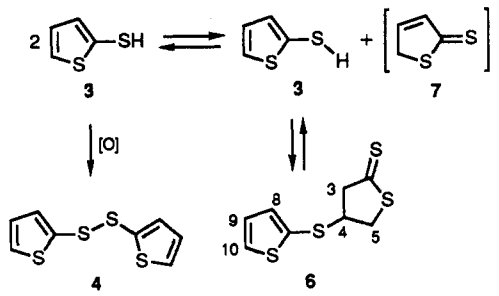
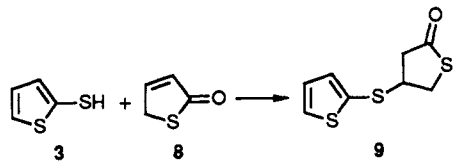
from ^{13}C NMR spectroscopy[10] are also in complete accord with structure **6**.

On investigating the chemical properties of **6**, it was discovered that the dimer is readily converted to the monomer **3** (bp_{15} 59–60 °C; lit.[11] bp_5 54 °C). Alternatively, treatment of **6** with Et_3N in THF in the absence of an acrylic acid also transforms **6** to **3** as evidenced by HPLC and ^1H NMR analysis. Thus, these studies demonstrate that the dimer reaction is easily reversed to regenerate usable 2-mercaptothiophene (**3**).

The behavior of **3** toward dimerization may be rationalized in terms of a slow tautomerization of **3** to 2,5-dihydro-2*H*-2-thioxothiophene (**7**) followed by a rapid Michael addition of 2-mercaptothiophene onto the acceptor **7** to yield **6**. Based on the isolation and characterization of the dimer as **6**, the existence of this highly reactive intermediate **7** appears mechanistically reasonable in spite of the fact that **7** was not detected by ^1H NMR spectroscopy.



Since 2-hydroxythiophene is known to exist predominately as 2,5-dihydro-2*H*-2-oxothiophene (**8**),[12] the Michael addition of **3** onto **8** (neat, 18 h, 25 °C) was next examined. From this reaction, a quantitative yield of **9** was isolated, and the compound was analogous to dimer **6**. The structural assignment of **9** was based on ^1H NMR and mass spectral analyses.[13] Thus, this result further substantiates the existence of intermediate **7** in the above sequence.



Acknowledgment. We thank Dr. John J. Baldwin and Professor Samuel J. Danishefsky for helpful discussions, Dr. Harri G. Ramjit for mass spectral analysis, and Vera W. Finley for preparation of the manuscript. In addition, we wish to thank Dr. Thomas J. Blacklock of Process Research for a sample of disulfide **4**.[7]

Registry No. **3**, 7774-74-5; **4**, 6911-51-9; **6**, 120665-65-8; **8**, 3354-32-3; **9**, 120638-04-2.

(10) Carbon NMR spectra were obtained at 75 MHz (Varian XL-300) in $CDCl_3$. Chemical shifts are referenced to the $CDCl_3$ triplet at 77.0 ppm. The carbon resonances were assigned with the aid of a carbon–proton correlation experiment (HETCOR). The assignments for C-8 and C-10 are based on the observation that $^1J_{CH}$ couplings for thiophene α-carbons are generally larger than for the corresponding β-carbons. Chemical shift in ppm (assignment): 241.1 (C-2), 59.57 (C-3), 50.97 (C-4), 44.17 (C-5), 129.3 (C-7), 136.8 (C-8), 128.1 (C-9), and 131.7 (C-10).

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(13) The HPLC was run as described in ref 6 and under these conditions, **8** was eluted in 3.12 min and **9** in 15.35 min. The mass spectrum calculated for $C_8H_8OS_3$ 215.9737, found 215.9756. Chemical shift in ppm (splittings in hertz, assignment): 2.58 (16.8, 9.9, H-3a), 2.83 (17.0, 7.1, 0.7, H-3b), 3.77 (10.0, 8.8, 6.4, 5.9, H-4), 3.43 (11.5, 8.8, H-5a), 3.56 (11.2, 5.6, 0.7, H-5b), 7.22 (3.6, 1.3, H-8), 7.06 (5.3, 3.5, H-9), and 7.48 (5.4, 1.2, H-10).

Bromination of α-Substituted Alkylbenzenes: Synthesis of (*p*-Bromophenyl)acetylene

Jihad Dakka and Yoel Sasson*

Casali Institute of Applied Chemistry, Graduate School of Applied Science and Technology, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

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Introduction

Ring halogenation of α-substituted alkyl aromatic compounds in presence of Lewis acid catalysts is practically impossible due to competing alkylation, which usually leads to polymerization and tar formation. Benzyl derivatives like bromide, chloride, alcohol, or acetate cannot be halogenated in the presence of iron or aluminum salts. It is also well-known that benzyl chloride cannot even be distilled in the presence of traces of iron due to excessive tar formation.

We have recently reported that quaternary ammonium salts can function as an alternative Friedel–Crafts aromatic bromination catalysts.[1] This group of catalysts, despite being less active than iron or aluminum salts, are water resistant and can therefore also catalyze oxybromination of aromatic compounds in presence of aqueous hydrogen peroxide as an oxidant.[1]

Results

We have now examined the bromination of benzyl derivatives in the presence of e.g. aliquat 336 (tricaprylmethylammonium chloride) catalyst. It was found that in the presence of 10 mol % catalyst, upon the gradual addition of 1 equiv of bromine at 60 °C, benzyl bromide was completely converted to *o*- and *p*-bromobenzyl bromide in the ratio of 9:11, respectively. The two isomers were separated by gas chromatography and identified by comparison with authentic samples. No alkylation or polymerization were observed.

When the same procedure was applied to benzyl chloride, nuclear bromination took place as well, but facile halogen exchange of the benzylic chlorine occurred simultaneously; 10 mol % excess of bromine is required in this experiment for complete conversion of the substrate. This phenomenon was utilized for the preparation of *o*- and *p*-bromobenzyl bromides directly from benzyl chloride. The isomer distribution is essentially the same as in the bromination of benzyl bromide.

More complicated were our attempts to brominate benzyl alcohol under the same conditions. Although some ring bromination was observed, at least 25% of the alcohol was oxidized by the bromine to benzaldehyde,[2] which is inert to bromination. In addition, some meta bromination (up to 5 mol %) of the alcohol took place simultaneously with 36% and 24% ortho and para bromination, respectively. No attempt was made to isolate these products.

Of particular interest to us was the bromination of (1-bromoethyl)benzene (BEB). This compound is an important raw material for various substituted styrenes, but, unfortunately, it cannot be halogenated under traditional conditions. We have examined the bromination of BEB in the presence of quaternary ammonium catalysts and were surprised to learn that the reaction took an unexpected route of simultaneous dehydrobromination–bromination (eq 1).

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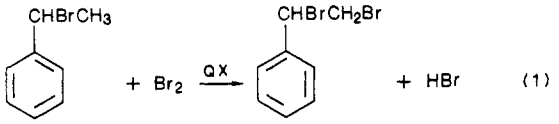
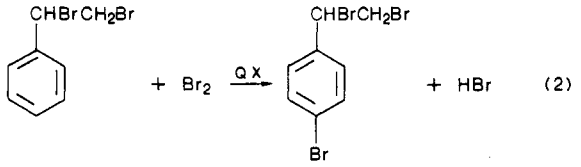
(2) Dakka, J.; Sasson, Y. *Bull. Soc. Chim. Fr.* **1988**, 756.

0022-3263/89/1954-3224$01.50/0



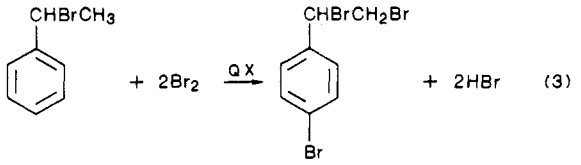
(1)

Ring bromination of BEB is, therefore, impossible. However, the product of reaction 1, (1,2-dibromoethyl)benzene, is brominated in situ (eq 2).



(2)

At 80 °C reactions 1 and 2 take place simultaneously according to the following stochiometry (eq 3).

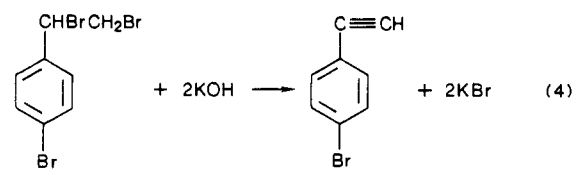


(3)

It was observed that the bromination is selective in nature and the main product obtained was 1-(1,2-dibromoethyl)-4-bromobenzene, with only a minor amount of the corresponding ortho isomer. This selectivity was also dependent on the nature of the quaternary ammonium catalyst. The para selectivity increased with catalysts with shorter alkyl chains. Thus at 80 °C in presence of 5 mol % catalyst at 90% conversion the para selectivity was 85% with aliquat 336, 92% for tetra-*n*-butylammonium bromide, and 98% for tetraethylammonium bromide. Examination of catalysts with different counteranion had no effect because these were instantly exchanged with bromide in presence of the hydrogen bromide.

Although the rate was increased upon the application of larger amount of catalyst the ortho/para ratio was not affected.

The product of reaction 3 is an excellent starting material for the synthesis of (*p*-bromophenyl)acetylene via double dehydrobromination. We have carried out this process according to a known procedure in presence of potassium hydroxide in methanol or with polyethylene glycol (PEG) catalyst[3] (eq 4).



(4)

Discussion

We have reported in the past that quaternary ammonium compounds can catalyze the HBr elimination from both (α-bromoethyl)- and (β-bromoethyl)benzene.[4] When a base is present or a strong vacuum is applied the products are styrene derivatives.[5] However in the absence of a base, under atmospheric pressure the eliminated hydrobromic acid cannot escape the system and mainly isomerization of (α-bromoethyl)- to (β-bromoethyl)benzene and vice versa is observed.[4]

In reaction 1 the fast elimination yields styrene, which instantly adds free bromine to its double bond. In the second stage a normal nuclear bromination is taking place. The aromatic bromination is catalyzed via formation of adducts with the general structure R_4NBr_n or $R_4NBr\cdot(HBr)_n$ (n = 3 or 5) in which the bromine molecule(s) is polarized and activated.[1] Tetrabutylammonium tribromide, for example, is a mild and selective brominating agent for phenols or anilines which yields mainly para bromination.[6,7]

In our aromatic bromination experiments no particular selectivity was observed except for the very bulky substrate (1,2-dibromoethyl)benzene. This selectivity was higher for the smaller onium catalysts than for the larger ones so the size of the attacking species is not an important factor in determining the selectivity. We suggest that the stability of the adduct and the nature of the interaction bromine quaternary salt is the main source of selectivity. With the smaller catalysts the adduct is more stable and the complexed bromine molecule is more strongly polarized, and these apparently contribute to higher para selectivity.

Experimental Section

Materials. Chemicals, reagents, and quaternary ammonium catalysts were all purchased from Aldrich and used without further purification.

***o*- and *p*-Bromobenzyl Bromide.** To a solution of 4.0 g of aliquat 336 in 17.1 g of benzyl bromide (0.1 mol), which was kept at constant temperature of 65 °C, 16 g of bromine is added dropwise over a period of 3 h with stirring. The mixing at 65 °C is continued for an additional hour. The mixture is distilled under vacuum to yield 22.2 g (88%) of bromobenzyl bromide (mixture of 45.5% ortho and 54.5% para).

(1-Bromoethyl)benzene. Bromine (80 g, 0.5 mol) is added dropwise (during 2 h) to a well-stirred glass flask containing 53 g of ethylbenzene (0.5 mol) kept at a constant temperature of 50 °C and irradiated with a 200-W tungsten lamp from a distance of 10 cm. The mixing is continued under light for an additional hour; 89 g of (1-bromoethyl)benzene is obtained, which was found to be 97% pure (GC analysis). This material was used without any purification for the next step.

1-(1,2-Dibromoethyl)-4-bromobenzene. (1-Bromoethyl)benzene (37 g, 0.2 mol) and 1.9 g of tetraethylammonium bromide (9.25 mmol) are mixed at 90 °C; 64 g of bromine (0.4 mol) is added dropwise with stirring during a period of 3 h. The mixing was continued for an additional hour at a constant temperature of 90 °C. After cooling the mixture was washed twice with water, dried over magnesium sulfate, and evaporated to yield a colorless solid, mp 57–60 °C (when prepared via addition of bromine to 4-bromostyrene the melting point of the pure compound was found to be 60–61 °C[8]). The material was analyzed by NMR and elemental analysis and was found to contain 1-(1,2-dibromoethyl)-4-bromobenzene with purity of over 96%. This crude material was used for the next step without any purification. ^{1}H NMR ($CDCl_3$): δ 7.12 (d, 2 H), 7.39 (d, 2 H), 5.11 (dd, 1 H), 4.01 (m, 2 H).[9] Anal. Calcd: C, 27.98; H, 2.04. Found: C, 27.88; H, 2.03.

1-Bromo-4-ethynylbenzene. 1-(1,2-Dibromoethyl)-4-bromobenzene (34.3 g 0.1 mol) are added to a solution of 11.3 g of potassium hydroxide (0.2 mol) in 160 g of methanol. The solution is stirred at 25 °C for 2 h, filtered, and evaporated. The solid product was recrystallized from ether to yield 15.5 g (85%)

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of pure (*p*-bromophenyl)acetylene, mp 64 °C (lit. mp 64–65 °C,[10,11] 63.5–63.7 °C[12]).

Similar results were obtained by using the elimination procedure of Kimura and Regen.[3] ^{1}H NMR ($CDCl_3$): δ 3.12 (s, 1 H), 7.47 (d, 2 H), 7.35 (d, 2 H).[13]

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Synthesis of Hexacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]undecane-8-carboxylic Acid (Homopentaprismane-8-carboxylic Acid)

Alan P. Marchand* and Mahendra N. Deshpande

Department of Chemistry, University of North Texas, Denton, Texas 76203-5068

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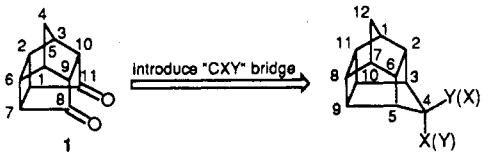
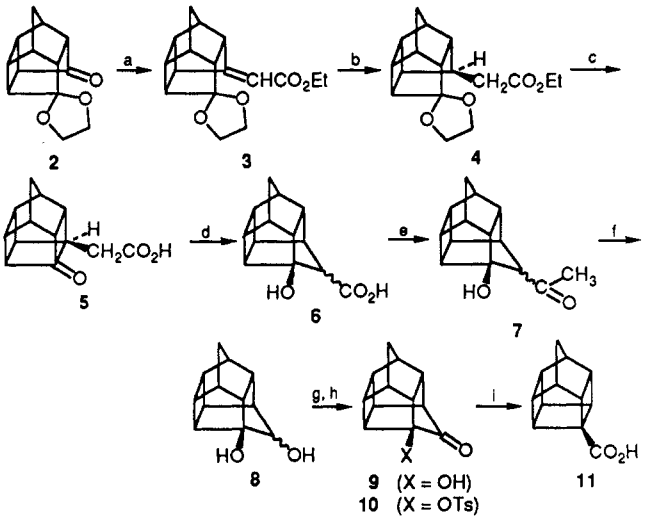
As part of a continuing program concerned with the synthesis and chemistry of novel polycyclic systems,[1] we are seeking new synthetic entries into highly strained cage molecules. In a previous study,[2] a synthesis of 1,3-bishomopentaprismane was developed that involved introduction of a methylene bridge across the 8,11-positions of a readily available[3] cage dione, pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (**1**, Scheme I). More recently, another, potentially general method has been developed to introduce a *functionalized* methylene bridge across the 8,11-positions of **1**. We now report the successful application of this strategy for the synthesis of the title compound (**11**). The parent hydrocarbon, homopentaprismane,[3,4] and several substituted homopentaprismanes have been synthesized previously in our laboratory[4] and by other investigators.[5-7]

Our synthesis of **1** is outlined in Scheme II. Wadsworth–Emmons reaction[8,9] of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione monoethylene ketal (**2**)[5a] with ethyl (diethoxyphosphinyl)acetate afforded the corresponding 8-carbethoxymethylene derivative, **3**, in 92% yield. This material was obtained as a mixture of two isomers as judged by the fact that its ^{13}C NMR spectrum contained 34 resonances (i.e., twice the number expected from the formula of **3**). Tandem gas chromatography–mass spectral (GC/MS) analysis revealed that these two isomers were present in ratio 68:32.

Scheme I



Scheme II[a]



[a] (a) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, reflux 36 h (93%); (b) H_2 (1 atm), Pd–C, EtOAc, room temperature, 2 days (100%); (c) 10% aqueous H_2SO_4, dioxane, reflux 2 days (90%); (d) NaH, DMF–THF, 20 h (91%); (e) MeLi, THF (80%); (f) $(CF_3CO)_2O$, 90% aqueous H_2O_2, 1 day, followed by 5% aqueous NaOH, MeOH, 50 °C, 17 h (60%); (g) NCS, Me_2S, Et_3N, −25 °C (77%) *or* $(COCl)_2$–DMSO, −60 °C → −40 °C (42%); (h) TsCl, py (88%); (i) 20% aqueous KOH, reflux 7 h (94%).

The corresponding *endo*-11-carbethoxymethylene derivative, **4**, was prepared in quantitative yield by catalytic hydrogenation of **3**.[2] Treatment of **4** with aqueous sulfuric acid hydrolyzed both the ester and ketal moieties to produce **5** (90% yield). The ^{13}C NMR spectrum of **5** displays singlet resonances at δ 178.33 and 221.02 that correspond to the CO_2H and ketone carbonyl carbon atoms, respectively, in this compound.

The key step in the synthesis, i.e., the introduction of a functionalized methylene bridge across the 8,11-position, was achieved by treatment of **5** in dimethylformamide–tetrahydrofuran with excess sodium hydride [or, somewhat less conveniently, with excess lithium diethylamide (LDA)]. A substituted 1,3-bishomopentaprismane, **6**, was thereby obtained in 91% yield. This material was obtained as a mixture of two isomers (ratio 69:31 by GC/MS analysis); its ^{13}C NMR spectrum contained 26 resonances.

Some difficulty was experienced when we attempted to decarboxylate **6** oxidatively. Thus, efforts to introduce an SMe group into **6** or into its methyl ester by using the method of Trost and Tamaru[10] resulted only in quantitative recovery of starting material. Our attempts to introduce an α-hydroperoxyl group into **6** by use of LDA–oxygen at −78 °C[11] also were unsuccessful.

Net oxidative decarboxylation of **6** ultimately was performed successfully as follows. Carboxylic acid **6** was

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