epoxidation of 1. Accordingly, a study of the reaction was carried out under different conditions, and the corresponding results are depicted in Table II.

Best results were achieved when a 2:1:0.4 molar ratio of KF–MCPBA–1 in CH_2Cl_2 was used. After 20 h at room temperature the starting material was completely transformed and a 90% yield of epoxide **2** could be isolated from the reaction mixture. The use of higher or lower KF molar proportions reduced drastically the yield of **2**, whereas clean but incomplete epoxidation was observed when the above 2:1 KF–MCPBA complex ratio proportion vs. olefin amount was diminished.

The use of other solvents afforded poorer yields: in hexane **1** was recovered almost unreacted, whereas in 2-propanol and methanol, besides incomplete epoxidation, decomposition was also observed.

From these results we conclude that MCPBA–KF complex suspended in CH_2Cl_2 affords a system active and persistent enough to promote complete epoxidation of α-methylstyrene and to allow the isolation of the resulting epoxide **2** in almost quantitative yield, plausibly due to the inactivation of any acid-catalyzed side reaction.

Experimental Section

Proton nuclear magnetic spectra (^1H NMR) were recorded on a Perkin-Elmer R12B spectrometer with Me_4Si as an internal standard. Gas–liquid chromatography was performed with a Perkin-Elmer Model 990 using a glass column packed with 3% OV-101 on silanized Chromosorb W. Commercially available *m*-chloroperoxybenzoic acid (Fluka) and α-methylstyrene (Fluka) were used without further purification. Solvents were dried and purified by standard procedures.

Preparation and Activity Evaluation of MCBPA–KF Complex. General Procedure. (a) To a suspension of 70–120 mg of freshly activated KF [1 h at 120 °C (0.1 torr)] in 25 mL of CH_2Cl_2 was added the appropriate amount of MCPBA, and the mixture was virgorously stirred for 30 min at room temperature. Then the complex was filtered off, washed thoroughly with CH_2Cl_2, dried under vacuum for 45 min, and stored at the temperature indicated in Table I. After the given time the complex was decomposed by addition of H_2O, the aqueous solution was extracted with CH_2Cl_2, and the active oxygen content was determined iodometrically in the organic layer.[9] Titration of the aqueous layer showed a residual oxygen content of less that 1%.

(b) Activity evaluation in the presence of a solvent was carried out by preparing the complex directly in the desired solvent, stirring the mixture for the given period of time (Figure 1), decomposing the complex, and titrating for the active oxygen content. For hexane and CH_2Cl_2, water was added and the organic layer worked up as in part a; for 2-propanol and methanol, AcOH was added, and titration was carried out directly in the alcohol–acetic acid mixture.

Epoxidation of α-Methylstyrene with MCPBA–KF Complex. General Procedure. The complex prepared as in b was stirred for 30 min at room temperature, the appropriate ratio of olefin was added, and the reaction mixture was stirred at room temperature for the given period of time. When reaction was completed (GLC monitoring), MCPBA–KF and/or MCBA complexes were removed by filtration and washed thoroughly with the same solvent, and the joint filtrates were dried over Na_2SO_4. When hexane or CH_2Cl_2 was used, complex elimination was complete, whereas significant amounts of acidic products were present in the filtrate when working with hydroxylic solvents.

Acknowledgment. Financial support from the Comisión Asesora de Investigación Cientifica y Técnica and the Comité Conjunto Hispano-Norteamericano para la Cooperación Cientifica y Ténica (Grant 0394/11) is gratefully acknowledged.

Registry No. 1, 98-83-9; 2, 2085-88-3.

(9) Gilbert, L. S.; Siegel, E.; Swern, D. *Org. Synth.* **1963**, *43*, 93.

New Synthetic Route to an α-Alkoxy-α-arylacetic Ester Using Formaldehyde Dimethyl Dithioacetal *S,S*-Dioxide

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Formaldehyde dimethyl dithioacetal S,S-dioxide (**1**) is a useful organic reagent. For example, β,γ-unsaturated carboxylic esters could be synthesized by allylation of **1** followed by oxidation and acid-catalyzed decompposition in methanol.[1] Recently, a new method for making acyclic and cyclic ketones was effected by dialkylation of **1** and subsequent acid hydrolysis.[2] We have further investigated the synthetic utility of **1**, and find that **1** provides a new route from an aromatic aldehyde (**2**) to an α-alkoxy-α-arylacetic ester (**5**).

As outlined in Scheme I, the present route comprises three steps: (i) a Knoevenagel-type condensation of **1** with **2** to give 2-aryl-1-(methylsulfonyl)-1-(methylthio)ethene (**3**); (ii) oxidation of **3** to the corresponding *S,S,S'*-trioxide (**4**); (iii) treatment of **4** with an acid (HCl or H_2SO_4) in an appropriate alcohol (ROH), leading to **5**.

For the first step with benzaldehyde as **2**, several conditions (NaH in DMF;[3] *t*-BuOK in *t*-BuOH;[3] EtONa in EtOH; K_2CO_3 in THF,[4] MeOH, EtOH, or *i*-PrOH; piperidine in MeOH[4]) were examined and the use of K_2CO_3 (2 mol equiv) in refluxing *i*-PrOH gave the best result. In this reaction, only one geometric isomer was produced, and its geometry was deduced to be *E* by analogy of the present reaction to the condensation of benzaldehyde with formaldehyde dimethyl dithioacetal *S*-oxide.[5] Under similar conditions, other aromatic aldehydes (**2b–2e**) could be converted to the corresponding **3** in good to high yields. Oxidation of **3** into **4** was easily accomplished with H_2O_2 (1.1 mol equiv) in AcOH at room temperature for 2 days. When the thus obtained **4** was subjected to the reaction of HCl in refluxing MeOH, acid-catalyzed addition of MeOH, a Pummerer-type reaction, and hydrolysis successively occurred and methyl α-methoxy-α-arylacetate (**5**, R = CH_3) was produced (Scheme II). Table I summarizes these results.

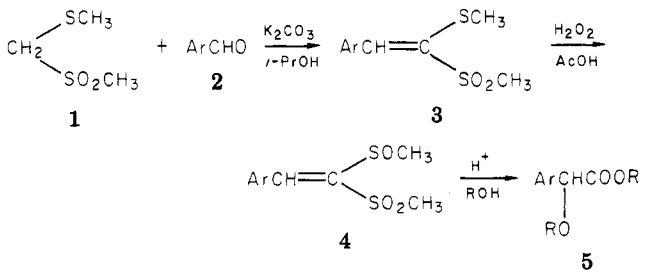
When *i*-PrOH was employed as an alcohol in the final transformation, a more complicated result was observed. Refluxing a solution of **4a** in the presence of HCl in *i*-PrOH gave 1-chloro-2-isopropoxy-1-(methylsulfonyl)-1-(methylthio)-2-phenylethane (Ph(*i*-PrO)CHCCl(SCH_3)(SO_2CH_3), **10**) as a major product which might be formed by trapping the intermediary cation (**8**, R = *i*-Pr) of Scheme II with chloride anion. However, treatment of **4a** with H_2SO_4 in refluxing *i*-PrOH resulted in production of **5a** (R = *i*-Pr) and the methanethiol ester (**11**) of α-isopropoxy-α-

$$\mathbf{4a} \xrightarrow[i\text{-PrOH}]{H_2SO_4} \underset{R = i\text{-Pr}}{\mathbf{5a}} + \underset{\mathbf{11}}{Ph(i\text{-PrO})CHCOSCH_3} \rightarrow \underset{\mathbf{12}}{Ph(i\text{-PrO})CHCOOH}$$

(1) Ogura, K.; Watanabe, J.: Iida, H. *Tetrahedron Lett.* **1981**, *22*, 4499.
(2) Ogura, K.; Suzuki, M.; Watanabe, J.; Yamashita, M.; Iida, H.; Tsuchihashi, G. *Chem. Lett.* **1982**, 813.
(3) A complex mixture was given.
(4) No reaction took place.
(5) Ogura, K.; Ito, Y.; Tsuchihashi, G. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2013.
(6) When **4a** was treated with H_2SO_4 in *t*-BuOH, the corresponding **5a** (R = *t*-Bu) was not produced.

0022-3263/82/1947-5404$01.25/0

Scheme I[a]



[a] a, Ar = C_6H_5; b, Ar = 4-ClC_6H_4; c, Ar = 4-$(CH_3O)C_6H_4$; d, Ar = 3,4-$(CH_3O)_2C_6H_3$; e, Ar = 2-thienyl.

Scheme II

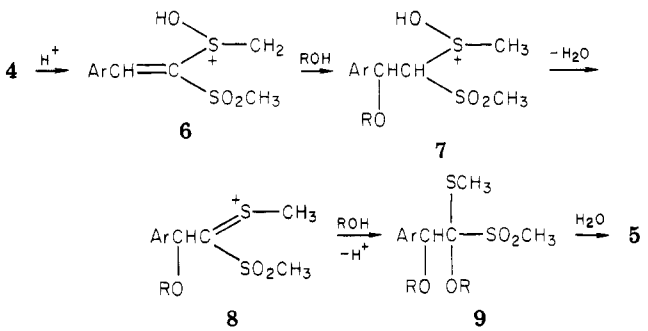


Table I. Yields (%) in Synthesis of Methyl α-Methoxy-α-arylacetate (5, R = CH_3) Using 1

	2 ⟶ 3[a]	3 ⟶ 4[b]	4 ⟶ 5
2a	70	87 (98)	76
2b	62	88 (100)	80
2c	60	74 (100)	76
2d	52	70 (100)	76
2e	88	65 (98)	72

[a] 1.5 mol equiv of 2 was used. [b] The value in parentheses is the yield based on unrecovered 3.

phenylacetic acid (12) in 47% and 29% yields, respectively. Since both the products can be converted by alkaline hydrolysis to 12, the present sequence provides a useful method for synthesizing 12[7] from benzaldehyde. Furthermore, it should be noted that the reaction of 4a with H_2SO_4 in refluxing EtOH gave ethyl α-ethoxy-α-phenylacetate (5a, R = C_2H_5) in 88% yield.

Thus, we have established a convenient method for synthesis of α-alkoxyarylacetic esters starting from aromatic aldehydes.

Experimental Section

Melting points were determined on a hot-stage microscope (Yamagimoto) and are uncorrected. ^1H NMR spectra were obtained in $CDCl_3$ on a Hitachi R-600 spectrometer. Mass spectra were recorded on a Hitachi RMU 7M high-resolution spectrometer. Infrared spectra were determined with a Jasco A-200 spectrometer. Infrared and ^1H NMR data for **3b–e**, **4b–e**, an **5b–e** (R = Me) were consistent with the structures, and satisfactory analytical data were reported for all these compounds.

Condensation of Benzaldehyde with 1. A Typical Procedure. A mixture of 1 (4.002 g, 28.53 mmol), benzaldehyde (4.54 g, 42.8 mmol), and K_2CO_3 (7.89 g, 56.8 mmol) in *i*-PrOH (32 mL) was heated under a reflux for 18 h. After addition of water (100 mL) and extraction with CH_2Cl_2 (4 × 50 mL), the organic layer was washed with water, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue was column chromatographed on silica gel with PhH and AcOEt as eluents to give the unchanged 1 (1.03 g, 26%) and **3a** (4.08 g, 70%) as a colorless oil which soon crystallized: mp 55–55.5 °C (from hexane–PhH); ^1H NMR δ 2.46 (3 H, s), 3.09 (3 H, s), 7.30–7.60 (3 H, m), 7.88–8.06 (2 H, m), 8.06 (1 H, s); IR (KBr) 1598, 1315, 1295, 1130, 967, 757, 690 cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_2S_2$: C, 52.61; H, 5.30. Found: C, 52.66; H, 5.27.

By the same procedure, the following compounds were obtained: **3b**, mp 105 °C (from EtOH); **3c**, mp 60.5 °C (from EtOH); **3d**, mp 103–104 °C (from EtOH); **3e**, mp 86–87 °C (from EtOH).

Oxidation of 3a. A Typical Procedure. To a solution of **3a** (909 mg, 3.99 mmol) in AcOH (10 mL) was added 35% aqueous solution of H_2O_2 (0.43 mL, 1.1 mol equiv), and the resulting mixture was stirred at room temperature for 2 days. After addition of water (60 mL) and extraction with CH_2Cl_2 (4 × 50 mL), the organic layer was washed with water, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue was separated by column chromatography on silica gel with PhH–AcOEt (19:1 and 1:1) to give the unchanged **3a** (102 mg, 11%) and **4a** (846 mg, 87%) as colorless crystals: mp 142 °C (from EtOH–AcOEt); ^1H NMR δ 3.22 (3 H, s), 3.37 (3 H, s), 7.48 (5 H, br s), 8.15 (1 H, s); IR (KBr) 1590, 1445, 1303, 1130, 1046, 958, 750 cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_3S_2$: C, 49.16; H, 4.95. Found: C, 49.23; H, 4.95.

Analogously, the following compounds were obtained: **4b**, mp 177–178 °C (from EtOH–AcOEt); **4c**, mp 133.5 °C (from PhH); **4d**, mp 176.5 °C (from PhH–AcOEt); **4e**, mp 113.5–114.5 °C (from PhH).

Production of 5a (R = CH_3). A Typical Procedure. To a solution of **4a** (507 mg, 2.08 mmol) in MeOH (14 mL) was added 11 M methanolic solution of HCl (3.5 mL), and the resulting solution was heated under a reflux for 18 h. After addition of water (40 mL) and extraction with Et_2O (4 × 40 mL), the organic layer was washed with water, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue was subjected to column chromatography on silica gel with hexane and PhH as eluents to give **5a** (R = CH_3; 284 mg, 76%) as a colorless oil which was identified by IR and ^1H NMR with the sample prepared by the reaction of mandelic acid with MeI (2 mol equiv) and NaH (2 equiv) in DMF at 0 °C–room temperature; ^1H NMR δ 3.32 (3 H, s), 3.62 (3 H, s), 4.70 (1 H, s), 7.34 (5 H, s); IR (neat) 1758, 1195, 1175, 1108, 1009, 699 cm^{-1}; exact mass for $C_{10}H_{12}O_3$ (M^+) *m/e* 180.0785, found *m/e* 180.0789.

In analogous manners, **5b–e** (R = Me) were obtained as colorless oils.

Treatment of 4a with H_2SO_4 in *i*-PrOH. To a solution of **4a** (283 mg, 1.16 mmol) in *i*-PrOH (10 mL) was added concentrated H_2SO_4 (0.2 mL), and the resulting mixture was heated under a reflux for 18 h. After addition of water (40 mL) and extraction with CH_2Cl_2 (4 × 30 mL), the organic layer was washed with water, dried over anhydrous $MgSO_4$, and evaporated in vacuo. The residue was column chromatographed on silica gel with hexane–PhH (1:1 and 1:2) to give **5a** (R = *i*-Pr; 130 mg, 47%) and 11 (76 mg, 29%). **5a** (R = *i*-Pr): a colorless oil; ^1H NMR δ 1.12 (3 H, d, *J* = 6 Hz), 1.20 (3 H, d, *J* = 6 Hz), 1.23 (3 H, d, *J* = 6 Hz), 1.25 (3 H, d, *J* = 6 Hz), 3.71 (1 H, septet, *J* = 6 Hz), 4.94 (1 H, s), 5.04 (1 H, septet, *J* = 6 Hz), 7.15–7.70 (5 H, m); IR (neat) 1750, 1728 (sh), 1176, 1104 cm^{-1}; exact mass for $C_{14}H_{20}O_3$ (M^+) *m/e* 236.1411, found *m/e* 236.1415; exact mass for $C_{14}H_{21}O_3$ (M^+ + H) *m/e* 237.1490, found *m/e* 237.1490 (relative intensity 2.0:13.9). 11 (colorless oil): ^1H NMR δ 1.20 (3 H, d, *J* = 6 Hz), 1.31 (3 H, d, *J* = 6 Hz), 2.20 (3 H, s), 3.78 (1 H, septet, *J* = 6 Hz), 4.95 (1 H, s), 7.18–7.70 (5 H, m); IR (neat) 1688, 1118, 1076, 1062 cm^{-1}; exact mass for $C_{12}H_{17}O_2S$ (M^+ + H) *m/e* 225.0948, found *m/e* 225.0957.

Production of 5a (R = Et). To a solution of **4a** (410 mg, 1.68 mmol) in EtOH (14 mL) was added concentrated H_2SO_4 (1.5 mL), and the resulting mixture was heated under a reflux for 18 h. After addition of water (60 mL) and extraction with CH_2Cl_2 (4 × 40 mL), the organic layer was washed with water, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue was separated by column chromatography on silica gel with hexane and PhH as eluents to give **5a** (R = Et; 307 mg, 88%; colorless oil): ^1H NMR δ 1.18 (3 H, t, *J* = 7 Hz), 1.26 (3 H, t, *J* = 7 Hz), 3.20–3.90 (2 H, m), 4.16 (2 H, q, *J* = 7 Hz), 4.86 (1 H, s), 7.24–7.51 (5 H, m); IR (neat) 1753, 1175, 1114 cm^{-1}; exact mass for $C_{12}H_{16}O_3$ (M^+) *m/e* 208.1097, found *m/e* 208.1072.

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(7) Fuson, R. C.; Rachlin, A. I. *J. Am. Chem. Soc.* **1962**, *64*, 1567.

Registry No. 1, 20163-71-7; **2a**, 100-52-7; **2b**, 104-88-1; **2c**, 123-11-5; **2d**, 120-14-9; **2e**, 98-03-3; (*E*)-**3a**, 58058-77-8; (*E*)-**3b**, 58058-79-0; (*E*)-**3c**, 83831-67-8; (*E*)-**3d**, 83831-68-9; (*E*)-**3e**, 83831-69-0; (*E*)-**4a**, 83831-70-3; (*E*)-**4b**, 83831-71-4; (*E*)-**4c**, 83831-72-5; (*E*)-**4d**, 83831-73-6; (*E*)-**4e**, 83831-74-7; **5a** (R = Me), 3558-61-0; **5a** (R = Et), 79309-63-0; **5a** (R = *i*-Pr), 83831-75-8; **5b** (R = Me), 10399-10-7; **5c** (R = Me), 59845-69-1; **5d** (R = Me), 83831-76-9; **5e** (R = Me), 19204-08-1; **11**, 83831-77-0; **12**, 5394-87-6.

Communications

(+)-Uskudaramine: A Novel Type Aporphine–Benzylisoquinoline Alkaloid

Summary: (+)-Uskudaramine (**1**) is the first aporphine–benzylisoquinoline dimer whose two constituent entities are bonded together through carbon to carbon coupling.

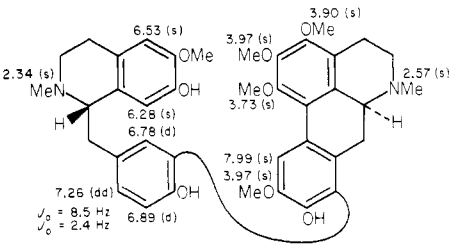
Sir: In a continuing investigation of the alkaloids of *Thalictrum minus* L. var. *microphyllum* (Ranunculaceae), collected in western Anatolia,[2] we have isolated the new amorphous triphenolic aporphine–benzylisoquinoline dimer (+)-uskudaramine (**1**), $C_{39}H_{44}O_8N_2$. This base is structurally isomeric with the known diphenolic alkaloid (+)-istanbulamine (**2**) found in the same plant.[2,3]

The 360-MHz (FT) NMR spectrum in deuteriochloroform of uskudaramine has been summarized around expression **1**, and for comparison purposes that of istanbulamine is cited around expression **2**. Each spectrum shows the presence of five methoxyl and two *N*-methyl singlets, as well as an aromatic singlet near δ 8.00 specifically associated with H-11 of an aporphine. But whereas the istanbulamine spectrum exhibits absorptions for a total of seven aromatic protons, the uskudaramine spectrum has only six such protons. More specifically, the aromatic peak present in the spectrum of istanbulamine (**2**) and conspicuously missing in that of uskudaramine (**1**) is the singlet at δ 6.84 assigned to H-8.

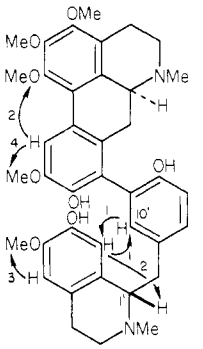
The logical conclusion is thus to move the terminal of the connecting bridge between the two moieties making up the aporphine–benzylisoquinoline dimer from the oxygen atom at C-9 of istanbulamine (**2**) to the adjacent C-8 position in uskudaramine (**1**). Such a structural change would satisfy the NMR spectral requirement by eliminating an aromatic proton in **1**, while at the same time creating an extra phenolic function at C-9 that would be congruent with the fact that uskudaramine (**1**) is triphenolic while its companion, istanbulamine (**2**), is only diphenolic.

In analogy with the mass spectrum of istanbulamine (**2**),[2] the mass spectrum of uskudaramine (**1**) displays a small molecular ion m/z 668 and base peak m/z 192 due to the dihydroisoquinolinium cation a formed through facile fission of the C-1′ to C-α′ bond. In both instances, there is a small but significant m/z 476 peak due to cation b that corresponds to $(M - a)^+$ (Table I).

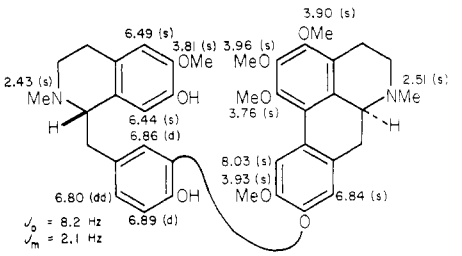
The UV spectrum of uskudaramine (**1**; Table I) exhibits an absorption at 312 nm diagnostic of an aporphine system.



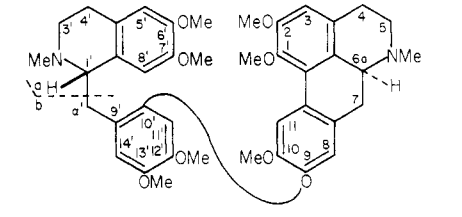
1



1a



2



3

The spectrum also shows the expected bathochromic shift in base due to the phenolic functions. More importantly, there is also a hyperchromic effect that accompanies the bathochromic shift. This hyperchromic effect is associated with the presence of a phenolic function at either C-3 or C-9 of the aporphine moiety, with C-9 being in the present case the more logical site for the phenol.[4]

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(2) Guinaudeau, H.; Freyer, A. J.; Minard, R. D.; Shamma, M. *Tetrahedron Lett.* **1982**, *23*, 2523.

(3) There is a particular tendency for benzylisoquinolines of *Thalictrum* species to acquire an extra oxygen at C-5. Such a species would then provide an aporphine oxygenated at C-3 as in alkaloids **1** and **2**.

(4) Abu Zarga, M. H.; Shamma, M. *J. Nat. Prod.*, **1982**, *45*, 471. Shamma, M.; Yao, S. Y.; Pai, B. R.; Charubala, R. *J. Org. Chem.* **1971**, *36*, 3253.

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