million (δ scale) by employing Me_4Si or $CHCl_3$ (entry 2, Table I) as an internal standard. Infrared spectra were obtained on a Perkin-Elmer 843-IR spectrophotometer.

Column chromatography was performed on silica gel (60–120 mesh) impregnated with silver nitrate (10%). TLC was done on glass plates coated with silica gel-G impregnated silver nitrate (10%).

General Procedures. Hydroboration. The acetoxyborohydride (20 mmol) was prepared according to the literature procedure[6] as follows: A dry 100 mL flask equipped with magnetic stirring bar, septum inlet, and reflux condenser was flushed with nitrogen. The flask was charged under nitrogen with sodium borohydride (20 mmol) followed by the addition of 40 mL of dry THF via syringe. The flask is immersed in an ice bath, and 10 mmol of mercuric acetate was added slowly under a blanket of nitrogen. The contents were allowed to stir for 1 h at 0 °C. The reaction mixture was brought to room temperature, and the diene (30 mmol) was added dropwise. The contents were further stirred for 16 h at room temperature for complete hydroboration.

Oxidation. The organoborane prepared as above in THF was cooled to 0 °C and 8 mL of 3 M aqueous sodium hydroxide was added slowly to the reaction mixture. Hydrogen peroxide, 8 mL of 30% aqueous solution, was introduced dropwise to the stirred reaction mixture. The temperature was then raised slowly, and the reaction mixture was heated at 70 °C for 1 h, during which the mercury coagulated. The contents were brought to room temperature, decanted to separate mercury, and saturated with sodium chloride. Isolation of the product was accomplished by pouring the cooled, two-phase reaction mixture into a separatory funnel, and the aqueous layer was extracted with ethyl ether (3 × 20 mL). The combined THF–ethyl ether extract was washed with water (2 × 10 mL) and brine (1 × 10 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. The product was isolated by column chromatography over silver nitrate (10%) impregnated silica gel using hexane/ether (5%).

Iodination. To a solution of organoborane prepared as above from acetoxyborohydride (20 mmol) was added iodine (25 mmol) all at once at room temperature, followed by the dropwise addition of 10 mL of 3 M solution of sodium hydroxide in methanol (30 mmol). After stirring for 10 min at room temperature the reaction mixture was decanted from mercury and poured into 50 mL of cold water containing 1 g of sodium thiosulfate to remove excess iodine. The aqueous layer was extracted with ether (3 × 20 mL). The combined THF–ether layer was dried and distilled and the product isolated as above.

Spectral Data. Alcohol (entry 1): ^1H NMR 4.70 (s, 2 H), 3.45–3.75 (m, 1 H), 2.20–2.50 (br, 1 H exchangeable), 1.73 (s, 3 H), 0.97 (d, J = 7 Hz, 3 H); IR (neat, cm^{-1}) 3380, 1640, 1450, 1370, 1020, 880. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.79; H, 11.59.

Iodo compound (entry 1): ^1H NMR 4.80 (s, 2 H), 3.40–3.70 (m, 1 H), 1.70 (s, 3 H), 0.97 (d, J = 6 Hz, 3 H); IR (neat, cm^{-1}) 1640, 882. Anal. Calcd for $C_{10}H_{17}I$: C, 45.47; H, 6.49. Found: C, 45.65; H, 6.41.

Alcohol (entry 2): ^1H NMR 5.97 (m, 1 H), 5.20 (m, 2 H), 3.85 (br, 1 H exchangeable), 3.35 (m, 1 H), 1.20 (s, 3 H), 0.88 (d, J = 6 Hz, 6 H); IR (neat, cm^{-1}) 3320, 2920, 1635, 1450, 1360, 1040. Anal. Calcd for $C_{13}H_{28}SiO_2$: C, 63.88; H, 11.54. Found: C, 63.70; H, 11.69.

Iodo compound (entry 2): ^1H NMR 6.0 (m, 1 H), 5.20 (m, 2 H), 2.91–3.20 (m, 1 H), 1.31 (s, 3 H), 0.97 and 1.0 (2 s, 6 H); IR (neat, cm^{-1}) 2930, 1640, 1450, 1370, 1040. Anal. Calcd for $C_{13}H_{27}OSiI$: C, 44.06; H, 7.67. Found: C, 44.21; H, 7.54.

Alcohol (entry 3): ^1H NMR 6.20 (m, 1 H), 5.03 (m, 4 H), 3.55 (m, 1 H), 2.40 (br, 1 H exchangeable), 1.0 (d, J = 7 Hz, 6 H); IR (neat, cm^{-1}) 3350, 1637, 1470, 1455, 890. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.98; H, 11.62.

Iodo compound (entry 3): ^1H NMR 6.20 (m, 1 H), 5.0 (m, 4 H), 3.1 (m, 1 H), 1.03 (d, J = 7 Hz, 6 H); IR (neat, cm^{-1}) 2920, 1640, 1460, 892. Anal. Calcd for $C_{10}H_{17}I$: C, 45.47; H, 6.49. Found: C, 45.61; H, 6.58.

Alcohol (entry 4): ^1H NMR 4.90 and 5.0 (2 s, 2 H), 3.90 (br, 1 H exchangeable), 3.60–3.75 (m, 1 H), 1.10 (d, J = 7 Hz, 3 H), 0.90 (s, 6 H); IR (neat, cm^{-1}) 3320, 1640, 882, 837. Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.78. Found: C, 80.85; H, 11.57.

Iodo compound (entry 4): ^1H NMR 4.90 and 5.0 (2 s, 2 H), 3.5 (m, 1 H), 1.10 (d, J = 7 Hz, 3 H), 0.90 (s, 6 H); IR (neat, cm^{-1}) 1640, 882. Anal. Calcd for $C_{15}H_{25}I$: C, 54.22; H, 7.58. Found: C, 54.04; H, 7.69.

Alcohol (entry 5): ^1H NMR 3.40 (m, 1 H), 3.10 (br, 1 H, exchangeable), 1.05 (s, 3 H), 1.0 (s, 3 H), 0.90 (d, J = 7 Hz, 3 H), 0.50–0.84 (m, 2 H); IR (neat, cm^{-1}) 3350, 2920, 1370, 1355, 1140. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.75; H, 11.94.

Iodo compound (entry 5): ^1H NMR 3.40–3.60 (m, 1 H), 1.03 (s, 3 H), 1.0 (s, 3 H), 0.93 (d, J = 7 Hz, 3 H), 0.55–0.84 (m, 2 H); IR (neat, cm^{-1}) 2930, 1370, 1360. Anal. Calcd for $C_{10}H_{17}I$: C, 45.47; H, 6.49. Found: C, 45.23; H, 6.58.

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Registry No. Limonene, 138-86-3; limlonene (alcohol), 619-01-2; limonene (iodo compound), 110851-26-8; silated linalool, 59632-77-8; silated linalool (alcohol), 110851-25-7; silated linalool (iodo compound), 110851-27-9; myrcene, 123-35-3; myrcene (alcohol), 24202-03-7; myrcene (iodo compound), 110851-28-0; caryophyllene, 87-44-5; caryophyllene (alcohol), 69855-00-1; caryophyllene (iodo compound), 110851-29-1; 3-carene, 13466-78-9; 3-carene (alcohol), 16725-98-7; 3-carene (iodo compound), 110851-30-4; acetoxyborohydride, 71604-09-6.

Palladium-Catalyzed Syn 1,4-Additions of Silyl-Derived Carboxylates and Phenoxides to Cyclopentadiene Monoepoxide. A Stereo- and Regiocontrolled Route to Differentially Protected *cis*-2-Cyclopentene-1,4-diols[1]

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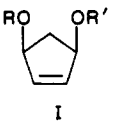
Cyclopentanoids are known to the synthetic practitioner as pivotal ingredients in the total synthesis of many biologically important molecules.[2] A recent escalation in their use has actuated the search for more elegant routes to these highly functionalized compounds. Toward this end, we now report that unsymmetrically protected versions of *cis*-2-cyclopentene-1,4-diol (I) can be conveniently prepared from cyclopentadiene monoepoxide in just one step. Our involvement in this area stems from a continued synthetic fascination with carbocyclic nucleosides.



I

Previously, we communicated[3] an especially direct route to the monoesters (**2a**) and symmetrical diesters (**2b**) of

(1) Presented in part by D.R.D. at the Pacific Conference on Chemistry and Spectroscopy (Western Regional Meeting), October 9–11, 1985, San Francisco, CA.

(2) For a review, see: Harre, M.; Raddatz, P.; Walenta, R.; Winterfeldt, E. *Agnew. Chem., Int. Ed. Engl.* **1982**, *21*, 480.

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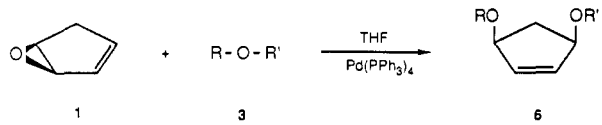
0022-3263/88/1953-0189$01.50/0

Table I. Synthesis of Differentially Protected *cis*-2-Cyclopentene-1,4-diols

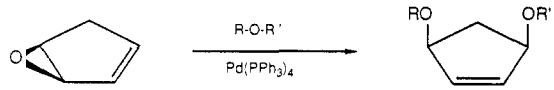


1 3 6

entry	compd	R	R'	ratio[a]	yield,[b,c] %
1	**6a**	Me_3Si	Ac	1.1:1	83
2	**6b**	Et_3Si	Ac	1.5:1	62
3	**6c**	$PhMe_2Si$	Ac	1.1:1	65
4	**6d**	Me_3Si	Bz	1.5:1	76
5	**6e**	Me_3Si	Ph	2:1	23
6	**6f**	Me_3Si	*p*-NO_2Ar	1.1:1	87

[a] This ratio indicates reactant stoichiometry in the format silyl substrate–cyclopentadiene monoepoxide. [b] These are all isolated yields. [c] The yield figures are probably better than indicated; however, the volatile nature of these silyl adducts undoubtedly leads to a loss of material during workup.

cis-2-cyclopentene-1,4-diol by using palladium(0) technology. Carboxylic acids and their corresponding anhydrides were shown to add to cyclopentadiene monoepoxide (**1**) in an exclusively syn 1,4-fashion upon exposure to palladium catalyst (eq 1). Mildly acidic phenols furnish

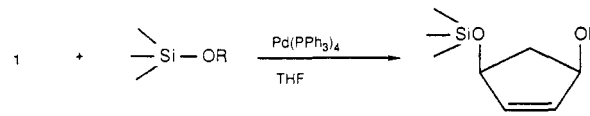


(1)

1

2a, R = Ac, Bz; R' = H
b, R = R' = Ac, Bz
c, R = Ar; R' = H

2c when subjected to similar reaction conditions. At this juncture, we elaborate on these earlier findings and disclose that silyl phenoxides (**3a**) and silyl carboxylates (**3b**) react analogously with **1** to afford the unsymmetrically protected diols **4a** and **4b** (eq 2). The isolated yields range from



(2)

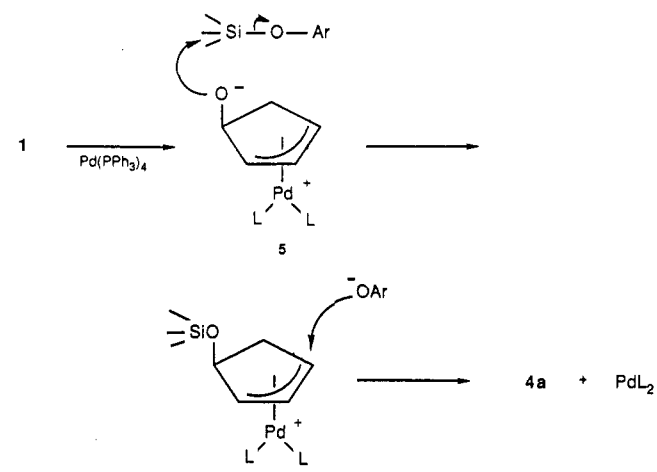
3a, R = Ar
b, R = COR'

4a,b

modest to very good and are tabulated along with other pertinent data in Table I. The cis 1,4-stereochemistry was unambiguously assigned by 200-MHz ^1H NMR measurement.[4]

As expected, the addition reaction between **1** and **3** proceeds with remarkable stereo- and regiochemical specificity. This result is fully consistent with our earlier observations[3] and is undoubtedly a consequence of the transient palladium π-allyl complex[5] **5**. The mechanism for the reaction of intermediate **5** with phenoxy substrates (**3a**) appears straightforward (Scheme I). We and others have recently demonstrated[3,5,6] that the zwitterionic oxygen in **5** may function either as a base or a nucleophile, depending on the nature of the substrate. It would appear likely, therefore, that the initial step in this mechanistic sequence involves alkoxide attack on the electropositive silicon atom with the concomitant displacement of a resonance-stabilized phenoxide ion. The subsequent external

Scheme I



delivery[7] of phenoxide to the distal end of the π-allyl system then yields **4a**.

Support for this mechanism can be evidenced from the stark contrast in adduct yields (Table I) between phenoxy substrate trimethylsilyl *p*-nitrophenoxide (87%, entry 6) and its parent compound trimethylsilyl phenoxide (23%, entry 5). Presumably, these data reflect the relative stabilities of the corresponding phenoxide ions.

Unfortunately, the mechanism for the reaction between intermediate **5** and silyl carboxylates **3b** is not quite as easily discerned. Silyl carboxylates contain two electron-deficient centers, both of which are capable of reaction with alkoxides.[8] Ordinarily, attack on silicon rather than the carbonyl carbon is the preferred route for alkoxy nucleophiles. However, this preference is reversed as steric congestion about silicon is increased.[8] Both modes of reaction are diagramed in Scheme II. Curiously, one obtains the same product regardless of which mechanism is operational because the *cis*-2-cyclopentene-1,4-dioxyl moiety manifests C_s symmetry. Path A (Scheme II) mirrors the mechanism previously described for silyl phenoxides (Scheme I) with one exception: the displaced anion is carboxylate instead of phenoxide. The sequence terminates with the formation of adduct **4b**. In contrast, pathway B involves alkoxide attack at the carbonyl group of **3b**. This generates the acylated palladium π-allyl and trialkylsiloxy anion, which eventually combine to form **4b** as well.

In conclusion, we feel this operationally simple, synthetic shortcut to differentially protected *cis*-2-cyclopentene-1,4-diols should find immediate application in the preparation of highly functionalized cyclopentanoids.

Experimental Section

^1H NMR spectra were measured on a Varian EM 360A (60 MHz) or an IBM AF 200 (200 MHz) spectrometer with $CDCl_3$ as solvent. Infrared spectra were recorded on a Perkin-Elmer 397 spectrometer. High-resolution mass spectrometry was carried out by the Midwest Center for Mass Spectrometry. Elemental analyses were performed by Desert Analytics, Tucson, AZ. The Baker precoated silica gel Si 250F plates (0.25-mm thickness) used for TLC were visualized with anisaldehyde reagent in ethanol. All chromatographic separations employed Baker silica gel (60–200 or 40–140 mesh). Tetrahydrofuran was continuously distilled under nitrogen from a deep blue solution of sodium benzophenone ketyl. Trimethylsilyl phenoxide, trimethylsilyl acetate, triethylacetoxysilane, phenyldimethylacetoxysilane, and *p*-(tri-

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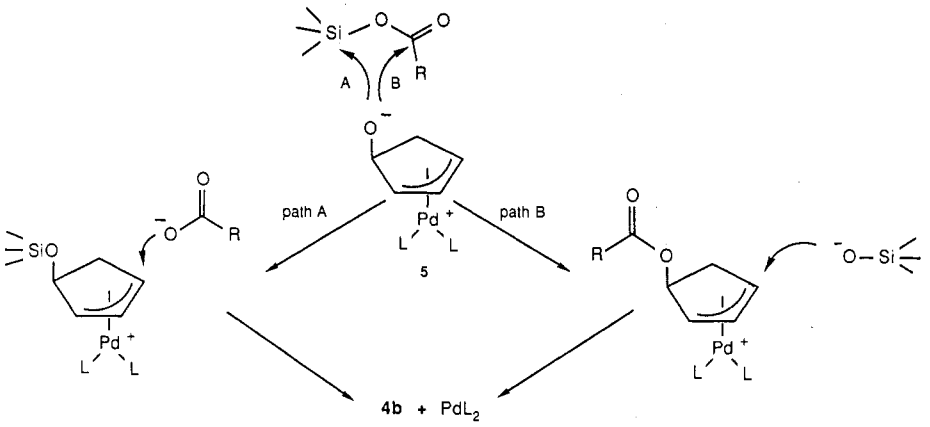
Scheme II



methylsiloxy)nitrobenzene were purchased from Petrarch Systems, Inc. and distilled prior to use. Cyclopentadiene monoepoxide[9] and trimethylsilyl benzoate[10] were prepared according to literature procedures. Tetrakis(triphenylphosphine)palladium was purchased from Aldrich and used without further purification. All reactions were carried out under anhydrous conditions with an inert blanket of nitrogen or argon.

General Procedure for the Preparation of Differentially Protected *cis*-2-Cyclopentene-1,4-diols. To a stirred, ice-cooled solution of trimethylsilyl acetate (463 mg, 3.50 mmol) and tetrakis(triphenylphosphine)palladium(0) (33 mg, 0.029 mmol, 0.95 mol %) in 3 mL of dry tetrahydrofuran was added dropwise over 10 min 250 mg (3.05 mmol) of cyclopentadiene monoepoxide. When addition was complete, the ice bath was removed, and the reaction progress was monitored via TLC (SiO_2, 4:1 hexane–ethyl acetate, R_f 0.53). Complete consumption of starting material generally takes less than 15 min. The reaction was terminated by passing the yellowish solution through a plug of SiO_2 (4.5 g) with absolute ether. The filtrate was carefully concentrated under aspirator pressure, and the residue was chromatographed over SiO_2 (28 g) with pentane–ether (9:1) as the eluent. Removal of the solvent afforded 0.539 (83%) of trimethylsilyl acetate **6a** as a clear, colorless oil: ^{1}H NMR (60 MHz) δ 0.0 (s, 9 H, Me_3Si), 1.61 (dt, J = 5 and 14 Hz, 1 H, β-CH_2), 2.03 (s, 3 H, Ac), 2.79 (overlapping dt, J = 7 and 14 Hz, 1 H, α-CH_2), 4.54–4.84 (m, 1 H, CHOSi), 5.31–5.61 (m, 1 H, CHOAc), 5.95 (br s, 2 H, CH=CH); IR (neat) 2970, 1735 (CO), 1373, 1250 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_3Si$: C, 56.02; H, 8.47. Found: C, 56.01; H, 8.59.

Silyl ethers **6b–f** were prepared under essentially the same conditions.

Triethylsilyl acetate 6b: oil; 62% yield; R_f 0.64 (4:1 hexane–ethyl acetate); ^{1}H NMR (200 MHz) δ 0.60 (q, 6 H, CH_2Si), 0.94 (t, 9 H, CH_3CSi), 1.60 (dt, J = 4.9 and 13.9 Hz, 1 H, β-CH_2), 2.03 (s, 3 H, Ac), 2.78 (overlapping dt, J = 7.3 and 13.9 Hz, 1 H, α-CH_2), 4.67 (m, 1 H, CHOSi), 5.45 (m, 1 H, CHOAc), 5.87 (m, 1 H, CH=CH), 5.96 (m, 1 H, CH=CH); IR (neat) 2960, 1735, (CO), 1370, 1240 cm^{-1}; MS, m/z (relative intensity) 197 (1), 145 (100), 103 (26); HRMS calcd for $C_{13}H_{24}O_3Si$ (M^+) 256.1495, found 256.1500.

Dimethylphenylsilyl acetate 6c: oil; 65% yield; R_f 0.51 (4:1 hexane–ethyl acetate); ^{1}H NMR (60 MHz) δ 0.0 (br s, 6 H, Me_2Si), 1.65 (dt, J = 4.2 and 14 Hz, 1 H, β-CH_2), 2.04 (s, 3 H, Ac), 2.72 (overlapping dt, J = 7 and 14 Hz, 1 H, α-CH_2), 4.52–4.82 (m, 1 H, CHOSi), 5.27–5.57 (m, 1 H, CHOAc), 5.91 (br s, 2 H, CH=CH), 7.25–7.75 (m, 5 H, Ph); IR (neat) 1735 (CO), 1370, 1245 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_3Si$: C, 65.16; H, 7.30. Found: C, 65.11; H, 7.35.

Trimethylsilyl benzoate 6d: oil; 76% yield; R_f 0.64 (4:1 hexane–ethyl acetate); ^{1}H NMR (60 MHz) δ 0.0 (s, 9 H, Me_3Si), 1.64 (dt, J = 5 and 14 Hz, 1 H, α-CH_2), 2.74 (overlapping dt, J = 7 and 14 Hz, 1 H, β-CH_2), 4.43–4.83 (m, 1 H, CHOSi), 5.40–5.79 (m, 1 H, CHOBz), 5.81 (br s, 2 H, CH=CH), 7.08–7.56 (m, 3 H, Ar), and 7.73–8.05 (m, 2 H, Ar); IR (neat) 3160, 1815 (CO), 1375, 1205 cm^{-1}; MS, m/z (relative intensity) 276 (M^+, 0.71), 179 (28), 154 (48), 122 (7), 105 (100); HRMS calcd for $C_{15}H_{20}O_3Si$ (M^+) 276.1182, found 276.1180.

Trimethylsilyl phenyl ether 6e: oil; 23% yield; R_f 0.70 (4:1 hexane–ethyl acetate); ^{1}H NMR (200 MHz) δ 0.01 (s, 9 H, Me_3Si), 1.79 (dt, J = 5.0 and 13.7 Hz, 1 H β-CH_2), 2.86 (overlapping dt, J = 7.1 and 13.7 Hz, 1 H, α-CH_2), 4.74 (m, 1 H, CHOSi), 5.11 (m, 1 H, CHOPh), 6.15 (br s, 2 H, CH=CH), 6.93 (m, 3 H, Ar), 7.29 (m, 2 H, Ar); IR (neat) 2960, 1600, 1495, 1375 cm^{-1}; MS, m/z (relative intensity) 176 (M^+ – Me_3Si, 4), 95 (7), 94 (100), 82 (13); HRMS calcd for $C_{11}H_{12}O_2$ (M^+ – Me_3Si) 176.0832, found 176.0844.

Trimethylsilyl *p*-nitrophenyl ether 6f: oil; 87% yield; R_f 0.51 (4:1 hexane–ethyl acetate); ^{1}H NMR (200 MHz) δ 0.12 (br s, 9 H, Me_3Si), 1.79 (dt, J = 4.6 and 13.9 Hz, 1 H, β-CH_2), 2.91 (overlapping dt, J = 7.2 and 13.9 Hz, 1 H, α-CH_2), 4.78 (m, 1 H, CHOSi), 5.18 (m, 1 H, CHOAr), 6.06 (m, 2 H, CH=CH), 6.95 (m, 2 H, Ar), 8.16 (m, 2 H, Ar); IR (neat) 1514 (NO_2), 1374, 1343 (NO_2), 1255 cm^{-1}; MS, m/z (relative intensity) 293 (M^+, 0.1), 278 (4), 196 (12), 155 (81), 73 (100); HRMS calcd for $C_{14}H_{19}NO_4Si$ (M^+) 293.1083, found 293.1075.

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Registry No. 1, 7129-41-1; **3a**, 2754-27-0; **3b**, 5290-29-9; **3c**, 17887-60-4; **3d**, 2078-12-8; **3e**, 1529-17-5; **3f**, 1014-66-0; **6a**, 111001-25-3; **6b**, 111001-26-4; **6c**, 110874-60-7; **6d**, 110874-61-8; **6e**, 110874-62-9; **6f**, 110874-63-0; $Pd(PPh_3)_4$, 14221-01-3.

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Dual Resonance Functionality in Pyridine 1-Oxides. A Double Multinuclear NMR Approach

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Pyridine 1-oxides have a characteristic N–O functionality that can act as both a π-electron donor and a π-

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