DDD, which was the precursor of the stilbene. This result indicates a difference of behavior of DDT and DDD under the same conditions: DDT is only dechlorinated to DDD while DDD rearranges to the dichlorostilbene.

In order to compare our system with the above reaction, which, according to Castro and Kray[14] should proceed via carbenoid intermediates, we reacted DDT with vitamin B_{12s}. A mixture of products was obtained, of which the 4,4′-dichlorostilbene comprised about 45%. The chlorinated stilbene, RCH=C(Cl)R, which should arise from a direct rearrangement of DDT, in a manner analogous to the DDD rearrangement, was not formed. Our results thus parallel the reaction of DDT with chromous chloride in the sense that, here again, DDD behaved differently in the presence of B_{12s}. DDT, contrary to DDD, does not rearrange but simply dechlorinates to DDD.

In conclusion, the present paper reports an interesting rearrangement of geminal dichloroethanes **3** in the presence of vitamin B_{12s} analogues. Although the reaction is not restricted to cobalt complexes, the smoothness and ease of the conversion, as compared to those of other methods, are noteworthy. Thus, rearrangements take place at room temperature in 5–15 min with reasonable yields. Much longer reaction times and more drastic conditions are required to effect the same transformation with other metal salts, and the yields are much lower. The reported reaction is also interesting from a mechanistic point of view. Our results point to a cobalt carbenoid complex as the rearranging species in the formation of stilbenes from dichloroethanes **3**. Many questions regarding the exact nature of this species remain to be answered. Nevertheless, our results represent a contribution to a better understanding of metal carbenoid chemistry, in particular to the little explored field of alkylcobaloxime rearrangements.

Experimental Section

^{1}H NMR spectra were determined on a Varian Model T-60 with $(CH_3)_4Si$ as an internal reference. Infrared spectra were measured with a Perkin-Elmer 720 apparatus. Gas chromatographic analyses were obtained with a CG 370 chromatograph. Melting points were taken with a Koffler hot-stage apparatus and are not corrected.

1,1-Dichloro-2,2-bis(*p*-chlorophenyl)ethane (DDD), 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (DDT), and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene were purchased from Aldrich Chemical Co., and vitamin B_{12} was purchased from Sigma Chemical Co. The following 1,1-dichloro-2,2-diarylethanes **3** were prepared by reaction of the corresponding arenes with dichloroacetaldehyde diethyl acetal[16] in the presence of sulfuric acid;[8] 1,1-dichloro-2,2-diphenylethane, mp 76 °C (lit.[17] mp 74 °C); 1,1-dichloro-2,2-bis(*p*-methylphenyl)ethane, mp 79 °C, (lit.[17] mp 80 °C); 1,1-dichloro-2,2-bis(*p*-ethylphenyl)ethane, mp 55 °C (lit.[17] mp 56–57 °C); 1,1-dichloro-2,2-bis(*p*-methoxyphenyl)ethane, mp 116 °C (lit.[18] mp 115–116 °C); 1,1-dichloro-2,2-bis(*p*-bromophenyl)ethane, mp 135 °C (lit.[19] mp 133 °C).

Preparation of Stilbenes 4. General Procedure. Sodium borohydride (0.46 g, 12 mmol) was added under nitrogen to a suspension of bis(dimethylglyoximato)cobalt(II)[20] (0.65 g, 1.8 mmol) in methanol–water (3:1, 5 mL). To the resulting dark blue solution was then added, after the gaseous evolution had subsided (2–3 min), a solution of a dichlorodiarylethane (**3**, ca. 1.2 mmol) in methanol (ca. 20 mL) previously flushed with nitrogen. The stilbene **4** began to crystallize out of the reaction mixture after 5 min. The product was filtered after 40 min and recrystallized from ethanol or acetic acid. All stilbenes **4** thus obtained were characterized by their IR and NMR spectra, identical with the spectra of authentic samples. Specific melting points and yields are given in Table I.

Reaction of DDD with B_{12s}. In a similar procedure vitamin B_{12} (0.1 g, 0.074 mmol) and sodium borohydride (0.46 g, 12 mmol) reacted with DDD (0.4 g, 1.2 mmol) to give *trans*-4,4′-dichlorostilbene: 0.196 g (63%); recrystallized from acetic acid; mp 176 °C (lit.[21] mp 175–176 °C); IR (KBr) 3050, 1590, 1490, 1090, 970, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.0 (2 H, s), 7.4 (8 H, m).

Reaction of DDD with Co^{I}Salen. Bis(*N*,*N*′-disalicylalethylenediamine)cobalt(II)[22] (0.65 g, 1.8 mmol) and sodium borohydride (0.46 g, 12 mmol) reacted with DDD (0.4 g, 1.2 mmol) to give *trans*-4,4′-dichlorostilbene (0.12 g, 38%), characterized as above.

Reaction of DDT with Vitamin B_{12s}. A solution of DDT (0.1 g, 2.6 mmol) in methanol (60 mL) was added under nitrogen to a solution of vitamin B_{12s}, generated by treatment of B_{12} (0.1 g, 0.074 mmol) with sodium borohydride (0.1 g, 2.6 mmol) in water (6 mL). After 1 h of reaction, the solution was rotary evaporated, the residue extracted with chloroform (30 mL), and the organic layer analyzed by gas chromatography (column OV-17, column temperature 190 °C). Comparison with authentic samples revealed DDD (18%), *trans*-4,4′-dichlorostilbene (44%), and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (20%) as major components of the product mixture.

Reaction of DDD with Copper. A suspension of DDD (1.28 g, 4 mmol), powdered copper (0.63 g, 10 mmol), and iodine (0.254 g, 1 mmol) in toluene (15 mL) was refluxed for 65 h. The suspension was then filtered and the filtrate analyzed by GLC (column OV-17, temperature 200 °C); only DDD and *trans*-4,4′-dichlorostilbene, in a 92:8 ratio, were detected in the mixture.

Acknowledgment. Financial help from the Conselho Nacional de Pesquisa (CNPq) is gratefully acknowledged.

Registry No. 1,1-Dichloro-2,2-bis(*p*-chlorophenyl)ethane, 72-54-8; 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane, 50-29-3; dichloroacetaldehyde diethyl acetal, 619-33-0; 1,1-dichloro-2,2-diphenylethane, 2387-16-8; 1,1-dichloro-2,2-bis(*p*-methylphenyl)ethane, 26204-07-9; 1,1-dichloro-2,2-bis(*p*-ethylphenyl)ethane, 72-56-0; 1,1-dichloro-2,2-bis(*p*-methoxyphenyl)ethane, 7388-31-0; 1,1-dichloro-2,2-bis(*p*-bromophenyl)ethane, 5216-53-5; benzene, 71-43-2; methylbenzene, 108-88-3; ethylbenzene, 100-41-4; methoxybenzene, 100-66-3; bromobenzene, 108-86-1; sodium borohydride, 16940-66-2; bis(dimethylglyoximato)cobalt(II), 36451-49-7; vitamin B_{12s}, 18534-66-2; bis(*N*,*N*′-disalicylalethylenediamine)cobalt(I), 26220-77-9; copper, 7440-50-8.

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Mechanism of Bromination of 1,5-Diacetoxynaphthalene

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Bromojuglone derivatives have proven to be extremely useful in controlling the regiochemistry of Diels–Alder reactions, particularly in synthetic approaches toward a variety of anthracyclines.[2] Until recently, the reported

(1) Camille and Henry Dreyfus Teacher–Scholar, 1978–1983; Fellow of the Alfred P. Sloan Foundation, 1979–1981.

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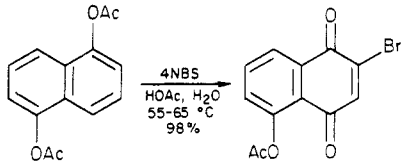
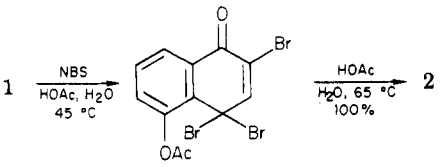
syntheses of 2- and 3-bromojuglone and their derivatives suffered from either very low yields[3] or involved multistep procedures.[4] These difficulties were overcome by Heinzman and Grunwell,[5] who reported a high-yield, one-step synthesis of the acetates of 2- and 3-bromojuglone from 1,5-diacetoxynaphthalene (1) and 1,8-diacetoxynaphthalene, respectively. We report our observations regarding the mechanism of this useful reaction as applied to the preparation of 2-bromojuglone acetate (2).



1 2

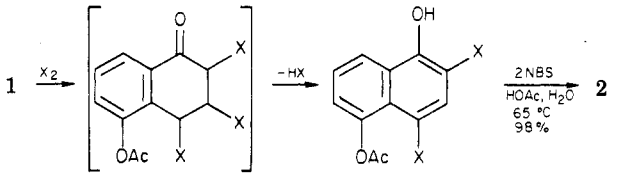
In connection with our work toward the synthesis of aclacinomycin,[6] we required 5-acetoxy-2-bromojuglone (2) as one of our initial intermediates. Reaction of 1,5-diacetoxynaphthalene (1) with *N*-bromosuccinimide (NBS) dissolved in dilute acetic acid at 55–65 °C did indeed give 5-acetoxy-2-bromojuglone (2) in excellent yield. However, on several occasions we observed a second product that could not be separated from the desired bromonaphthoquinone. Formation of this impurity proved to be temperature dependent and at lower temperatures it became the predominant reaction product. When the reaction temperature was lowered to 45 °C, a pale yellow solid could be isolated by filtration of the reaction mixture. Recrystallization of this solid from ligroin (60–90 °C) yielded colorless needles, mp 125–125.5 °C. We have identified this product as 5-acetoxy-2,4,4-tribromonaphthalen-1-one (3) by examination of its spectroscopic data, especially ultraviolet and mass spectra. Formation of compound 3 cannot be accounted for by the previously proposed mechanism[5] for this reaction.



3

Formation of acetoxytrihalonaphthalenones under similar reaction conditions is not unprecedented. Wheeler and Mattox[7] reported a trichloro compound obtained on treatment of 1,5-diacetoxynaphthalene with chlorine in glacial acetic acid. The structure was later shown by Thomson[8] to be the analogous 5-acetoxy-2,4,4-trichloronaphthalen-1-one. This compound when refluxed with aqueous alcohol was readily converted into 5-acetoxy-2-chlorojuglone. Similarly, our tribromonaphthalenone 3, on warming in aqueous acetic acid, is quantitatively converted into 5-acetoxy-2-bromojuglone (2), thus suggesting that this compound is an intermediate in the mechanism for the formation of 2 from 1.

The mechanism of formation of 3 may involve a rather complicated reaction sequence. de la Mare[9] has studied the chlorination of 1,5-diacetoxynaphthalene in glacial acetic acid in great detail. In this reaction, the initial product is 5-acetoxy-2,3,4-trichloro-3,4-dihydronaphthalen-1(2*H*)-one (4a) formed by addition of chlorine to the naphthalene system and chlorodeacylation. This intermediate is unstable under the reaction conditions, and subsequent dehydrochlorination gives 5-acetoxy-2,4-dichloronaphthol (5a). Calò[10] has suggested that, in the



4a, X = Cl
b, X = Br

5a, X = Cl
b, X = Br

reaction of phenol with NBS in acetic acid, the actual brominating agent is molecular bromine. Therefore, an analogous pathway might be suggested for the bromination of 1,5-diacetoxynaphthalene (1) with NBS in aqueous acetic acid. However, it is also possible that electrophilic bromodeacetylation occurs directly to give the monobromophenol, which then is rapidly brominated to give 5b. Although we favor the de la Mare type mechanism via 4b, we cannot prove it at present.

Electrophilic bromination of 5-acetoxy-2,4-dibromonaphthol (5b) in the 4-position would give the observed tribromo intermediate 3 directly. However, chlorination of 5-acetoxy-2,4-dichloronaphthol (5a) has been shown to occur in the 2-position initially, followed by a rapid rearrangement of chlorine to the 4-position.[9] This rearrangement is rapid in acetic acid, and we were unable to detect any of the 2,2,4-tribromo isomer. Hydrolysis of either of these isomers would give the observed reaction product, 5-acetoxy-2-bromojuglone (2).

Further evidence that 5-acetoxy-2,4-dibromonaphthol (5b) is indeed an intermediate in the conversion of 1 to 2 was shown by reaction of 5b, prepared by the procedure of Carter et al.,[3b] with NBS in aqueous acetic acid. Under these conditions the bromojuglone 2 is produced in 98% yield.

Therefore our investigation has given strong evidence that the mechanism of bromination of 1 with NBS in acetic acid involves initial formation of 5b (perhaps by elimination of 1 mol of HBr from 4b). Further bromination of 5b under the reaction conditions would lead to the 2,4,4-tribromo compound 3 (presumably via the 2,2,4-tribromo isomer), which is then hydrolyzed to the final product, 2-bromojuglone acetate (2).

Experimental Section

1,5-Diacetoxynaphthalene (1). This compound was prepared by acetylation of naphthalene-1,5-diol by a slight modification of the method of Leman.[11]

2-Bromojuglone Acetate (2) from 1. This preparation was carried out according to the method of Heinzmann and Grunwell.[5]

5-Acetoxy-2,4,4-tribromonaphthalen-1-one (3). To a solution of 7.2 g (40 mmol) of *N*-bromosuccinimide in 100 mL of acetic acid and 200 mL of H_2O, maintained at 45 °C, was added,

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dropwise with stirring, a warm solution of 2.4 g (10 mmol) of 1,5-diacetoxynaphthalene (1) in 100 mL of acetic acid. The solution was stirred at 45 °C for 40 min and then filtered to collect the pale yellow precipitate. The precipitate was washed several times with H_2O and then dried under vacuum. Recrystallization from ligroin (60–90 °C) gave 2.37 g (5.4 mmol, 54%) of **3** as colorless needles: mp 125–125.5 °C; IR ($CHCl_3$) 1775, 1685, 1195 cm^{-1}; UV_{max} (hexane) 261 nm (log ϵ 4.04), 313 (3.41); ^1H NMR ($CDCl_3$, 200 MHz) δ 2.52 (3 H, s), 7.58–7.63 (2 H, m), 7.96 (1 H, s), 8.10 (1 H, dd, J = 7.2 Hz); mass spectrum (isobutane chemical ionization), m/e 443, 442, 441, 440, 439, 437, 363, 362, 361, 359, 283, 281.

2-Bromojuglone Acetate (2) from 3. A solution of 0.117 g (0.266 mmol) of **3** in 10 mL of acetic acid and 10 mL of H_2O was heated at 70 °C for 50 min. The solution was diluted with 50 mL of H_2O and then cooled to 25 °C and extracted with $CHCl_3$ (3 × 50 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried over Na_2SO_4, and concentrated in vacuo to give 0.075 g (0.25 mmol, 96%) of **2** as an orange solid: mp 152–153 °C (lit.[5] mp 158 °C); IR ($CHCl_3$) 1772, 1684, 1682, 1600, 1190, 1098 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 2.42 (3 H, s), 7.36 (1 H, s), 7.38 (1 H, dd, J = 8, 1.5 Hz), 7.72 (1 H, t, J = 8 Hz), 8.13 (1 H, dd, J = 8, 1.5 Hz).

2-Bromojuglone Acetate (2) from 5b. To a solution of 1.78 g (10 mmol) of *N*-bromosuccinimide in 50 mL of acetic acid and 100 mL of H_2O maintained at 65 °C was added, dropwise with stirring, a solution of 1.8 g (5.0 mmol) of **5b** (prepared by the known method)[3b] in 50 mL of warm acetic acid. The solution was stirred at 65 °C for 50 min and then diluted with 100 mL of H_2O. The cooled solution was extracted with $CHCl_3$ (4 × 100 mL), and the combined extracts were washed with H_2O (3 × 50 mL) and brine (1 × 50 mL), dried over Na_2SO_4, and concentrated in vacuo to give 1.45 g (4.9 mmol, 98%) of **2** as an orange solid: mp 152–153 °C (lit.[5] mp 158 °C); IR ($CHCl_3$) 1772, 1684, 1682, 1600, 1190, 1098 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 2.42 (3 H, s), 7.36 (1 H, s), 7.38 (1 H, dd, J = 8, 1.5 Hz), 7.72 (1 H, t, J = 8 Hz), 8.13 (1 H, dd, J = 8, 1.5 Hz).

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Registry No. 1, 605-89-0; 2, 77189-69-6; 3, 87712-57-0; **5b**, 87728-27-6.

2-(Dimethoxymethyl)benzyl Alcohol: A Convenient Isobenzofuran Precursor

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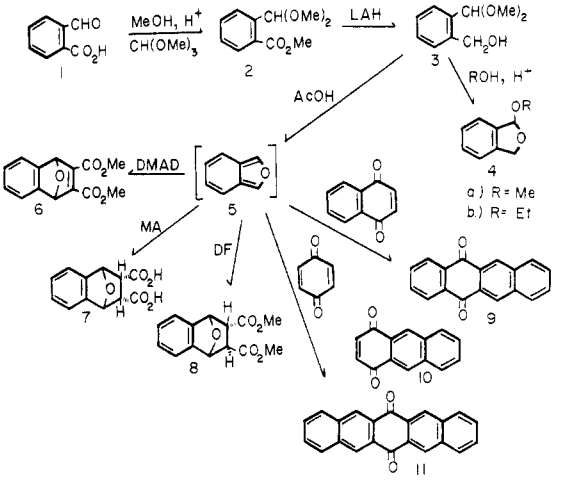
Isobenzofuran (**5**) and its derivatives have assumed some prominence of late as synthetically useful reactive intermediates.[1] Insofar as isobenzofuran itself is concerned, it has been generated by reverse Diels–Alder reactions,[2] by base-induced elimination reactions of 1-alkoxyphthalans,[3] and by thermal decomposition of 1-alkoxyphthalan.[4] This report describes a simple, convenient preparation of isobenzofuran precursors and some of their reactions.

Scheme I. Reaction of 2-(Dimethoxymethyl)benzyl Alcohol



Treatment of commercially available 2-carboxybenzaldehyde (**1**) with excess refluxing methanol in the presence of Dowex resin and trimethyl orthoformate gave methyl 2-(dimethoxymethyl)benzoate (**2**). This product, **2**, was distilled and reduced by lithium aluminum hydride (LAH) to 2-(dimethoxymethyl)benzyl alcohol (**3**).

This last compound, **3**, is obviously a protected form of 2-(hydroxymethyl)benzaldehyde (or 1-hydroxyphthalan in the ring-closed form[5]). It was readily converted to 1-alkoxyphthalans (**4a,b**) by treatment with the appropriate alcohol at ambient temperatures in the presence of Dowex resin as a catalyst.

The use of 1-methoxyphthalan to generate isobenzofuran in situ has already been demonstrated.[3,4] However, 2-(dimethoxymethyl)benzyl alcohol (**3**) proved quite satisfactory as an isobenzofuran precursor (see Scheme I). Thus, treating **3** in hot aqueous acetic acid with 1,4-naphthoquinone led to the formation of tetracene-5,12-dione (**9**), and with *p*-benzoquinone either 1,4-anthraquinone (**10**) or pentacene-6,13-dione (**11**) arose, depending on the molar ratio of the reagents. With dimethyl fumarate (DF), dimethyl acetylenedicarboxylate (DMAD), or maleic anhydride (MA), **3** produced the expected Diels–Alder adducts of isobenzofuran, i.e., *trans*-2,3-dicarbomethoxy-1,4-epoxy-1,2,3,4-tetrahydronaphthalene (**8**), 2,3-dicarbomethoxy-1,4-epoxy-1,4-dihydronaphthalene (**6**), and 1,4-epoxy-1,2,3,4-tetrahydro-*endo,cis*-2,3-naphthalenedicarboxylic acid (**7**). Compound **6**, an oil, was hydrogenated to *endo,cis*-2,3-dicarbomethoxy-1,4-epoxy-1,2,3,4-tetrahydronaphthalene.

In summary, this report describes the simple preparation of **3** and **4** and introduces the utilization of **3** as a source of isobenzofuran.

Experimental Section

Melting points were determined in open capillaries with a Mel-Temp apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Beckman Acculab 10 spectrometer, and NMR spectra were determined on a Bruker WP-80 spectrometer with tetramethylsilane (Me_4Si) as an internal standard. Chemical analyses were determined by Uniroyal Research Laboratories, Guelph, Ontario, and MHW Laboratories, Phoenix, AZ.

Methyl 2-(Dimethoxymethyl)benzoate (2). To 350 mL of absolute methanol were added 23.5 g (0.157 mol) of 2-carboxybenzaldehyde (**1**), 80 mL of trimethyl orthoformate, and 12 g of Dowex 50W-X8 resin. The mixture was refluxed with stirring

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