee, R. P.; Prasanna, S.; Weinreb, S. M.; Dodd, J. H. *Synthesis* **1980**, 72.

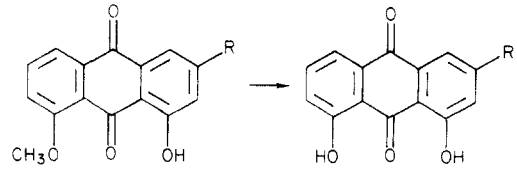
0022-3263/82/1947-0383$01.25/0

Table I. Yields and Melting Points of Tetrahydroanthracen-1-ones 3a-e and Hydroxyanthraquinones 4a-e

R_1	R_2	R_3	compd	% yield	mp, °C	compd	% yield	mp, °C
H	H	H	3a	82	167-168	4a	84	195-196 [a]
H	H	CH_3	3b	88	166-168	4b	65	183-184 [b]
H	CH_3	H	3c	81	168-169	4c	72	177-178 [c]
OCH_3	CH_3	H	3d	80	178-180	4d	68	197 [d]
OCH_3	CO_2CH_3	H	3e	85	188-190	4e	86	224-225 [e]

[a] Lit.[9a] mp 194-195 °C. [b] Lit.[9b] mp 185-186 °C. [c] Lit.[10] mp 176-177 °C. [d] Lit.[12] mp 198 °C. This product was demethylated[8] to chrysophanol: 93%; mp 195-196 °C (lit.[10] mp 194-195 °C. [e] This product on demethylation[8] yielded the methyl ester of rhein: 94%; mp 177-178 °C (lit.[11] mp 174 °C). Saponification of the methyl ester (10% NaOH, THF, 30 min) yielded rhein: 96%; mp 319-321 °C (lit.[11] mp 318-319 °C).

the unsubstituted and 5- and 6-substituted 2-cyclohexen-1-ones **2**[6] produced the tetrahydroanthracenones **3a-e** in high yield (Table I, Scheme I). Cold (0 °C), stirred solutions of anthracenones **3** were reacted with *N*-bromosuccinimide (3.3 equiv) added in small portions. The reaction mixture was allowed to come to room temperature over 1 h and was then quenched with excess triethylamine to yield the anthraquinones **4** (Table I). Direct preparations of the naturally occurring anthraquinones 1-hydroxyanthraquinone (**4a**), 1-hydroxy-2-methylanthraquinone (**4b**), and pachybasin (**4c**) were thus achieved. Final transformation of **4d** to chrysophanol (**5a**) was accomplished by demethylation with boron tribromide.[8] Demethylation (BBr_3) of **4e** gave ester **5b** which was subsequently hydrolyzed (10% NaOH/THF) to yield rhein (**5c**).



4d, R = CH_3
e, R = CO_2CH_3

5a, R = CH_3
b, R = CO_2CH_3
c, R = CO_2H

The detailed mechanism for the oxidative transformation of **3** to anthraquinones **4** is yet to be finalized. In preliminary work on the reaction, we noted that addition of a small amount of *N*-bromosuccinimide to a solution of **3a** produced a deep red color which rapidly faded to give a light yellow solution. Additional quantities of *N*-bromosuccinimide furnished a lasting red solution. Analysis of a thin-layer chromatogram (silica gel) of the reaction mixture, following complete addition of the NBS, showed total disappearance of the starting material and the production of an intermediate. Workup at this stage yielded a dark residue which decomposed to furnish a mixture which included the hydroxyanthraquinone and the starting hydroquinone. Immediate application of the workup residue to a chromatography column (silica gel) enhanced formation of the hydroxyanthraquinone and implied that either an acid or a base was required for completion of the reaction. Addition of acid ($HClO_4$) had little influence on the product composition; however, addition of triethylamine produced the hydroxyanthraquinone from the intermediate in good yields.

Further work to delineate the mechanism of the reaction and the structure of the intermediate and to extend this approach to more complex systems is in progress.

Acknowledgment. The work was generously supported by the National Cancer Institute of the National Institutes of Health (Grant No. CA 18141).

(6) Literature procedures were employed to prepare the 5- and 6-substituted 2-cyclohexen-1-ones. (a) 5-Methyl-2-cyclohexen-1-one: Blanchard, J. P.; Goering, H. L. *J. Am. Chem. Soc.* **1951**, *73*, 5863. (b) 6-Methyl-2-cyclohexen-1-one: Stotter, P. L; Hill, K. A. *J. Org. Chem.* **1973**, *38*, 2576. (c) 5-(Carbomethoxy)-2-cyclohexen-1-one: Hauser, F. M.; Prasanna, S. *Ibid.* **1979**, *44*, 2596.

(7) The tetrahydroanthracenones **3** and anthraquinones **4** and **5** were characterized through ^1H NMR and mass spectral analyses. Combustion analyses were obtained for **3a-e**.

(8) The demethylation was carried out by treating a cold (−78 °C) solution of the methyl ether (1 equiv) in methylene chloride with boron tribromide (2 equiv) and stirring the reaction mixture under nitrogen for 7 h at −50 °C.

(9) For a comprehensive list of naturally occurring anthraquinones see: (a) Thompson, R. H. "Naturally Occurring Quinones", 2nd ed.; Academic Press: London and New York, 1971; Chapter 5, 369. (b) *Ibid.*, p 370.

(10) Slater, G. P.; Haskins, R. H.; Hogge, L. R.; Nesbitt, L. R. *Can. J. Chem.* **1967**, *45*, 92.

(11) Nawa, H.; Uchibayashi, M.; Matsuoka, T. *J. Org. Chem.* **1961**, *26*, 979.

(12) Wagner, H.; Mueller, E. *Chem. Ber.* **1965**, *98*, 2859.

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