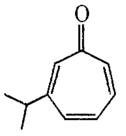

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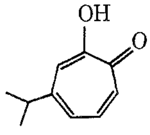

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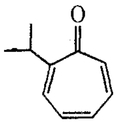

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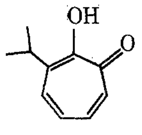

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age [$BF_3 \cdot OEt_2$–$(CH_3CO)_2O$, −10°, three products in 70%], bromination (1 equiv of NBS, 98%), and dehydrobromination (LiCl–DMF, 130°, 77%) gave the tropone **13**.[9] 3-Isopropylcyclohepta-2,6-dienone, one of the ether cleavage products, was also converted to **13** by treatment with DDQ–*p*-TsOH (benzene, 100°) in 80% yield. The tropone **13** was transformed to the tropolone **14** by the usual procedure ($NH_2NH_2 \cdot H_2O$ at 25° and then 2 *N* KOH at 80°, 100%).[10] The product was identical in all respects with the naturally occurring material.[11]

2-Isopropyltropone (**16**) has been prepared from **15** (derived from 1,1,3,3-tetrabromo-4-methylpentan-2-one and furan) by sequential treatments with H_2 over 10% Pd/C in C_2H_5OH (96%), BBr_3 in CH_2Cl_2 at −78–25° (giving 6-bromo-2-isopropylcyclohept-2-enone as major product in 70%), 1 equiv of Br_2 in CCl_4 (100%), and LiCl in DMF at 150° (20%). The tropone **16** can be converted to α-thujaplicin (**17**) by the known method.[12,13]

Acknowledgments. We thank Professors S. Itô and K. Takase and Drs. T. Toda and H. Fujise for a generous supply of natural thujaplicins. Partial financial support from the Takeda and Tokai Science Foundations is also acknowledged.

Supplementary Material Available. Illustrative experimental details will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number JOC-75-806.

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Received April 16, 1974

Direct Ring Fluorination of Aryl Oxygen Compounds with Xenon Difluoride

Summary: In the absence of hydrogen fluoride initiation, anisole, phenol, 2-naphthol, veratrole, catechol, and resorcinol react with xenon difluoride in methylene chloride or ether to give monofluoro substituted products in yields of 37–71%. Veratrole and catechol give the corresponding 4-fluoro compounds almost exclusively, while 2-naphthol is readily converted to 1-fluoro-2-naphthol.

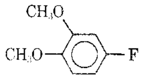
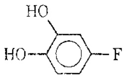
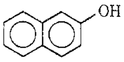
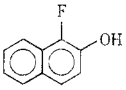
Sir: In the course of our studies on the synthesis of fluoro analogs of pharmacologically active compounds, we have examined the reaction of xenon difluoride with a variety of aryl oxygen compounds. The pioneering studies of Filler, Hyman, and Shaw[1–4] have demonstrated the utility of XeF_2 as a selective fluorinating reagent for aromatic hydrocarbons. In extending the scope of this reaction to include functionally substituted aryl compounds, we report here our results with methoxy- and hydroxy-substituted benzenes.

Xenon difluoride was prepared photochemically by a modification of Matheson's procedure.[5] The solvents dichloromethane and ether (Baker AR) were used without further purification. Anisole and veratrole were distilled before use, while phenol, catechol, resorcinol, and 2-naphthol were of reagent grade and used without further purification.

The procedure was adapted from that previously described.[1]

In a typical experiment, 4 g (37 mmol) of anisole (3-fold excess) dissolved in 12 ml of methylene chloride in a 30-cc Kel-F bottle was degassed to 5×10^{-6} Torr and poured onto 2.1 g (12.2 mmol) of xenon difluoride contained in an evacuated (5×10^{-6} Torr) Kel-F bottle at −196°. The resulting mixture was warmed gradually until the reaction commenced (as evidenced by the evolution of xenon gas and accompanying color change of the solution). Reactions usually occurred in the range of −10 to 25° and were complete within a matter of minutes for the monosubstituted benzenes and several hours for the disubstituted compounds. A small portion of the reaction mixture was treated with NaF pellets to remove the hydrogen fluoride produced and then analyzed by gas chromatography or mass spectrometry. For the remainder of the mixture, the solvent and HF were removed under reduced pressure (5–10 Torr) and the pure compounds were isolated by crystallization or fractional distillation. The results of these reactions are listed in Table I. In all cases, satisfactory yields (37–71%) of monofluorinated products were obtained. Mass spectral analysis failed to reveal any products due to fluorine addition. These reactions occur spontaneously upon warming to 25°. This behavior is in contrast to the reaction of XeF_2 and benzene which requires initiation by hydrogen fluoride. Presumably, the function of the HF is to polarize the Xe–F bond.[3] It is possible that this polarization can

Table I
Reactions of Oxygen-Substituted Benzenes with XeF_2

Substrate	Solvent	Fluorinated products[a]	% yield	Isomer distribn
$C_6H_5OCH_3$	CH_2Cl_2	$C_6H_4(OCH_3)F$	71.5	10:1:8[b]
C_6H_5OH	CH_2Cl_2	$C_6H_4(OH)F$	47	2:2:1[b]
1,2-$C_6H_4(OCH_3)_2$	CH_2Cl_2		37	
1,2-$C_6H_4(OH)_2$	$(C_2H_5)_2O$		38	
1,3-$C_6H_4(OH)_2$	$(C_2H_5)_2O$	$C_6H_3(OH)_2F$	45	Structure not yet established
	$(C_2H_5)_2O$		40	

[a] Column specifications for GLC separation of products: from anisole, 11 ft × ⅛ in., 2.5% Carbowax 20M on Chrom G (80–100 mesh); from phenol, 12 ft × ⅛ in., 10% Apiezon L on Chrom G (100–120 mesh); from veratrole, 6 ft × ⅛ in., 2.5% Carbowax 20M on Chrom G (80–100 mesh), non-acid-washed. The products from catechol, resorcinol, and 2-naphthol were solids which were purified by crystallization. The components of the mixtures of isomers of $C_6H_4(OCH_3)F$ and $C_6H_4(OH)F$ were identified and the yields were determined by comparison with authentic samples, using GLC. The fluoroveratrole, catechol, and 2-naphthol were isolated and compared with authentic samples. [b] Ortho:meta:para.

also be induced by dissolution of XeF_2 in a relatively polar solvent such as dichloromethane, perhaps via halogen–halogen interactions.

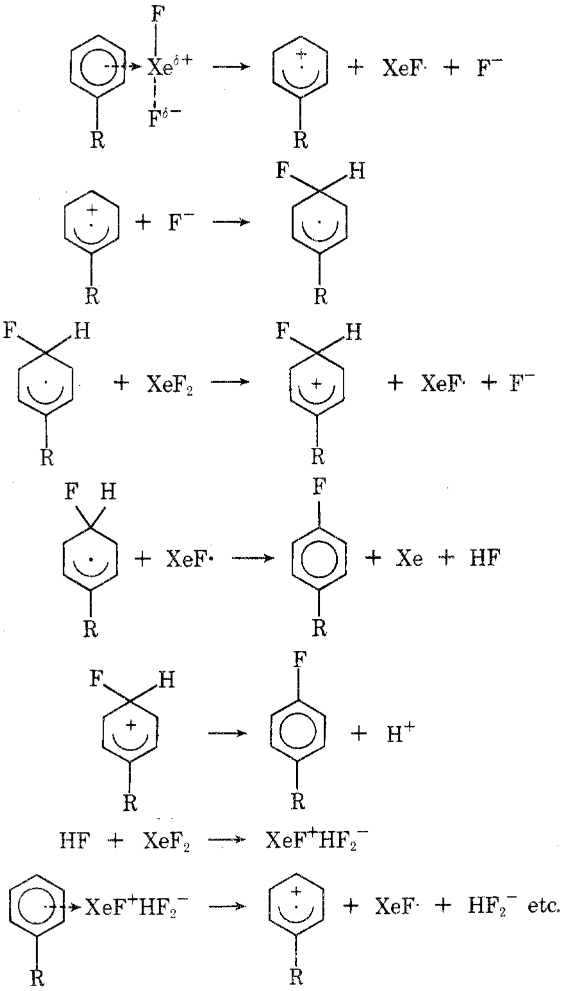
Since these reactions proceed without HF initiation, a modification of our previously proposed mechanism[3] is necessary. We tentatively suggest that substituted aromatic compounds, whose oxidation potentials are higher than that of benzene, induce the polarization of XeF_2 while transferring an electron, to form the colored cation radical (Scheme I). During the subsequent formation of fluorinated product, via a σ complex, hydrogen fluoride is generated and, as in the case of HF initiation, the rate of reaction is then markedly enhanced by the facile formation of the strongly oxidizing XeF^+. All of the compounds in this study possess oxidation potentials substantially higher than that of benzene.[6]

In the case of the phenols, the relatively high acidity ($pK_a \approx 9$–11)[7] does not appear to have any significant effect on the yield of fluorinated products. Apparently, the hydrolysis of XeF_2 by these phenols is much slower than nuclear fluorination. This is not surprising in view of the relatively slow aqueous hydrolysis of XeF_2 ($K_{15^\circ} = 1.27 \times 10^{-4}$ sec^{-1}),[8] which is also unaffected by the presence of acid. Although the aqueous hydrolysis of XeF_2 yields the explosive xenon trioxide,[9] the reaction with phenols did not reveal any products containing a xenon–oxygen bond.[10] Moreover, there was no evidence of the oxidation of the phenols, as was observed with pentafluorophenol, to yield $(C_6F_5)_2O_2$.[11]

Anisole is converted to the isomeric fluoroanisoles (10:1:8 ortho:meta:para) while the fluorophenols are obtained in a markedly different ratio (2:2:1 ortho:meta:para). With both veratrole and catechol, the products are almost exclusively the 4-fluoro isomers. This orientation is consistent with the previously observed behavior of catechol[12] and veratrole[13] with electrophiles. Resorcinol is converted to a monofluoro product whose structure has yet to be confirmed. 2-Naphthol gives 40% 1-fluoro-2-naphthol (1) as the exclusive fluorine-containing product. In contrast, CF_3OF and 2-naphthol give 14% 1 and 20% 1,1-difluoro-2-naphthone.[14]

These results amply demonstrate the usefulness of XeF_2 as a selective, direct fluorinating agent for aryl oxygen compounds, thereby obviating multistep routes to the desired products. The yields have not been optimized and the full potential of this method remains to be explored.

Scheme I
Fluorination of Aromatics In the Absence of HF Initiation



Acknowledgments. We wish to thank Miss Nina Shoshoo for synthesizing some of the reference fluoro compounds; Dr. M. Studier for his help with mass spectra; Dr. L. Kaplan, Dr. K. Wilzback, and Dr. W. Brown for their assistance with the gas chromatography work. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Supplementary Material Available. Description of a modified procedure for the preparation of XeF$_2$ and details for the reaction of the latter with anisole will appear following those pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JOC-75-807.

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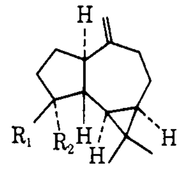
Received November 5, 1974

Photochemical Rearrangements of Cross-Conjugated Cyclohexadienones. Application to the Synthesis of (−)-4-Epiglobulol and (+)-4-Epiaromadendrene[1]

Summary: Photochemical rearrangement of (−)-dehydroepimaalienone (**5**) in aqueous acetic acid produced the tricyclic hydroazulene derivative **8** which was converted into (−)-4-epiglobulol (**2b**) and (+)-4-epiaromadendrene (**1b**).

Sir: In recent years there has been considerable interest in the synthesis of tricyclic sequiterpenes having a cyclopropane ring fused to a hydroazulene ring system, and syntheses of (−)-aromadendrene (the enantiomer of **1a**),[2] (±)-globulol (**2a**),[3] and (−)-cyclocolorenone (**3**)[4] have been reported. In our synthesis of (−)-cyclocolorenone the key step involved photochemical rearrangement of the carboxy cross-conjugated dienone **4b** to establish the ring skeleton of the natural product. We now wish to report the synthesis of (−)-4-epiglobulol (**2b**) and (+)-4-epiaromadrendene (**1b**) using photochemical rearrangement of the tricyclic dienone **5** to obtain the 5/7-fused system of these compounds.



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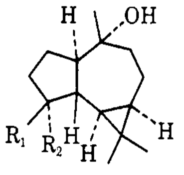

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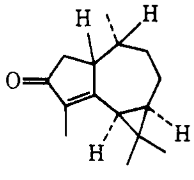

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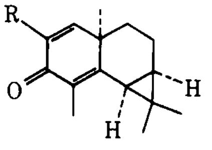
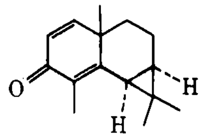
a, R$_1$ = H; R$_2$ = CH$_3$
b, R$_1$ = CH$_3$; R$_2$ = H



4a, R = H
b, R = CO$_2$H



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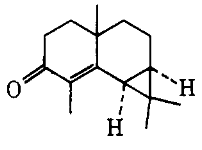

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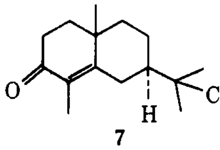

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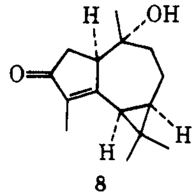
A logical precursor to **5** was (−)-epimaalienone (**6**). While this compound has been prepared in six steps from α-santonin by Ourisson and coworkers,[5] a much more convenient route involved treatment of the bicyclic chloroenone **7**, an intermediate in our recently reported synthesis of (+)-α-cyperone,[6] with sodium hydride in 1,2-dimethoxyethane. Under these conditions ring closure via the conjugate enolate of **7** occurred to give **6** in 75% yield. Oxidation of **6** with 2,3-dichloro-5,6-dicyanobenzoquinone in dioxane gave **5** (56%): bp 111–115° (0.05 mm); λ_{max} (95% EtOH) 244 nm (ϵ 10,400) and 305 (8400); ir ν_{max} (CCl$_4$) 1654 (conjd C=O), 1622 (conjd C=C), 1585 cm^{-1} (conjd C=C); NMR $\delta_{(CH_3)_4Si}$ (CCl$_4$) 1.14 (s, 6 H), 1.24 (s, 3 H), 1.84 (s, 3 H), 6.08 (d, J_{AB} = 10 Hz, 1 H), 6.78 ppm (d, J_{AB} = 10 Hz, 1 H); *m/e* (70 eV) 216.153 (calcd 216.151); $[\alpha]^{25}$D −367° (*c* 0.132, CHCl$_3$). Anal. Calcd for C$_{15}$H$_{20}$O: C, 83.28; H, 9.32. Found: C, 83.02; H, 9.39.

In contrast to its 10 epimer, **4a**, which has been shown to be stable to direct irradiation under a variety of conditions,[4,7] **5** was found to be photochemically labile.[8] Thus, on irradiation of a solution this dienone in 45% aqueous acetic acid at room temperature for 30 min using a 450-W Hanovia high-pressure mercury lamp housed in a Pyrex probe and chromatography of the photolysis mixture on silica gel, the tricyclic hydroxy ketone **8** was isolated in 50% yield. Compound **8** showed mp 93–95°; λ_{max} (95% EtOH) 251 nm (ϵ 11,300); ir ν_{max} (CCl$_4$) 3420 (OH), 1700 (conjd cy-



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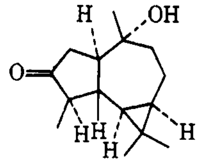

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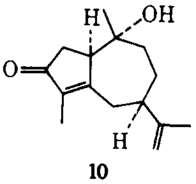

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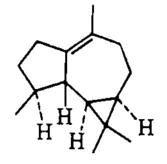

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