

Preparation of Some Unsymmetrical Methylenedionium Salts and Their Reaction with Nucleophiles

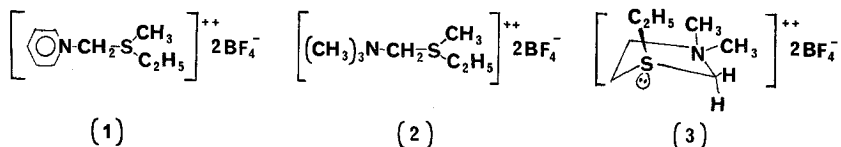
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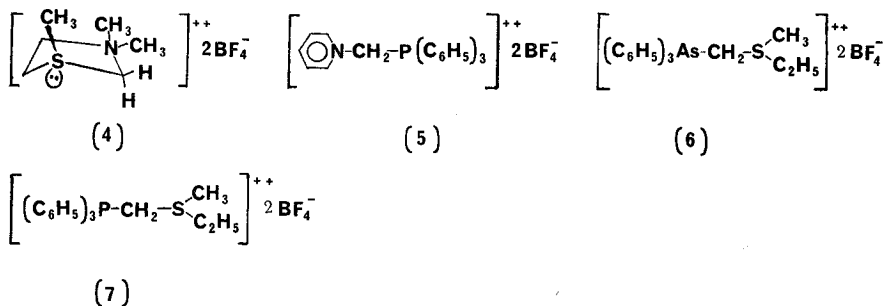
The synthesis of (ethylmethylsulfoniomethyl)pyridinium-, trimethyl(ethylmethylsulfoniomethyl)-ammonium-, 1-ethyl-3,3-dimethyl-1-thionia-3-azoniacyclopentane-, 1,3,3-trimethyl-1-thionia-3-azoniacyclopentane-, (triphenylphosphoniomethyl)pyridinium-, ethylmethyl(triphenylarsoniomethyl)sulfonium- and (ethylmethylsulfoniomethyl)triphenylphosphonium bistetrafluoroborate is described. The NMR spectra of these unsymmetrical methylenedionium salts, with particular reference to the methylene protons resonance between two onium groups, are discussed. The reaction of these onium salts with numerous nucleophiles such as pyridine, piperidine, triethylamine, triphenylphosphine and triphenylarsine, is also discussed.

KEY WORDS: Synthesis of unsymmetrical methylenedionium salts/ NMR spectra of unsymmetrical methylenedionium salts/ Reaction of unsymmetrical methylenedionium salts/

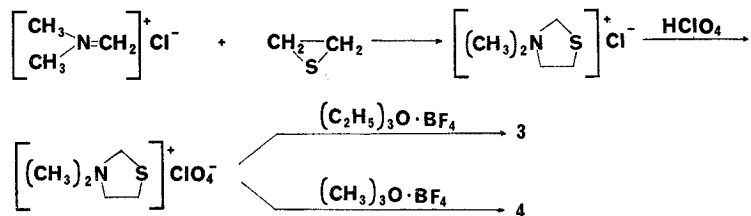
Symmetrical methylenebisonium salts, such as methylenebisammonium, methylenebissulfonium and methylenebisphosphonium salts are rather easily obtainable and have been targets of research both in the fields of physical organic and synthetic chemistry. However, the unsymmetrical ones have received relatively little study. The most common examples are the stable trialkyl(dialkylsulfoniomethyl)ammonium bistetrafluoroborates, which are available by reaction of dialkyl(alkylthiomethyl)amines or trialkyl(alkylthiomethyl)ammonium salts with trialkyloxonium tetrafluoroborates.¹⁾ It is also well known that dialkyl(triphenylphosphoniomethyl)sulfonium bistetrafluoroborates were synthesized by Gosselck and his co-workers and converted to the stable ylide salts.²⁾ In connection with these studies, we have investigated the reaction of various types of unsymmetrical methylenedionium salts with nucleophiles such as pyridine, piperidine, triethylamine, triphenylphosphine and triphenylarsine. The onium salts prepared in the present investigation are indicated below.



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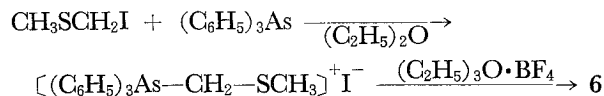
(Ethylmethylsulfoniomethyl)pyridinium- (1) and trimethyl(ethylmethylsulfoniomethyl)ammonium bistetrafluoroborate (2) were synthesized according to the method proposed by Böhme and his co-workers.¹⁾ Thus, chloromethyl methyl sulfide was reacted with pyridine in neat or trimethylamine in ether to provide the intermediate (methylthiomethyl)pyridinium- or trimethyl(methylthiomethyl)ammonium chloride, which was easily converted to 1 or 2 by brief refluxing with triethyloxonium tetrafluoroborate in dichloromethane. In the reaction as outlined below, dimethyl(methylene)ammonium chloride was allowed to react with ethylene sulfide to produce 3,3-dimethylthiazolidinium chloride, which was exchanged for the corresponding perchlorate by perchloric acid. Treatment of the perchlorate with triethyl- or trimethyloxonium tetrafluoroborate afforded 1-ethyl-3,3-dimethyl- (3) or 1,3,3-trimethyl-1-thionia-3-azoniacyclopentane bistetrafluoroborate (4), the latter compound has been already synthesized by Böhme and his co-workers.¹⁾



On prolonged stirring in acetonitrile with triphenylphosphine, 1 gave (triphenylphosphoniomethyl)pyridinium bistetrafluoroborate (5) in a good yield.



Chloromethyl methyl sulfide failed to produce (methylthiomethyl)triphenylarsonium chloride when allowed to react with triphenylarsine in benzene. Using iodomethyl methyl sulfide instead, we have been able to prepare (methylthiomethyl)-triphenylarsonium iodide, which has been converted to ethylmethyl(triphenylarsoniomethyl)sulfonium bistetrafluoroborate (6) by triethyloxonium tetrafluoroborate in the manner described above.



The last compound, (ethylmethylsulfoniomethyl)triphenylphosphonium bistetrafluoroborate (**7**) has been prepared by the procedure cited by Gosselck and his co-workers.²⁾ This onium salt was purified to give melting point in agreement with literature value and provided NMR spectrum supporting its structure.

The NMR spectra of the unsymmetrical methylenedonium salts above mentioned were measured in trifluoroacetic acid (Table I).

Table I. NMR Spectra of Some Unsymmetrical Methylenedonium Bistetrafluoroborates (δ ppm, in $\text{CF}_3\text{CO}_2\text{H}$)

Compound	Methylene H ^{a)}	Others
1	6.55 (s, 2H)	9.5–8.3 (m, 5H), 3.85 (q, 2H), 3.31 (s, 3H), 1.70 (t, 3H)
2	5.65 (s, 2H)	3.97 (q, 2H), 3.65 (s, 9H), 3.47 (s, 3H), 1.77 (t, 3H)
3	5.52 (d, 1H), 5.30 (d, 1H)	4.6–4.2 (m, 4H), 3.78 (q, 2H), 3.60 (s, 3H), 3.43 (s, 3H), 1.58 (t, 3H)
4	5.52 (d, 1H), 5.30 (d, 1H)	4.6–4.2 (m, 4H), 3.60 (s, 3H), 3.43 (s, 3H), 3.30 (s, 3H)
5	6.65 (d, 2H)	8.9–7.5 (m, 20H)
6	5.23 (s, 2H)	7.6–7.5 (m, 15H), 3.71 (q, 2H), 3.09 (s, 3H), 1.57 (t, 3H)
7	5.31 (d, 2H)	8.4–7.8 (m, 15H), 3.71 (q, 2H), 3.07 (s, 3H), 1.57 (t, 3H)

a) Methylene protons between two onium groups.

As can be seen from Table I, the signal assigned to the protons attached to the carbon atom between two onium groups remove to upper field with decreasing electronegative character in the order of ammonium > phosphonium > arsonium group. In the case of **1**, due to a strong electron-withdrawing nature as well as a magnetic anisotropic effect of the pyridinium group the signal of the methylene protons of **1** shifts 1.0–1.2 ppm to down field compared with those of **2**, **3** and **4**. The same tendency is observed in the case of **5**. In the cases of **3** and **4**, the diastereotopic methylene protons appear as two doublets at δ 5.52 and 5.30, in which the down field signal is assigned to the *syn* proton to the sulfur lone pair, and the upper field signal to the *anti* one on the basis of the results of Barbarella and his co-workers.^{3,4)}

We have described just now a versatile synthetic route to **5** which consists in the exchange reaction between **1** and triphenylphosphine in acetonitrile. This may be understood in terms of the strongly nucleophilic character of triphenylphosphine. Thus, we have examined the reaction of the above onium salts with a variety of nucleophiles including the triphenylphosphine. The reaction was performed using an onium salt and 1 equivalent of a nucleophile in acetonitrile according to the general procedure described in experimental section. The results are summarized in Tables II and III.

In the reaction of **1** with pyridine or piperidine, the nucleophilic attack to the carbon between the pyridinium and ethylmethylsulfonium groups in **1** is predominant. When the nucleophile is diphenyl sulfide or triphenylarsine, the attack occurs on methyl or ethyl group bounded to the S atom. In the reaction of **2** with nucleophiles, only such a transfer of methyl or ethyl group in **2** to the applied nucleophile was recognized, probably because the close approach of the attacking molecule is hindered

Reaction of Some Unsymmetrical Methylenedonium Salts

Table II. Reaction of Onium Salts (1 and 2) with Some Nucleophiles in Acetonitrile

Run	Onium salt	Nucleophile	Products and yields ^{a)} (%)
1	1		$\left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{N} \left(\text{C}_5\text{H}_5 \right) \right]^{++} 2\text{BF}_4^- (71), \left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{SC}_2\text{H}_5 \right]^+ \text{BF}_4^- (21),$ $\left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{SCH}_3 \right]^+ \text{BF}_4^- (7)$
2	1		$\left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{N} \left(\text{C}_5\text{H}_9 \right) \right]^{++} 2\text{BF}_4^- (100)$
3	1	$(\text{C}_2\text{H}_5)_3\text{N}$	$\left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{N}(\text{C}_2\text{H}_5)_3 \right]^{++} 2\text{BF}_4^- (33), \left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{SC}_2\text{H}_5 \right]^+ \text{BF}_4^- (66)$
4	1	$(\text{C}_6\text{H}_5)_2\text{S}$	$\left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{SC}_2\text{H}_5 \right]^+ \text{BF}_4^- (15), \left[(\text{C}_6\text{H}_5)_2\text{S}-\text{CH}_3 \right]^+ \text{BF}_4^- (15),$ $\left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{SCH}_3 \right]^+ \text{BF}_4^- (14), \left[(\text{C}_6\text{H}_5)_2\text{S}-\text{C}_2\text{H}_5 \right]^+ \text{BF}_4^- (14)$
5 ^{b)}	1	$(\text{C}_6\text{H}_5)_3\text{As}$	$\left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{SC}_2\text{H}_5 \right]^+ \text{BF}_4^- (89), \left[\text{C}_5\text{H}_5\text{N}-\text{CH}_2-\text{SCH}_3 \right]^+ \text{BF}_4^- (11)$
6	2		$\left[(\text{CH}_3)_3\text{N}-\text{CH}_2-\text{SC}_2\text{H}_5 \right]^+ \text{BF}_4^- (75), \left[(\text{CH}_3)_3\text{N}-\text{CH}_2-\text{SCH}_3 \right]^+ \text{BF}_4^- (25)$
7	2		
8	2	$(\text{C}_2\text{H}_5)_3\text{N}$	$\left[(\text{CH}_3)_3\text{N}-\text{CH}_2-\text{SC}_2\text{H}_5 \right]^+ \text{BF}_4^- (100)$
9	2	$(\text{C}_6\text{H}_5)_3\text{As}$	
10	2	$(n\text{-Bu})_3\text{P}$	$\left[(\text{CH}_3)_3\text{N}-\text{CH}_2-\text{SC}_2\text{H}_5 \right]^+ \text{BF}_4^- (100), \left[(n\text{-Bu})_3\text{P}-\text{CH}_3 \right]^+ \text{BF}_4^- (100)$

a) The yields of the products were obtained by NMR analyses, and the difference to 100 is unreacted starting materials in all runs. b) Reacted at 80°C.

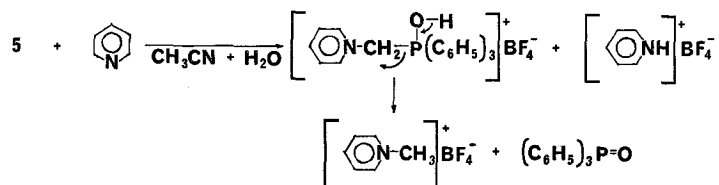
by the bulky trimethylammonium group. Even in the case with pyridine or piperidine, we were unable to find any product arising from attack of the nucleophile to the carbon between trimethylammonium and ethylmethylsulfonium groups within the limits of our detection. When the nucleophile is triethylamine, triphenylarsine or tributylphosphine the attack occurs only on the methyl group but not on the ethyl group, probably due to the bulkiness of the attacking molecules. In addition, the reaction of 6 or 7 with triphenylphosphine as well as the reaction of 7 with triphenylarsine have also resulted in only the transfer of methyl group to the applied nucleophiles. The reaction of 5 with pyridine was performed in a mixture of acetonitrile and water instead of acetonitrile. The analysis of products obtained in this reaction has led to the following equation. In an analogous manner, 7 also reacted smoothly with triethylamine in aqueous acetonitrile to afford triphenylphosphine oxide,

Table III. Reaction of Onium Salts (5, 6 and 7) with Some Nucleophiles in Acetonitrile

Run	Onium salt	Nucleophile	Products and yields ^{a)} (%)	
1 ^{b)}	5		(C ₆ H ₅) ₃ P=O (100), $\left[\text{pyridine-N-CH}_3\right]^+ \text{BF}_4^-$ (100), $\left[\text{pyridine-NH}\right]^+ \text{BF}_4^-$ (100)	
2	6	(C ₆ H ₅) ₃ P	$\left[(\text{C}_6\text{H}_5)_3\text{As-CH}_2\text{-SC}_2\text{H}_5\right]^+ \text{BF}_4^-$ (100), $\left[(\text{C}_6\text{H}_5)_3\text{P-CH}_3\right]^+ \text{BF}_4^-$ (100)	
3 ^{b)}	7	(C ₂ H ₅) ₃ N	(C ₆ H ₅) ₃ P=O (100), $\left[(\text{CH}_3)_2\text{S-C}_2\text{H}_5\right]^+ \text{BF}_4^-$ (100), $\left[(\text{C}_2\text{H}_5)_3\text{NH}\right]^+ \text{BF}_4^-$ (100)	
4	7	(C ₆ H ₅) ₃ As	$\left[(\text{C}_6\text{H}_5)_3\text{P-CH}_2\text{-SC}_2\text{H}_5\right]^+ \text{BF}_4^-$ (100), $\left[(\text{C}_6\text{H}_5)_3\text{As-CH}_3\right]^+ \text{BF}_4^-$ (100)	
5	7	(C ₆ H ₅) ₃ P	$\left[(\text{C}_6\text{H}_5)_3\text{P-CH}_2\text{-SC}_2\text{H}_5\right]^+ \text{BF}_4^-$ (100), $\left[(\text{C}_6\text{H}_5)_3\text{P-CH}_3\right]^+ \text{BF}_4^-$ (100)	

a) The yields obtained by NMR analyses were almost quantitative. b) Aqueous acetonitrile was used as a solvent instead of acetonitrile.

dimethylethylsulfonium- and triethylammonium tetrafluoroborate.



The conversion of some dialkyl(triphenylphosphoniomethyl)sulfonium bistetrafluoroborates or of some methylenebis(dialkylsulfonium) bistetrafluoroborates to the corresponding ylide salts, isolated as stable crystalline compounds, have already been reported.^{2,5)} The possibility was entertained that 1, 2, 3, 5 or 6 described above might be converted to an analogous ylide salt. Thus, we have examined whether the ylide salt can be isolated or generated in organic solvents on treatment with the appropriate base. However, we could not afford the ylide salt under the conditions used in the preparation of triphenylphosphonium(dialkylsulfonium)methylides²⁾ and bis(dialkylsulfonium)methylides.⁵⁾ In a typical experiment, 1 was treated with equimolar amounts of potassium hydroxide or sodium methoxide in methanol at -10°C , by the following addition of benzoyl chloride, or in the presence of benzaldehyde. In both cases 1 was submitted to the nucleophilic attack by methoxide ion to afford N-(methoxymethyl)pyridinium tetrafluoroborate quantitatively with liberation of ethyl methyl sulfide. Benzoyl chloride was converted to methyl benzoate and benzaldehyde to benzaldehyde dimethyl acetal which would be derived from the acid-catalyzed reaction of benzaldehyde and methanol by tetrafluoroboric acid produced in the course of reaction.

EXPERIMENTAL

(Ethylmethyisulfoniomethyl)pyridinium Bistetrafluoroborate (1). To 14.5 g (0.15 mol) of chloromethyl methyl sulfide was added dropwise 12 g (0.15 mol) of pyridine at 0°C. The mixture was stirred at room temperature for 72 hr. The resulting precipitate was filtered with suction through a sintered glass funnel, washed with ether and dried under reduced pressure. The (methylthiomethyl)pyridinium chloride (26.5 g, 0.15 mol) thus obtained was added to 100 g (0.53 mol) of triethyloxonium tetrafluoroborate dissolved in 140 ml of dichloromethane, which, after refluxing for 2 hr under nitrogen, was set aside at room temperature. The obtained **1** was collected, washed with dichloromethane and dried. Yield 46 g (89%), mp 128–129°C.

Trimethyl(ethylmethyisulfoniomethyl)ammonium Bistetrafluoroborate (2). This onium salt was synthesized in a 73% yield by reaction of trimethyl(methylthiomethyl)ammonium chloride with triethyloxonium tetrafluoroborate in dichloromethane in the manner described for **1**, mp 121–122°C.

1-Ethyl-3,3-dimethyl-1-thionia-3-azoniacyclopentane Bistetrafluoroborate (3). A solution of dimethyl(methylene)ammonium chloride (17 g, 0.18 mol) in acetonitrile (50 ml) was added dropwise to a solution of ethylene sulfide (11 g, 0.18 mol) in acetonitrile (20 ml). The mixture was allowed to stand at room temperature for 5–6 hr. After cooling, 12.5 g (45% yield) of 3,3-dimethylthiazolidinium chloride was collected. The chloride (12.5 g, 0.081 mol) dissolved in acetonitrile (130 ml) was treated with 70% perchloric acid (11 ml, 0.128 mol) at 0°C. The mixture was then diluted with excess ether, the resulting 3,3-dimethylthiazolidinium perchlorate was collected and washed with anhydrous ether. Yield 17.8 g (100%), mp 276–279°C. The perchlorate (1.5 g, 6.9 mmol) was added in portions to a stirred solution of triethyloxonium tetrafluoroborate (4.6 g, 24.2 mmol) in dichloromethane (15 ml). The mixture was refluxed for 2 hr under nitrogen and allowed to stand at room temperature overnight. The resulting precipitate was collected, washed with anhydrous dichloromethane and purified by a dissolution and precipitation cycle in acetonitrile-dichloromethane to afford **3**. Yield 1.4 g (63%), mp 183–184°C.

1,3,3-Trimethyl-1-thionia-3-azoniacyclopentane Bistetrafluoroborate (4). 3,3-Dimethylthiazolidinium perchlorate (1.5 g, 6.9 mmol) was added portionwise to a stirred solution of trimethyloxonium tetrafluoroborate (3.6 g, 24.3 mmol) in nitromethane (25 ml) at –10°C. The mixture was stirred for 72 hr at room temperature and allowed to stand at low temperature overnight. The resulting white precipitate was collected, washed with dichloromethane and further with ether. Yield 1.0 g (47%), mp 221–222°C (lit.¹³ 230°C).

(Triphenylphosphoniomethyl)pyridinium Bistetrafluoroborate (5). To a solution of 3.8 g (11.1 mmol) of **1** in acetonitrile (80 ml) at 0°C was added portionwise 2.94 g (11.2 mmol) of triphenylphosphine. The solution was stirred under nitrogen for 19 hr at room temperature, wherein the solution was light yellow in color. After removal of the solvent, the residue was purified by a dissolution and precipitation

cycle in acetonitrile-ether. Yield 5.3 g (90%), mp 214–215°C.

Ethylmethyl(triphenylarsoniomethyl)sulfonium Bistetrafluoroborate (6).

To a solution of 3.4 g (18.1 mmol) of iodomethyl methyl sulfide in ether (15 ml) at room temperature was added 4.6 g (15 mmol) of triphenylarsine. The mixture was refluxed for 3 hr under nitrogen and cooled below 0°C. The resulting precipitate was collected and washed with ether to give 4.2 g (57%) of (methylthiomethyl)-triphenylarsonium iodide, mp 135–136°C. The iodide was then converted to **6** by reaction with triethyloxonium tetrafluoroborate dissolved in dichloromethane in the manner described for **1**. Yield 75%, mp 171–173°C.

Reaction of Onium Salts with Nucleophiles in Acetonitrile. To a cold solution of an onium salt (5.0 mmol) in 20 ml of acetonitrile (in Runs 1 and 3 of Table III 20 ml of aqueous acetonitrile was employed instead) was added 5.0 mmol of a nucleophile. The mixture was stirred at room temperature for 16 hr under nitrogen. The solvent was removed thoroughly under reduced pressure, and the residue was washed carefully with anhydrous ether. The structure of each product thus obtained was confirmed by comparison with authentic specimen otherwise synthesized.

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