molar ratio of $AlCl_3$/1 from 1.1 to 1.7–2.0, the amount of **3** could be increased to 55%.

To circumvent the ethoxy exchange, the cleavage was run in benzene at 50 °C where yields of pure **2** of up to 84% were realized. On refluxing in benzene, about 8% of dicleaved material, **12**, was obtained, similar to that in acetophenones.[5] Identification of **12** was from conversion to its methylenedioxy derivative, **13**.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus. Melting and boiling points are uncorrected. Nuclear magnetic resonance spectra were recorded at 90 MHz on a Varian EM-390 using Me_4Si as the internal standard. Infrared spectra were recorded on a Perkin-Elmer 457. Microanalyses were performed by M-H-W Laboratories, Garden City, Mich.

2-Hydroxy-3,4,6-trimethoxybenzaldehyde (2). To a solution of 51.0 g (0.226 mol) of **1**[6] in 500 mL of dry benzene was added 33 g (0.248 mol) of anhydrous aluminum chloride. After being shaken for 5 min, the mixture was heated at 50 °C for 7.5 h. Water, 300 mL, was added, and the mixture was shaken to decompose the dark oil. Water, 2.5 L, benzene, 1 L, and 12 M hydrochloric acid, 125 mL, were added, and the mixture was stirred overnight. The clear colored phases were separated. The aqueous phase was extracted with ether and benzene. The combined organic phases were extracted six times with 100-mL portions of 5% sodium hydroxide solution. While being stirred and cooled, the basic solutions were acidified with 110 mL of 12 M hydrochloric acid. The tan solids were dissolved in 250 mL of hot methanol, diluted with 100 mL of hot water, and cooled to produce 40.0 g (84%) of **2** as yellow rods, mp 103–104 °C. Recrystallization from 25% methanol/water produced light yellow thick rods: mp 102.0–102.7 °C; IR (KBr) 2840, 1640, 1635 cm^{-1}; NMR ($CDCl_3$) δ 3.82, 3.89, 3.98 (s, 3 each, OCH_3), 5.97 (s, 1, ArH), 10.12 (s, 1, CHO), 12.27 (s, 1, OH).

Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.70; H, 5.69.

4,6-Dimethoxy-3-ethoxy-2-hydroxybenzaldehyde (3). To a solution of 11.3 g (0.05 mol) of **1** in 600 mL of anhydrous ether was added a solution of 9.35 g (0.07 mol) of anhydrous aluminum chloride in 150 mL of anhydrous ether. The yellow suspension was shaken for 5 min forming a brown oil. After standing at room temperature overnight, the mixture was refluxed 8 h on the steambath. Water, 50 mL, was added and then 6 M hydrochloric acid, 25 mL. After being stirred overnight, the two clear colored phases were separated. The aqueous phase was extracted five times with ether. The combined ethereal solutions were extracted eight times with 25-mL portions of 5% sodium hydroxide solution. The basic washes were acidified with 6 M hydrochloric acid, 55 mL, producing 8.76 g (83%) of a mixture of **2** and **3** containing 38% **3** (from NMR). After being dissolved in 500 mL of ether, the mixture was extracted three times with 100-mL portions of 5% sodium carbonate solution. The ethereal phase was washed with saturated salt solution and dried with anhydrous sodium sulfate. Solvent removal yielded 3.96 g of tan-yellow solids: mp 86–106 °C; NMR ($CDCl_3$) showed 67% of **3** present. Recrystallization from 1:1 ethanol/water resulted in pure **3** as yellow rods: mp 116.3–117.1 °C; IR (KBr) 2850, 1635; NMR ($CDCl_3$) δ 1.36 (t, 3, CH_3, J = 7.2 Hz), 3.90, 3.97 (s, 3 each, OCH_3), 4.04 (q, 2, OCH_2), 5.99 (s, 1, ArH), 10.17 (s, 1, CHO), 12.30 (s, 1, OH).

Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.36; H, 6.28. Acidification of the sodium carbonate washes and recrystallization of the solid produced **2** identical with that produced in aluminum chloride/benzene cleavage.

2-Ethoxy-1,3,5-trimethoxybenzene (10). 2,4,6-Trimethoxyphenol[4] reacts with ethyl sulfate and sodium hydroxide solution forming colorless rods from cyclohexane: mp 48.8–49.4 °C; IR (KBr) 2840, 1235, 1225, 1210 cm^{-1}; NMR ($CDCl_3$) δ 1.36 (t, 3, CH_3, J = 7.2 Hz), 3.80 (s, 3, OCH_3), 3.85 (s, 6, OCH_3), 4.00 (q, 2, OCH_2), 6.19 (s, 2, ArH).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.52; H, 7.47.

5-Ethoxy-1,2,3-trimethoxybenzene (11). Antiarol[7] reacts with ethyl iodide, potassium carbonate, and acetone forming a colorless oil: bp 111 °C (1.7 torr); IR (film) 2850, 1230 cm^{-1}; NMR ($CDCl_3$) δ 1.37 (t, 3, CH_3, J = 7.0 Hz), 3.80 (s, 3, OCH_3), 3.83 (s, 6, OCH_3), 3.97 (q, 2, OCH_2), 6.18 (s, 2, ArH).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.46; H, 7.62.

3-Ethoxy-2,4,6-trimethoxybenzaldehyde (6). A Vilsmeier reaction[8] on **10** produced colorless rods from cyclohexane: mp 60.0–60.9 °C; IR (KBr) 1670, 1255, 1215 cm^{-1}; NMR ($CDCl_3$) δ 1.33 (t, 3, CH_3, J = 7 Hz), 3.89, 3.93, 3.94 (s, 3 each, OCH_3), 3.99 (q, 2, OCH_2), 6.27 (s, 1, ArH), 10.30 (s, 1, CHO).

Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.11; H, 6.75. Also formed from **3** on reaction with methyl sulfate, potassium carbonate and acetone.

6-Ethoxy-2,3,4-trimethoxybenzaldehyde (7). A Vilsmeier reaction on **11** produced from benzene and then 25% methanol/water colorless microscopic rods: mp 57.7–58.5 °C; IR (KBr) 2850, 1680, 1250, 1200 cm^{-1}; NMR ($CDCl_3$) δ 1.47 (t, 3, CH_3, J = 7 Hz), 3.83 (s, 3, OCH_3), 3.96 (s, 6, OCH_3), 4.12 (q, 2, OCH_2), 6.30 (s, 1, ArH), 10.40 (s, 1, CHO).

Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.97; H, 6.75.

2,3-Dihydroxy-4,6-dimethoxybenzaldehyde (12). The procedure for the preparation of **2** was followed but the reaction mixture was refluxed for 8 h. Evaporation of the mother liquors from recrystallization left well-formed golden crystals, mp 114–137 °C. Further crystallization from benzene produced rhombahedral yellow plates: mp 147.8–148.3 °C; IR (KBr) 3340, 2850, 1660 cm^{-1}; NMR ($CDCl_3$) δ 3.90, 4.03 (s, 3 each, OCH_3), 5.13 (s, 1, 3-OH), 6.03 (s, 1, ArH), 10.20 (s, 1, CHO), 12.25 (s, 1, 2-OH).

Anal. Calcd for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C, 54.77; H, 4.99.

4,6-Dimethoxy-2,3-methylenedioxybenzaldehyde (13). From **12** using the procedure of Bonthrone and Cornforth[9] colorless needles formed: mp 166–167 °C; IR (KBr) 2880, 2775, 1675 cm^{-1}; NMR ($CDCl_3/C_6D_6$) δ 3.35, 3.57 (s, 3 each, OCH_3), 5.56 (s, 2, CH_2O_2), 5.70 (s, 1, ArH), 10.32 (s, 1, CHO).

Anal. Calcd for $C_{10}H_{10}O_5$: C, 57.14; H, 4.80. Found: C, 57.27; H, 4.78.

Registry No.—**1**, 41038-46-4; **2**, 65162-31-4; **3**, 69832-50-4; **6**, 69832-51-5; **7**, 69832-52-6; **8**, 20491-92-3; **9**, 642-71-7; **10**, 69832-53-7; **11**, 69832-54-8; **12**, 69832-55-9; **13**, 69832-56-0.

References and Notes

(1) The monocleaved product is a hydroxytrimethoxybenzaldehyde. The peak in the NMR at 12.27 shows the hydroxy group is hydrogen bonded to the adjacent aldehyde. Only two compounds are possible, the 2-hydroxy-3,4,6-trimethoxybenzaldehyde and the 6-hydroxy-2,3,4-trimethoxybenzaldehyde. This latter compound is known,[7] having mp 65 °C. This leaves the 2-hydroxy compound as the only other possibility.
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Vitamin B_{12s} Catalyzed Dechlorination of 1,1-Dichloro-2,2-bis(*p*-chlorophenyl)ethane. Novel Synthesis of Substituted Stilbenes

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The bioinorganic chemistry of vitamin B_{12} and related molecules, in aqueous and micellar environments, is well documented.[1-6] From a purely chemical point of view, vitamin B_{12s} is an extraordinary nucleophile whose participation in dechlorination reactions would not be unexpected. It is our purpose to report a novel, vitamin B_{12s}-catalyzed synthesis of substituted stilbenes starting with readily available materials.

The reaction consists essentially of the addition of a methanol solution of 1,1-dichloro-2,2-bis(*p*-chlorophenyl)-ethane, DDD, to an aqueous solution of vitamin B_{12s} under

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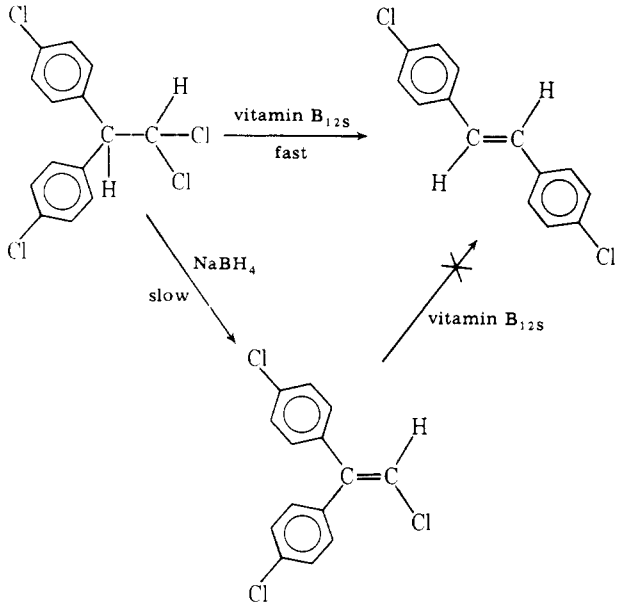
Scheme I



a nitrogen atmosphere in the absence of light. The products obtained in the reaction were *trans*-4,4′-dichlorostilbene, DCS, and trace amounts of 1-chloro-2,2-bis(*p*-chlorophenyl)ethylene, DDMU. The latter was proven not to be an intermediate, since it does not react with vitamin B_{12s} under identical conditions.

Scheme I describes the reactions occurring under our experimental conditions.

Vitamin B_{12s}, generated by the reduction of aquocobalamin, appears to be the reactive species in solution displacing chloride ion (detected by $AgNO_3$ titration) through nucleophilic substitution. Indeed, vitamin B_{12r}, generated by photolysis of methylcobalamin in a N_2 atmosphere, does not react with DDD to produce DCS. Apparently, the reaction occurs with formation of cobalt–carbon intermediates followed by homolytic bond rupture, a mechanism which is common for vitamin B_{12}-catalyzed reactions. An alternative mechanism could be a Co–Cl α-elimination to yield a carbene or carbenoid type intermediate which would then rearrange to the product. It is important to remark that $CoCl_2$ or $Co(NO_3)_2$ under identical conditions do not react with DDD to produce *trans*-4,4′-dichlorostilbene. Indeed, the cobalt I nucleophilicity is highly increased in vitamin B_{12s} due to the effect of the corrin ring.

A similar reaction using 1,1-dichloro-2,2-bis(*p*-ethylphenyl)ethane resulted in the production of *trans*-4,4′-diethylstilbene. The simplicity of the present method as compared to the Wittig reaction, decarboxylation of phenylcynnamic acid, Clemmensen reduction of benzoins, and other available methods,[7] added to the fact that only the trans isomer is formed, more than substantiates its use at the laboratory level for synthesis of substituted *trans*-stilbenes.

Experimental Section

All melting points are uncorrected. IR spectra were determined with a Perkin-Elmer 720 spectrophotometer. NMR spectra were run in $CDCl_3$ on a Varian HA-100 spectrometer using Me_4Si as the internal standard. UV spectra were obtained in methanol by means of a Varian 634 spectrophotometer.

Vitamin B_{12a}, aquocobalamin, was purchased from Merck Chemical Co., DDD from Aldrich Chem. Co., and 1,1-dichloro-2,2-bis(*p*-ethylphenyl)ethane from Chemical Service. The purity of the three reagents mentioned above was found to be satisfactory by thin-layer chromatography. All the other compounds were of the best reagent grade available.

Typically, a solution of aquocobalamin (400 mg in 25 mL of water) was purged with purified nitrogen in a closed vessel through rubber septa for 2 h. A capillary tube punched just through the rubber septa provided the vent. Subsequent to deoxygenation, 200 mg of $NaBH_4$ was added, and the mixture was allowed to react for 10 min. A solution of 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane (DDD) (1330 mg in 250 mL of methanol, also purged for 2 h with purified nitrogen) was added and allowed to react. The reaction was monitored by TLC (using silica gel GF_{254}, type 60, Merck, in 200 × 200 × 0.30 mm plates, and petroleum ether, fraction 30–60, Ecibra, as developing solvent). In addition, $NaBH_4$ was added to the reaction mixture until DDD disappeared on the TLC plate. The reaction was complete in about 20 min.

As the reaction proceeded, a white precipitale was formed and filtered off. The colored solution was then extracted with several portions of chloroform to remove the organic fraction. The chloroform extract was then rotary evaporated to dryness, mixed with the previously filtered white precipitate, and dried in vacuo in an Abderhaldem type apparatus over P_2O_5. A total weight of 1070 mg of the organic fraction was recovered and used for subsequent analysis. TLC showed the presence of a fluorescent compound (R_f 0.60) and traces of 1-chloro-2,2-bis(*p*-chlorophenyl)ethylene (DDMU) as identified by its UV and IR spectrum after separation by preparative layer chromatography (see the spectral data below).

A blank reaction in which vitamin B_{12a} was absent was carried out under identical experimental conditions (see above) and showed only DDD and DDMU. The appearance of the later occurred very slowly, with the reaction being half complete in 72 h. DDMU was purified (mp 64–65 °C) and its UV (λ_{max} 242 nm and a shoulder at 257 nm), IR (main bands at 3030, 1600, 1580, 1480, 1390, 1080, 1010, 855, and 800 cm^{-1} in KBr pellet), and NMR spectra (7.23 aromatic protons multiplet and 6.57 ppm ethylenic proton singlet, integration 8:1) were found to be identical with those of a sample prepared by dehydrochlorination of DDD with alcoholic KOH. Furthermore, a sample of DDMU treated with $NaBH_4$ in the presence of vitamin B_{12a} as previously described does not react. Accordingly, it cannot be an intermediate in the production of the fluorescent compound.

The organic fraction containing the fluorescent product was crystallized several times from 95% ethanol until DDMU could not be detected by thin-layer chromatography and dried in vacuo over P_2O_5 (mp 173–174 °C). The fluorescent compound was identified as *trans*-4,4′-dichlorostilbene since its UV (λ_{max} 305 and 315 nm), NMR (aromatic A_2B_2 pattern centered at 7.22 ppm and a singlet at 6.88 ppm for the ethylenic protons, 4:1 integration), and infrared spectral data (KBr pellet, main bands at 1632, 1590, 1485, 1410, 1100, 1090, 1015, 970, and 830 cm^{-1} besides the aromatic and olefinic C–H stretching vibrations) were identical with those of an authentic sample.

The reaction can be carried out with higher catalyst to substrate ratio. Indeed, using 50 mg of vitamin B_{12a} the reaction goes to completion, but higher amounts of DDMU (ca 10%) are formed.

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Registry No.—Vitamin B_{12s}, 18534-66-2; vitamin B_{12a}, 13422-51-0; DDD, 72-54-8; DCS, 1657-56-3; DDMU, 1022-22-6.

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Partial Rate Factors for the Thallation of Toluene

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McKillop and Taylor and their associates have very successfully developed the aromatic thallation reaction into an important synthetic method useful for the preparation of

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