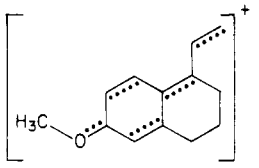
Pd^0 chemistry[10] to effect alkylation of the anion of **3**. However, even under the most favorable conditions that we could devise only a 40% yield of solely the *rearranged* oily acetate **7**[11] was obtained, because of concomitant dehydration. The source of the latter difficulty is the facile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



8

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.

Acknowledgment. We would like to thank Dr. K. M. R. Pillai for technical help in preliminary experiments.

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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(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.

S. G. Will, P. Magriotis, E. R. Marinelli
J. Dolan, Francis Johnson*

Department of Pharmacological Sciences
and Department of Chemistry
SUNY at Stony Brook
Stony Brook, New York 11794

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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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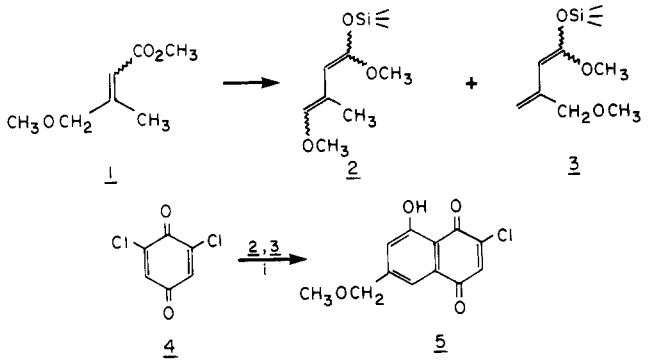
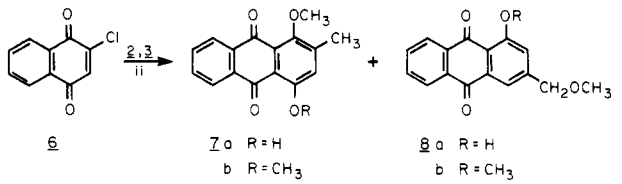
Scheme I[a]



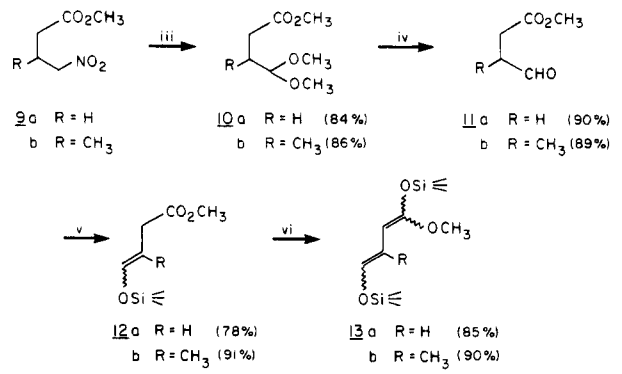
[a] (i) THF, room temperature; silica gel, C_6H_6.

Scheme II[a]



[a] (ii) C_6H_6, room temperature; silica gel, C_6H_6.

Scheme III[a]

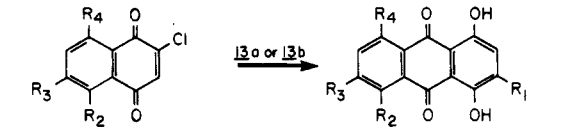


[a] (iii) CH_3ONa; H_2SO_4, CH_3OH, −10 °C; (iv) H_2O, Δ; (v) Et_3N, $ZnCl_2$, $ClSi(CH_3)_3$; (vi) LDA, $ClSi(CH_3)_3$, −78 °C.

A convenient solution to the problem was eventually found in the preparation of 1-methoxy-1,4-bis(trimethylsiloxy)butadiene **13a** and its 3-methyl derivative from the corresponding succinaldehydic esters by double enol silylation. 4-Nitrobutanoates,[8] readily available through Michael addition of nitromethane to α,β-unsaturated esters, undergo a modified Nef reaction,[9] giving acetals which are easily hydrolyzed to the required γ-formyl esters[10] (Scheme III).

Dienes **13a** and **13b** react with dichlorobenzoquinones in benzene at room temperature and give adducts which do not aromatize. These products have been shown in analogous cases to result from addition to one of the quinonic carbonyls, but in these instances decompose rapidly during hydrolysis or chromatography. A variety of naphthoquinones on the other hand combine smoothly with diene **13b** affording the expected anthraquinones regiospecifically and with very satisfactory yields (62–87%). Diene **13a**, however, exhibited poor affinity for quinone **17** and after 7 days without solvent at room temperature yielded only 27% of helminthosporin (**22**).

Scheme IV



	R_2	R_3	R_4
6	H	H	H
14	H	H	OH
15	OAc	H	H
16	H	OCH_3	OH
17	H	CH_3	OH

	R_1	R_2	R_3	R_4
18	CH_3	H	H	H
19	CH_3	H	H	OH
20	CH_3	OH	H	H
21	CH_3	H	OCH_3	OH
22	H	H	CH_3	OH

In a typical example, 2.00 mmol of the diene in 2 mL of dry benzene was added (3–5 min) to 1 mmol of the quinone (**6**, **14–16**) in 3 mL of the same solvent. The mixture was kept at room temperature for 1 h and then refluxed until the cycloaddition was complete (supplemental portions of diene being added as required for prolonged reactions). The crude adduct was stirred for 1 h in a mixture of THF (10 mL), concentrated HCl (2 mL), and then refluxed for 1 h. Extraction of the aromatized product with 2% NaOH, acidification, and purification by dry column chromatography on silica gel (C_6H_6–CCl_4, 1:1) gave the expected product.

The following natural products were obtained in this way: 2-methylquinizarin (**18**) (from **13b** and **6**) (138 h; mp 178 °C; 79%), islandicin (**19**) (from **13b** and **14**) (3 h; mp 218.5–219.0 °C; 77%), digitopurpone (**20**) (from **13b** and **15**) (32 h; mp 211–212 °C; 87%), erythroglaucin (**21**) (from **13b** and **16**) (45 h; mp 206.5–207.5 °C; 62%), and helminthosporin (**22**) (**13a** and **17**) (7 days; mp 227.5–228.5 °C; 27%) (Scheme IV).

Registry No. **1**, 98962-57-3; **2**, 99097-56-0; **3**, 93564-92-2; **4**, 697-91-6; **5**, 99097-57-1; **6**, 1010-60-2; **7a**, 78176-81-5; **7b**, 52541-72-7; **8a**, 93564-93-3; **8b**, 99097-58-2; **9a**, 13013-02-0; **9b**, 16507-06-5; **10a**, 4220-66-0; **10b**, 99097-59-3; **11a**, 13865-19-5; **11b**, 65038-34-8; **12a**, 99097-60-6; **12b**, 99097-61-7; **13a**, 99097-62-8; **13b**, 99097-63-9; **14**, 18855-92-0; **15**, 60549-39-5; **16**, 65120-69-6; **17**, 62993-89-9; **18**, 2589-39-1; **19**, 476-56-2; **20**, 34425-57-5; **21**, 476-57-3; **22**, 518-80-9.

Bruno Simoneau, Jacques Savard, Paul Brassard*

Département de chimie
Université Laval, Québec
Québec, Canada G1K 7P4

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Chelation- and Non-Chelation-Controlled Additions to 2-*O*-Benzyl-3-*O*-(*tert*-butyldimethylsilyl)-glyceraldehyde

Summary: 2-*O*-Benzyl-3-*O*-(*tert*-butyldimethylsilyl)-glyceraldehyde, prepared from 1,3:4,5-di-*O*-benzylidenemannitol, undergoes chelation- or non-chelation-controlled Grignard-type and aldol additions, depending upon the nature of the organometallic reagent used ($TiCl_4/Me_2Zn$, $TiCl_4$/allylsilane, $SnCl_4$/enol silane, $RTi(OCHMe_2)_3$, and BF_3/allylsilane).

Sir: We have previously shown that Lewis acidic titanium reagents are ideal partners in chelation-controlled Grignard- and aldol-type additions to chiral α- and β-alkoxy carbonyl compounds. Furthermore, analogous titanium

0022-3263/85/1950-5434$01.50/0