A Regiospecific Synthesis of α-Methoxystilbenes

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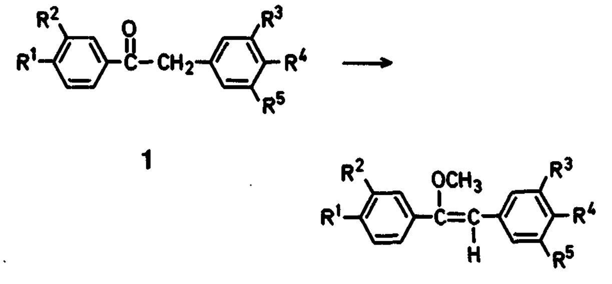
The synthesis of α-methoxystilbenes has been achieved by methoxy-bromination of stilbene with bromine in methanol followed by sodium methoxide elimination of hydrogen bromide[1]. Unfortunately, this approach is unsuitable for regiospecific synthesis of α-methoxystilbenes from unsymmetrical stilbenes. We here report that, in hexamethylphosphoric triamide solvent, enolate anions of deoxybenzoins can be predominately O-methylated using methyl fluorosulfonate[2] (Magic Methyl)[3]. By this procedure the first regiospecific synthesis of an α-methoxystilbene **2c** has been accomplished.



1

2

	R¹	R²	R³	R⁴	R⁵
a	H	H	H	H	H
b	OCH_3	H	H	OCH_3	H
c	$-O-CH_2-O-$		OCH_3	OCH_3	OCH_3

Table. Experimental Conditions and Results of the Synthesis of **2a** from **1a**

Solvent	Methylating Agent	Yield[a] (%)
DMSO	$(CH_3)_2SO_4$	23[b]
HMPT	$(CH_3)_2SO_4$	43[b]
HMPT	CH_3SO_2F	70[b,c]

[a] Isolated yields.

[b] Reaction conditions: 25°, 4 min.

[c] Reaction conditions: 5°, 4 min.

α-Methoxystilbene (2a) (Typical Methylation Procedure):
Deoxybenzoin[3] **1a** (1.0 g, 5.5 mmol) was dissolved in hexamethylphosphoric triamide (30 ml) under a nitrogen atmosphere and the solution was cooled to 5° by means of an ice bath. Potassium t-butoxide (1.7 g, 14.2 mmol) was added and the mixture was stirred 4 min. Methyl fluorosulfonate (1.8 g, 13 mmol) was added, the mixture was stirred 3 min, and then quenched by pouring into water (100 ml). The water solution was extracted with ether (3 × 50 ml). The combined ether layers were dried over magnesium sulfate, and the solvent was removed to afford an oil which solidified upon addition of a few ml of methanol. Recrystallization from methanol afforded *trans*-α-methoxystilbene; yield: 0.75 g (70%); m.p. 54.5–55° (lit.[1], 51.5–52°).

4,4′,α-Trimethoxystilbene 2b:
The general procedure utilizing deoxyanisoin[3] **1b** (1.0 g) afforded white crystals of **2b**; yield: 0.8 g (77%); m.p. 114–115° (from methanol).

$C_{17}H_{18}O_3$	calc.	C 75.53	H 6.71
(270.3)	found	75.47	6.48

U.V. (CH_3OH): λ_{max} = 297 nm (log ε = 4.48).

3,4-Methylenedioxy-α-3′,4′,5′-tetramethoxystilbene 2c:
The general procedure utilizing **1c**[4] (0.55 g) afforded yellow crystals of **2c**; yield: 0.4 g (70%); m.p. 130.5–131° (from methanol).

$C_{19}H_{20}O_6$	calc.	C 66.27	H 5.85
(344.4)	found	65.97	5.59

U.V. (CH_3OH): λ_{max} = 314 mm (log ε = 4.28), 222 nm (log ε = 4.51).

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[2] J. B. Press, H. Schecter, *Tetrahedron Lett.* **1972**, 2677.

[3] Available from Aldrich Chemical Company.

[4] G. Krow, E. Michener, unpublished work.