Acknowledgment. We thank The Dow Chemical Company for a generous gift of dichlorodifluoroethylene[16] and the National Institutes of Health for a grant (AI-19709) which made this work possible.

Registry No. **1a**, 108-95-2; **1b**, 98-54-4; **1c**, 95-48-7; **1d**, 150-76-5; **1e**, 90-43-7; **1f**, 108-46-3; **2a** (X = Cl), 456-61-1; **2b** (X = Cl), 99299-68-0; **2c** (X = Cl), 328-00-7; **2d** (X = Cl), 99299-69-1; **2e** (X = Cl), 99299-70-4; **2f** (X = Cl), 736-32-3; **3a**, 81787-62-4; **3b**, 99299-71-5; **3c**, 99299-72-6; **3d**, 99299-73-7; **3e**, 99299-74-8; **3f**, 99299-75-9; 1,1-dichloro-2,2-difluoroethylene, 79-35-6.

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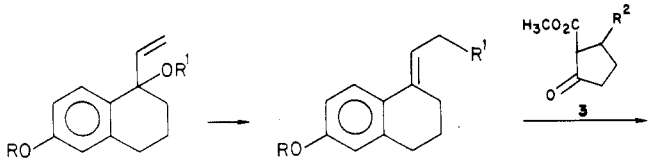
Halocarbon Chemistry. 2. Use of the 1,1-Difluoro-2,2-dichloroethyl Group for Phenol Protection. Regulation of Ionization during the Torgov Steroid Synthesis[1]

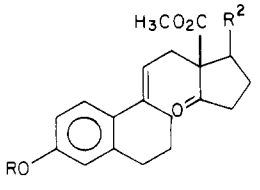
Summary: The use of the easily cleavable (dilute base) HCl_2CCF_2O in place of CH_3O in the Torgov steroid intermediate completely inhibits solvolysis of the tertiary alcohol during acetylation and the derived acetate, via a (π-allyl)Pd complex, is extremely useful for the previously difficult alkylation of cyclic β-keto esters that are precursors of ring D in steroids.

Sir: In many syntheses of estra-1,3,5(10)-trienes the Torgov approach[2] is utilized because of its brevity and simplicity. Early work[3] employing this route utilized **1**, but attempts to convert this alcohol to the more desirable **2** in which R^1 is either OH or a good leaving group (e.g.,



1, R = CH_3; R = H
6, R = CH_3; R^1 = Ac
9, R = CF_2CHCl_2; R^1 = H
10, R = CF_2CHCl_2; R^1 = Ac

2, R = CH_3
5, R = CH_3; R^1 = $SC(NH_2)_2^+OAc^-$
7, R = CH_3; R^1 = OAc



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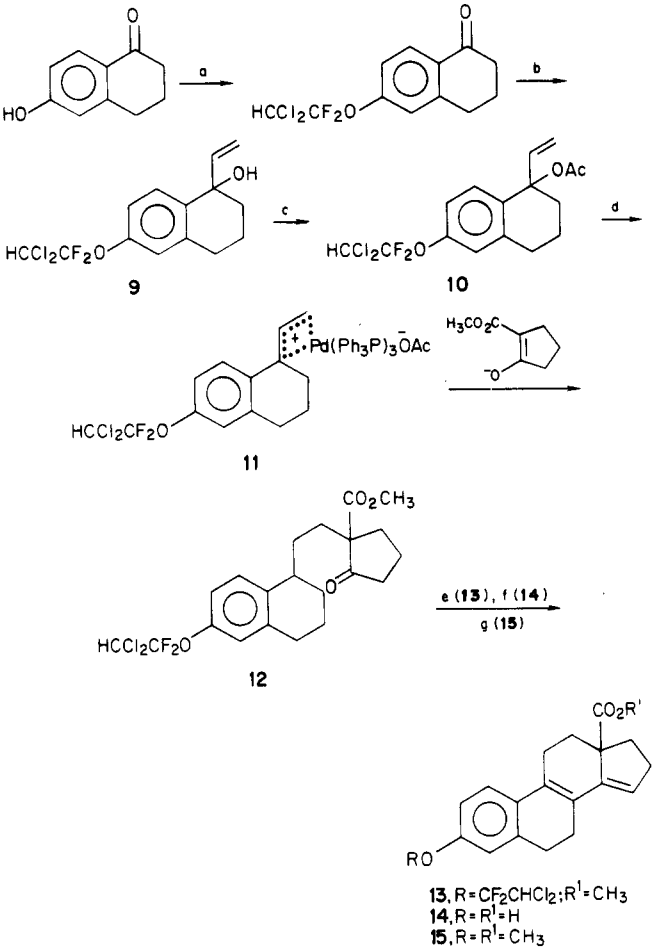
Br, Cl, or OTs) were thwarted by either the facility with which **1** undergoes dehydration[4] and then dimerization or by poor yields.[5] The only truly useful derivative that has emerged is the isothiouronium acetate[6] **5**, but its use until recently was limited to the alkylation of relatively acidic cyclic 1,3-diketones.[2,6,7] Our own work[8,9] has extended the range of application of **5** to the β-keto esters **3** but we were dissatisfied with the yields (50–70%) of the alkylation products **4** (R = CH_3).

In order to circumvent the problems associated with known Torgov intermediates we elected to try to obtain the acetate **6** or its isomer **7**, with the objective of utilizing

Scheme I[a]



[a] Reagents: (a), 40% KOH, $Bu_4N^+OH^-$, $CF_2=CCl_2$, CH_2Cl_2, room temperature, 92%; (b) $CH_2=CHMgBr$, THF, 0 °C, room temperature, 24 h, 91%; (c) Ac_2O, DMAP, CH_2Cl_2, room temperature, 12 h, 91%; (d) $Pd^0(PPh_3)_4$ (0.05 equiv), toluene, room temperature, 1 h, 2-(methoxycarbonyl)cyclopentanone, DBU, toluene, room temperature, 1 h, mixed, then 80 °C, 24 h, 80%; (e) TFA, room temperature, 5 min, 85%; (f) 6% KOH in H_2O/Me_2SO (6:1), room temperature, 12 h then (g) CH_2N_2, Et_2O 85%.

(1) For part 1 of this series, see the preceding communication. This communication (part 2) should also be regarded as part 4 of a series of papers on steroids. For part 3 of the steroid series, see ref 9.

(2) Blickenstaff, R. T.; Gosh, A. C.; Wolf, G. C. In "Total Synthesis of Steroids"; Blomquist, A. T., Wasserman, H., Eds.; Academic Press: New York, 1974; p 86 ff.

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(8) Magriotis, P. A.; Murray, W. V.; Johnson, F. *Tetrahedron Lett.* **1982**, *23*, 1983.

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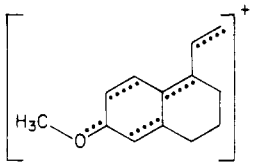
Pd^0 chemistry[10] to effect alkylation of the anion of **3**. However, even under the most favorable conditions that we could devise only a 40% yield of solely the *rearranged* oily acetate **7**[11] was obtained, because of concomitant dehydration. The source of the latter difficulty is the facile formation of the highly delocalized cation**8**. In an attempt



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to curb oxygen lone-pair participation we synthesized the haloether **9** based on the idea that the $CHCl_2CF_2O$ group should behave like a halogen atom in its influence[12] on an aromatic ring. Thus its deactivating effect could be expected to inhibit benzylic ionization. Much to our satisfaction, acetylation under the conditions specified (Scheme I) led to the *unrearranged* acetate **10** in 92% yield. Utilizing the (π-allyl)palladium acetate **11** derived from **10**, in an alkylation reaction of the anion of the β-keto ester **3** (R^2 = H), led to **12** as an oil in 80% yield.[13] Acid-catalyzed cyclization of the latter then afforded the crystalline pentaene **13** (mp 110–111 °C; 92%), which when treated with mild base gave **14**. This was methylated directly with diazomethane to give **15** (mp 123–124 °C, identical in all respects with an authentic racemic sample.[14]

This solution to what has been a vexing synthetic problem not only demonstrates the value of the OCF_2CHCl_2 substituent in *limiting the ionization of an alcohol that is simultaneously tertiary, allylic, and benzylic* but also points up the usefulness of this haloalkyl moiety as *a protective group for phenols*,[15] given the reactions of Scheme I that it survives. Further studies on the use of polyhaloethyl groups to control both benzylic reactivity and the substitution pattern of polyaromatic systems are being pursued.

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Registry No. **9**, 98922-04-4; **10**, 98922-05-5; **11**, 98942-17-7; **12**, 98922-06-6; **13**, 98922-07-7; **14**, 98922-08-8; **15**, 82806-26-6; 2-(methoxycarbonyl)cyclopentanone, 10472-24-9; 5-hydroxy-α-tetralone, 3470-50-6; 5-(2,2-dichloro-1,1-difluoroethoxy)-α-tetralone, 98922-09-9; $F_2C{=}CCl_2$, 79-35-6.

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(11) All new compounds reported in this article were shown to be homogeneous by TLC and gave physical data that confirmed the assigned structures.

(12) Sheppard, W. A. *J. Am. Chem. Soc.* **1963**, *85*, 1314; **1961**, *83*, 4860.

(13) A similar yield of the methyl ether analogue **4** (R = CH_3, R^2 = H) was obtained when **7** was substituted for **10** in the reaction scheme.

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(15) For a general method of preparing these haloalkyl phenolic ethers, see ref 3 of the preceding communication.

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New Reagents for the Regiospecific Synthesis of Naturally Occurring Quinizarins

Summary: A modified Nef reaction applied to 4-nitrobutanoates gives the corresponding acetals which after hydrolysis and enol silylation yield the new 1,3-dienes 1-methoxy-1,4-bis(trimethylsiloxy)butadiene and its 3-methyl derivative. The latter reacts smoothly with chloronaphthoquinones and provides simple and efficient syntheses of 2-methylquinizarin, islandicin, digitopurpone, and erythroglaucin.

Sir: Substituted quinizarins constitute an important group of frequently encountered natural products[1] and have also been proposed as models or starting materials for the elaboration of anthracyclinones.[2] Effective methods for preparing 1,4-di- and 1,3,4-trioxygenated anthraquinones[4,5] have recently been devised; however the larger group of 3-alkylated analogues does not seem to have been obtained previously by such simple regiospecific procedures.

In a preliminary investigation, enolization of 3-(methoxymethyl)crotonate (**1**) and immediate silylation gave a mixture of structural isomers (**2** and **3**) that could not be readily separated (for a different result, see ref 6). Reaction of this mixture of dienes with 2,6-dichlorobenzoquinone (**4**) gave only 3-chloro-5-hydroxy-7-(methoxymethyl)naphthoquinone (**5**) (mp 122.0–123.5 °C) in 54% yield. This result is, however, not unexpected considering the notorious difficulty of annulating benzoquinones with 4-substituted vinylketene acetals[4,7] (Scheme I).

With 2-chloronaphthoquinone (**6**), the same reagents (**2**, **3**) gave a complex mixture which was separated by chromatography (silica gel; $CHCl_3$–CCl_4, 1:1): 4-hydroxy-1-methoxy-2-methylanthraquinone (**7a**), mp 169–171 °C (6%); 1-hydroxy-3-(methoxymethyl)anthraquinone (**8a**), mp 139–140 °C (34%); 1,4-dimethoxy-2-methylanthraquinone (**7b**), mp 130–131 °C (5%); and 1-methoxy-3-(methoxymethyl)anthraquinone (**8b**), mp 153–154 °C (17%). Although this array of products can be converted through methylation or acid hydrolysis of intermediates into only two substances, the approach is effectively eliminated as a useful method for the preparation of alkylquinizarins (Scheme II).

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