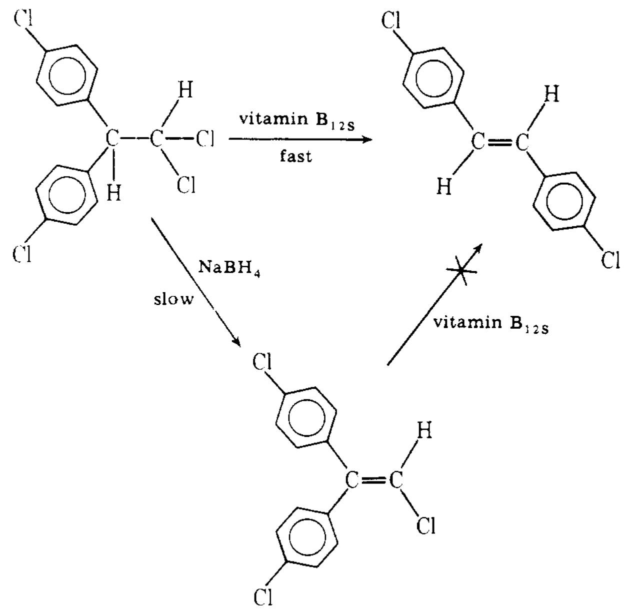
Scheme I



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$_4$Si 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$_2$O$_5$. 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$_2$O$_5$ (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$_2$B$_2$ 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.

Acknowledgments. One of us (Faruk Nome) gratefully acknowledges CNPq, for support of this work.

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

Table I. Relative Rate Constants for the Reaction of Thallium(III) Trifluoroacetic Acid at 25 °C

concn, M			rel rate,
$[CH_3C_6H_5]$	$[C_6H_6]$	$[Tl(O_2CCF_3)_3]$	k_T/k_B
0.401	2.16	0.194	38.8
0.200	2.00	0.097	45.4
0.202	2.07	0.107	43.7
0.200	2.30	0.096	43.9
0.106	2.45	0.051	45.8

many compounds.[1] The thallation reaction is often described as a typical electrophilic aromatic substitution reaction similar, for example, to mercuration. However, studies of the quantitative aspects of the reaction have not yielded consistent results. Briody and Moore attempted to measure the absolute rate constants for the thallation of toluene and benzene. The reaction of thallium(III) trifluoroacetate with benzene in trifluoroacetic acid was too fast for convenient study.[2] To circumvent this difficulty, they studied the reaction in mixtures of acetic acid and trifluoroacetic acid at 25 °C. They reported that the toluene to benzene rate ratio was about 7 under these conditions. Subsequently, they studied the perchloric and sulfuric acid-catalyzed thallation of benzene and toluene in mixtures of acetic acid and water at 70 °C.[3] Unfortunately, the kinetic data did not conform to a simple rate law presumably because there are numerous thallium(III) reagents present in the acidic aqueous acetic acid solution. The toluene to benzene rate ratios determined in this study ranged from 1.9 to 15.5. Briody and Moore also determined the isomer distribution for the acid-catalyzed reaction in aqueous acetic acid at 70 °C. These data also varied considerably. Olah and his students reported that k_T/k_B was 33 for this reaction in trifluoroacetic acid.[4]

We were puzzled by the different values determined for the k_T/k_B ratio. Inasmuch as thallium(III) trifluoroacetate is a good oxidizing agent, we thought that the deviations from this linear free-energy relationship might be real and might indicate that the thallation reaction proceeded by a novel mechanism, e.g., electron transfer.

Accordingly, we have measured the toluene to benzene rate ratio and the isomer distribution under the conditions used in most preparative work, i.e., for the reaction of the aromatic compounds with thallium(III) trifluoroacetate in trifluoroacetic acid at 25 °C. These conditions were chosen to avoid the equilibration of the thallium(III) ligands which occurs in mixed solvents to avoid the isomerization of the products which occurs at higher temperature.

Results and Discussion

Competition methods were used in this work to avoid the inaccuracies which develop because the reaction rate is large. Five independent experiments were performed in which the toluene to benzene ratio varied from about 0.2 to 0.05 and in which the thallium(III) trifluoroacetate concentration changed by a factor of 2. The reaction solutions were poured into aqueous potassium iodide to quench the reaction and to convert the arylthallium bis(trifluoroacetates) to aryl iodides for convenient analysis. The results are summarized in Table I.

The iodomethylbenzenes were separated from the other product of the reaction by gas chromatography. The isomer distribution was determined by nuclear magnetic resonance spectroscopy to be 9.7 ± 1.0% 2-, 3.5 ± 0.5% 3-, and 86.8 ± 1.1% 4-tolylthallium bis(trifluoroacetate). These observations are in good accord with a previous measurement of the isomer distribution for this reaction.[1a] Our experimental results are in reasonable agreement with Olah's observations.[4]

The partial rate factors for thallation are compared with the information for mercuration in Table II.

The selectivity factors, log (p_f^{Me}/m_f^{Me}), for these reactions at 25 °C are 1.3 and 1.8 indicative of ρ^+ values of about −5.0 and −7.0 respectively for mercuration and thallation. The values of log p_f^{Me}/log m_f^{Me} are 4.1 and 3.6, respectively. These results are well within the range determined for many conventional electrophilic substitution reactions, 4.0 ± 0.5.[5] These observations offer strong support for the view that thallation does indeed proceed via a conventional mechanism presumably through the Wheland intermediate.

Experimental Section

Materials. The starting materials and reference compounds used in this work were obtained from commercial sources. The aryl iodides were purified by distillation prior to their use as reference compounds. These materials were shown to be free of contamination by sensitive analytical methods.

Competition Experiments. Preliminary work indicated that the reaction could be quite conveniently studied by competition methods. In a typical experiment, thallium(III) trifluoroacetate (20 mmol) in trifluoroacetic acid (5.00 mL) at 25 °C was added to a solution of benzene (22.0 mmol) and toluene (4.30 mmol) in trifluoroacetic acid (5.00 mL) at 25 °C. The reagents were thoroughly mixed and the reaction was allowed to proceed for 7 min. The reaction was quenched by the addition of potassium iodide (0.5g) in water (10 mL). The aryl iodides were isolated by the procedure described by McKillop and his associates.[1a] A known quantity of 4-methylnitrobenzene was added to the ether solution of the products. The ether was then carefully removed by fractionation. The iodobenzene to iodotoluene ratio was determined by gas chromatography using SE 30 on Chromosorb W. The relationship between the areas and the product ratios and yield was established by the analysis of known mixtures of the reference compound and the aryl iodides. The relative rates were assessed by the Ingold–Shaw expression.

Isomer Distribution. The study of the iodomethylbenzenes and their mixtures established that the resonance signals of the three isomers observed at 270 MHz were sufficiently distinctive to provide a confident analysis of the isomer distribution. The ortho to meta ratio was readily established by the well-separated resonances of H_6 in the 1,2 isomer at 7.80 ppm and H_4 in the 1,3 isomer at 7.08 ppm. Known mixtures containing about 10% 2-, 90% 4-, and 2.0, 3.0, or 3.8% 1-iodo-3-methylbenzene were used to define the relationship between the areas of the resonances and the mole ratios. The ortho to meta and para ratio was determined in several ways. In the high-field region, the singlet resonance for the 2 isomer at 2.43 ppm was compared to the overlapping resonances of the 3 and 4 isomers at 2.30 ppm. In the low-field region, the doublet resonance of H_6 of the 2 isomer at 7.80 ppm was compared with the overlapping multiplet resonance of H_2 of the 4 isomer and H_2 and H_6 of the 3 isomer near 7.56 ppm. This H_6 resonance of the 2 isomer was also compared with the overlapping

Table II. Relative Rate Data and Isomer Distributions for the Mercuration and Thallation Reactions

		isomer distribution			partial rate factor		
reaction, conditions	k_T/k_B	ortho	meta	para	o_f	m_f	p_f
mercuration, $Hg(O_2CCF_3)_2$, CF_3CO_2H, 25 °C[a]	9.89	12.2	8.6	79.2	3.62	2.55	46.9
mercuration, 0 °C[b]	18	17.4	5.9	76.7	18.8	3.18	82.8
thallation, $Tl(O_2CCF_3)_3$, CF_3CO_2H, 25 °C	43.5	9.7	3.5	86.8	12.7	4.5	226
thallation, 25 °C[b]	33	9.7	5.8	84.6	9.6	5.7	168

[a] Reference 6. [b] Reference 4. This study.

multiplet resonances of H_3 of the 4 isomer and H_5 of the 3 isomer and H_3 of the 2 isomer. All these approaches yielded results that were in good agreement.

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Registry No.—$Tl(O_2CCF_3)_3$, 23586-53-0; $CH_3C_6H_5$, 108-88-3; C_6H_6, 71-43-2; 2-tolylthallium bis(trifluoroacetate), 42006-01-9; 3-tolylthallium bis(trifluoroacetate), 55288-00-1; 4-tolylthallium bis(trifluoroacetate), 23586-55-2.

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Lithium Vapor Synthesis for 1,5-Dilithiopentane and 1,6-Dilithiohexane and the Reaction of Lithium Vapor with Dihalopropanes

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Previously, the one direction taken in our work directed toward the development of general synthetic methods for polylithium organic compounds[1-5] was an investigation of the reaction of alkanes which were halogen substituted at several sites. We reported[3] that the products were completely lithium-substituted alkanes and lower molecular weight fragments. The principal product was found to be the completely lithium-substituted analogue of the parent alkane. For example, the reaction of 1-bromopropane gave a 20% yield of a solid polymeric lithium compound, octalithiopropane.[3]

$$Li_{(g)}(900\ °C) + BrCH_2CH_2CH_3 \rightarrow \underset{20\%}{CLi_3CLi_2CLi_3} + \text{completely lithium-substituted fragments}$$

The abstraction reaction of lithium vapor with the carbon–halogen bond is an extremely exothermic reaction, (i.e., ~110 kcal/mol), and the subsequent lithium atom reaction with the alkyl radical forms a 56 kcal/mol bond. The subsequent monolithium-substituted product is undoubtedly vibrationally excited, enabling the reaction to proceed toward more extensive lithium substitution for hydrogen.

We have found that alkanes will not react with lithium vapor until they are heated to temperatures on the order of 800 °C before being mixed with lithium vapor, and are thus vibrationally excited over a continuum of vibrational states. Based on our studies in this area,[3] the effect of vibrational excitation occurs only through approximately three carbon–carbon bonds, so that longer chain compounds are not completely substituted by lithium.

In the present study, milder reaction conditions have been sought and a modified reactor system (Figure 1) has been designed to facilitate more selective substitution of lithium at the carbon–chlorine bond and the synthesis of dilithio-substituted alkanes from dichloralkanes. 1,5-Dichloropentane, 1,6-dichlorohexane, 1,3-dichloropropane, and 1,3-dibromopropane were chosen for this study.

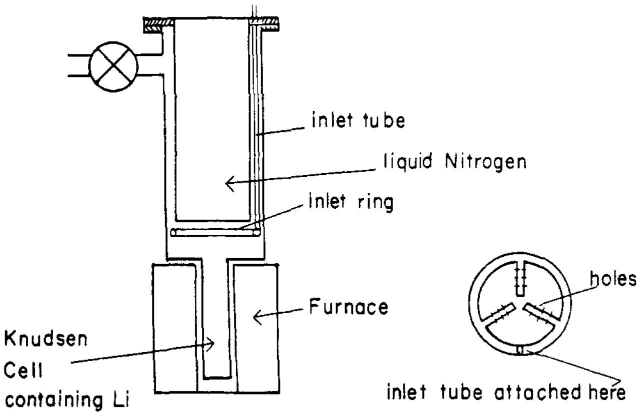

Figure 1. The improved reactor.

In a typical reaction, 1,5-dichloropentane was studied in a stainless steel reactor (Figure 1) with an Inconel Knudsen cell. One-quarter of a milliliter or 2×10^{-3} mol of 1,5-dichloropentane was admitted to the reactor over a 25-min period, a rate of 8×10^{-5} mol/min. The extremely reactive products were removed from the cold finger under argon and carefully hydrolyzed using D_2O on a vacuum line. Excess D_2O was removed using a −95 °C trap, and the products were then separated by gas chromatography. The same procedure was followed for 1,6-dichlorohexane, except that this reactant was admitted to the reactor at a rate of 8×10^{-5} mol/min for 25 min. The reactants 1,3-dihcloropropane and 1,3-dibromopropane were admitted over a 25-min period at a rate of 2×10^{-5} mol/min.

The primary methods of characterization of each fraction were mass spectroscopy and GLC retention times. The characterization of the deuterium substitution sites was unambiguous using mass spectroscopy, but for the title compounds the deuterium substitution was also confirmed by ^1H NMR.

The hexane, pentane, butane, and propane, etc., fractions were collected separately for high-resolution mass spectra to positively identify each species. The entire product mixture was also analyzed by low-resolution mass spectroscopy. The product distributions shown in Table I are averages of at least three runs, each with a reproducibility of ±5%.

Table I. Distribution of Hydrolysis Products (%)

	1,5-dichloropentane	1,6-dichlorohexane
C_2D_6	11	23
C_2D_4	1	3
C_2D_2	28	19
C_3D_8	7	7
C_3D_6	2	4
C_3D_4	19	8
C_4D_{10}	1	5[a]
$DCH_2(CH_2)_3CH_2D$	31	trace
$DCH_2(CH_2)_4CH_2D$		31

	1,3-dibromopropane	1,3-dichloropropane
C_2D_6	24	29
C_2D_4	1	1
C_2D_2	6	8
C_3D_8	12	33
C_3D_6	47	13
C_3D_4	trace	trace
C_4D_{10}	9	6

[a] For 1,6-dichlorohexane, the butane produced in hydrolysis was composed of a mixture of butanes containing 1–10 deuteriums.

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