a new reagent, diphosgene (Aldrich), methyl trichloromethyl carbonate, as follows. The sodium salt of malononitrile (0.92 g; 0.0104 mol) was mixed with 5 mL of dry THF under nitrogen. Diphosgene (1.01 g; 0.0052 mol) dissolved in an equal amount of ether, was added dropwise with cooling (ice bath). After being stirred at room temperature for 24 h, the mixture was refluxed for 1.5 h. After cooling, the mixture was filtered, and the precipitate was washed with ether, giving the sodium salt of trideuteriomethyl dicyanoethanoate, a hygroscopic solid, in 36% yield. Without further purification, the sodium salt of trideuteriomethyl dicyanoethanoate (0.29 g; 0.0022 mol) was dissolved in 9 mL of 2 N HCl. The solution was saturated with sodium chloride and filtered after treatment with activated charcoal. The filtrate was extracted 3× with methylene chloride. The combined organic layers were dried ($MgSO_4$) and concentrated to give the crude product (0.05 g; 17%). ^1H NMR and ^{13}C NMR were identical with those of **1a** except for splitting of each resonance by the deuterium substituents. The splitting patterns were consistent (vida infra) with approximately ${}^2/_3$ of the material being trideuteriomethyl and the remainder being methyl dicyanoethanoate. The mass spectrum [m/z (relative intensity at 9 eV) 15 (12), 16 (0), 17, (0), 18 (25), 59 (60), 60 (<2), 61 (<2), 62 (100)] confirmed the material contained a mixture of trideuteriated/undeuteriated product of 2:1.

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Simple Synthesis of Biphenyls with the 2-Carbomethoxy-3,5-dihydroxyphenyl Moiety

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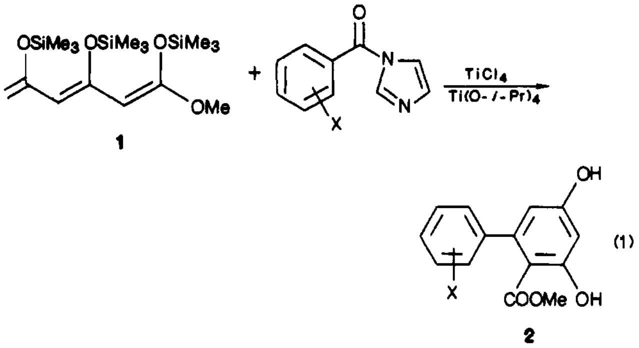
The Ullmann reaction and the Gomberg–Bachmann synthesis, extensively used for the preparation of biphenyl derivatives,[1] present some limitations:[2] the Ullmann synthesis does not give good yields unless one of the aryl halides has an activating group such as nitro, and it can be used for the preparation of unsymmetrical biaryls only if there is a difference in the reactivity of the two components; in the Gomberg–Bachmann reaction the yields are usually low, although recent examples[2] of biphenyl syntheses have improved the yields and used milder reaction conditions than the classical methods.[3-8]

We have recently reported[9] on the Ti^{IV}-promoted condensation of aliphatic imidazolides or equivalent active acylation reagents with 1,3,5-tris(trimethylsiloxy)-1-methoxyhexa-1,3,5-triene (**1**) to provide methyl 2,4-dihydroxy-6-alkylbenzoates in yields of up to 75% in a 5C + 1C condensation.

Table I. Unsymmetrical Biaryls 2

2X	yield, %	mp, °C	formula	HRMS[a] found	HRMS[a] calcd
2′-Cl	trace				
3′-Cl	65	131–132	$C_{14}H_{11}O_4Cl$	280.030	280.031
4′-Cl	60	148–149	$C_{14}H_{11}O_4Cl$	280.032	280.031
3′,4′-diCl	58	144–145	$C_{14}H_{10}O_4Cl_2$	313.993	313.993
3′,5′-diCl	65	152–154	$C_{14}H_{10}O_4Cl_2$	313.995	313.993
4′-CH_3	10	141–143	$C_{15}H_{14}O_4$	258.090	258.089
H[b]	40	117–118[c]	$C_{14}H_{12}O_4$	244.070	244.074
2′-F	11	127–129	$C_{14}H_{11}O_4F$	262.066	262.064
3′-F	42	102–104	$C_{14}H_{11}O_4F$	262.062	262.064
4′-F	38	136–138	$C_{14}H_{11}O_4F$	262.064	262.064

[a] High-resolution mass spectra were obtained at 60 eV on a Du Pont 21-492B instrument at 65 °C. [b] Prepared from the condensation of trimethyl orthobenzoate and 1. [c] Lit.[11] mp 119–121 °C.



1

2

(1)

In contrast to aliphatic acid chlorides, the condensation of aromatic acid chlorides with **1** did not lead to detectable amount of product.

We have now found that the condensation of **1** did proceed with aromatic imidazolides, thus providing an easy route to unsymmetrical biphenyls **2** (eq 1). In the present case, it was necessary to use 4 equiv of silyl ether to obtain yields in the range of 40–65%. Trimethyl orthobenzoate also reacted with **1** to provide the corresponding biphenyl, showing that both aliphatic and aromatic ortho esters can undergo the 5C + 1C condensation. A range of functionalized biphenyls can be prepared by this method, as summarized in Table I. This method appears to be particularly useful for the synthesis of unsymmetrical biphenyls with halogen substitution in one phenyl ring, since the classical Ullmann reaction or its modifications may lead to the problem of selective halogen activation or polycondensation, and in the Carney–Harris method[11] the introduction of halogen substituents in the phenyl ring of the triketo ester used for the subsequent cyclization was not attempted.

In the condensation of (2-chlorobenzoyl)imidazoline with **1** only a small amount of the expected biaryl was detected by NMR, whereas in the reaction of (2,6-dichlorobenzoyl)imidazoline no biaryl was detected. Steric hindrance of the imidazolide is believed to be the major limiting factor since (2-fluorobenzoyl)imidazoline did give the corresponding biphenyl.

The interpretation of the ^1H NMR of biaryls **2** is straightforward as the two protons of the 2-carbomethoxy-3,5-dihydroxyphenyl moiety appear as an AB quartet in the 6.2–6.5 ppm region, and the aromatic protons of the second ring appear further downfield in all of the compounds studied. The ester carbonyl stretching frequency

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in the IR spectra is characteristic and appears at 1660 cm^{-1}.

Experimental Section

1,3,5-Tris(trimethylsiloxy)-1-methoxyhexa-1,3,5-triene (1) was prepared in 80% overall yield in two steps from triacetic ester according to our published procedure.[9]

Preparation of Imidazolides. The imidazolides were prepared according to literature procedure:[10] the acid chloride and imidazole were mixed in a one to two molar ratio in THF and stirred for 15 h at room temperature. The resulting precipitate of imidazolinium chloride was discarded and the filtrate concentrated to give the product, which was often used crude. If desired, the imidazolide may be recrystallized from ethyl acetate/petroleum ether.

(2-Chlorobenzoyl)imidazoline: mp 68–69 °C (lit.[10] mp 68–69 °C).

(3-Chlorobenzoyl)imidazoline was obtained as a viscous oil (lit.[10] mp 44–45 °C).

(4-Chlorobenzoyl)imidazoline: mp 83–85 °C (lit.[10] mp 86.5–87.5 °C).

(4-Methylbenzoyl)imidazoline: mp 71–72 °C (lit.[10] mp 75 °C).

(3,4-Dichlorobenzoyl)imidazoline: mp 123–124 °C; IR (KBr) 3130, 1700, 1370, 1310, 1240, 920, 835, 740, 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1 (s, 1 H), 7.5 (s, 1 H), 7.6 (s, 2 H), 7.8 (s, 1 H), 8.0 (s, 1 H).

(3,5-Dichlorobenzoyl)imidazoline: mp 141–143 °C; IR (KBr) 3020, 1705, 1365, 1275, 1235, 745, 645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.0 (m, 1 H), 7.5 (m, 1 H), 7.6–7.8 (m, 3 H), 8.0 (m, 1 H).

(2-Fluorobenzoyl)imidazoline: mp 58–59 °C; IR (KBr) 3150, 3110, 1700, 1610, 1370, 900, 745, 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.95–7.95 (m).

(3-Fluorobenzoyl)imidazoline: mp 42–43 °C; IR (KBr) 3110, 3040, 1700, 1585, 1440, 1365, 1295, 810, 740, 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.08 (s, 1 H), 7.26–7.50 (m, 5 H), 8.00 (s, 1 H).

(4-Fluorobenzoyl)imidazoline: mp 79–81 °C; IR (KBr) 3120, 1695, 1590, 1230, 895, 840, 745, 630, 615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.0–7.2 (m, 3 H), 7.4 (s, 1 H), 7.7–7.8 (m, 2 H), 7.9 (s, 1 H).

Preparation of Biphenyls 2. The aromatic imidazolide (0.5 mmol) was weighed into a small flask and 40 mL of dry CH_2Cl_2 added. After the mixture was cooled to −78 °C under nitrogen, 2 mmol of silyl ether 1 was added followed by a mixture of 4 mmol of $TiCl_4$ and 4 mmol of $Ti(i\text{-}PrO)_4$ in 5 mL of CH_2Cl_2. The mixture was stirred for 4 h at −78 °C and overnight at room temperature. Then the reaction was carefully quenched with aqueous sodium bicarbonate and extracted 5 times with ether. The ether solution was dried, concentrated, and purified through column chromatography (eluent: 25/75 ethyl acetate–petroleum ether v/v) to give the product in 40–65% yield based on the electrophile (see Table I).

All the products gave NMR, IR, and MS (low and high resolution) spectra consistent with the proposed structures.

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The Solvolyses of Some Monoterpenoid 2,4-Dinitrophenyl Ethers

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The acid-catalyzed cyclization of nerol is one of the earliest recorded cyclization reactions in terpene chemistry.[1] Solvolyses of neryl derivatives remains a fertile testing ground for assessing the role of neighboring group participation by a remote double bond, where only modest rate enhancements are observed relative to reasonable model substrates, such as the corresponding geranyl derivatives.

Table I. Activation Parameters for the Solvolyses of Neryl and Geranyl 2,4-Dinitrophenolates

	neryl ether		geranyl ether	
solvent	$\Delta H^{\ddagger}$,[d] kcal mol^{-1}	$\Delta S^{\ddagger}$,[d] eu	$\Delta H^{\ddagger}$,[d] kcal mol^{-1}	$\Delta S^{\ddagger}$,[d] eu
100% EtOH[b]	26.3 ± 1.0	−5.4 ± 2.9	24.7 ± 1.3	−10.5 ± 3.8
80% EtOH[a]	25.1 ± 0.6	−4.6 ± 1.9	27.0 ± 1.1	−0.4 ± 3.4
60% EtOH[a]	22.6 ± 0.3	−9.3 ± 0.9	26.3 ± 0.7	0.4 ± 2.2
40% EtOH[a]	21.1 ± 0.4	−10.9 ± 1.2	23.1 ± 1.3	−6.2 ± 3.8
100% TFE[b]	17.3 ± 0.05	−22.1 ± 0.2	22.2 ± 0.2	−11.7 ± 0.5
acetic acid[c]	23.6 ± 0.4	−10.0 ± 1.3	27.3 ± 0.5	−1.4 ± 1.5

[a] Aqueous ethanol solutions (v/v), 0.05 M in sodium acetate. [b] Buffered with 1 mM 2,6-lutidine. [c] Taken from ref 2. [d] At 100 °C.

Table II. Product Analyses for the Solvolyses of Neryl and Geranyl 2,4-Dinitrophenolates

		neryl		geranyl	
solvent	*t*, °C	% cycliz	% elimin	% cycliz	% elimin
HAc[a]	95	77	58	4	39
100% EtOH	73	64	50	4	9
TFE	73	81	75	14	81

[a] Taken from ref 2.

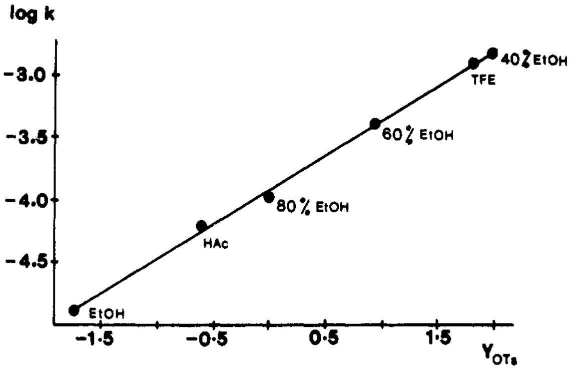
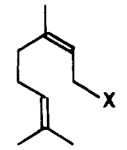


Figure 1. Logarithms of rate constants for solvolysis of neryl 2,4-dinitrophenolate vs. Y_{OTS}, $t = 73.6 \pm 0.1$ °C ($\log k = 0.55 Y_{OTS} - 3.91$).

In the present study, the solvolyses of neryl and geranyl 2,4-dinitrophenolates, 1 and 2, respectively, have been examined in a variety of solvents to assess the role of the remote double bond in the neryl system.



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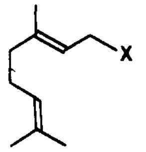

2

$X = OC_6H_3(NO_2)_2$

Table I gives the activation parameters for the solvents studies and indicates, with the exception of 100% EtOH, the consistently more negative $\Delta S^{\ddagger}$ for the neryl system. These results suggest the reliability of the analysis of $\Delta S^{\ddagger}$ differences in terms of combinatorial entropy proposed by Astin and Whiting,[2] i.e., the number of allowed conformations leading to cyclic products in the neryl case is much smaller than those leading to acyclic products for the geranyl ether, leading to a calculated entropy difference

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