

**4,5-Triazoloacenaphthene (XII) from 4,5-Diaminoacenaphthene.**—4-Nitro-5-aminoacenaphthene (I) (1.1 g., 0.005 mole) purified by crystallization from methyl Cellosolve was reduced in a Parr hydrogenator with the aid of 300 mg. of platinum oxide in 20 ml. of ethanol. The ethanol solution was filtered and diluted with water. Fine tan needles of 4,5-diaminoacenaphthene were formed. This diamine, because of its instability, was collected on a filter and quickly dissolved in glacial acetic acid, and 5 g. of sodium nitrite was added all at once. The mixture, which became green in color, was warmed to 80° on the steam-bath and then diluted with water. A brown solid separated which was collected and dried. Crystallization from glacial acetic acid with the aid of decolorizing charcoal gave a tan product which when mixed with the product of the decomposition of the diazonium salt of 4-amino-5-benzenesulfonamidoacenaphthene (IV), gave no depression of the melting point. The infrared spectra were identical.

**4,5-(1-Benzoyltriazo)-acenaphthene (XIII).**—Two grams (0.007 mole) of 4-amino-5-benzamidoacenaphthene (X) was suspended in 25 ml. of concentrated hydrochloric acid and warmed. The amine hydrochloride was only partially soluble in concentrated hydrochloric acid. The mixture was cooled to 0°, and 1.0 g. (0.015 mole) of sodium nitrite was added, with subsequent stirring for 30 minutes. The excess nitrous acid was destroyed by the addition of 2 g. of urea with stirring for 10 minutes. The mixture was decom-

posed by passing the solution through a steam line. A brown solid 1.2 g. (58%) was collected and crystallized from ethanol, m.p. 159.5–160.5°. The infrared spectrum showed no hydroxy absorption at 3500–3700 cm.<sup>-1</sup>,<sup>15b</sup> but did show carbonyl absorption at 1710 cm.<sup>-1</sup>,<sup>15a</sup>. This compound was insoluble in 10% sodium hydroxide solution. *Anal.* Calcd. for C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O: N, 14.04. Found: N, 13.85.

**Hydrolysis of 4,5-(1-Benzoyltriazo)-acenaphthene (XI-II).**—One-half gram (0.0017 mole) of the benzoyltriazo XIII was suspended in a mixture of 10 ml. of ethanol and 10 ml. of 50% sulfuric acid. The mixture was maintained at reflux temperature for 14 hours. During the first part of the reaction a strong odor of ethyl benzoate was noted, and later the odor of diethyl ether was detected. The reaction mixture was cooled to room temperature and the solvent removed under vacuum. The odor of ethyl benzoate was again noted. The residue was treated with 20 ml. of 10% sodium hydroxide solution and warmed for 0.5 hour on the steam-bath, cooled, and acidified with dilute hydrochloric acid. A white solid separated, m.p. 280° (block). Crystallization from glacial acetic acid gave a tan product which when mixed with 4,5-triazoloacenaphthene (XII) showed no depression in melting point. The infrared spectra of the two compounds were identical.

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[CONTRIBUTION FROM THE WETHERILL LABORATORY OF CHEMISTRY, PURDUE UNIVERSITY]

## Stereospecific Reactions of Nucleophilic Agents with Acetylenes and Vinyl-type Halides. VIII. The Mechanism of the Reaction of Tetrachloroethylene with *p*-Toluenethiolate Reagent<sup>1</sup>

BY WILLIAM E. TRUCE AND RUDOLPH KASSINGER

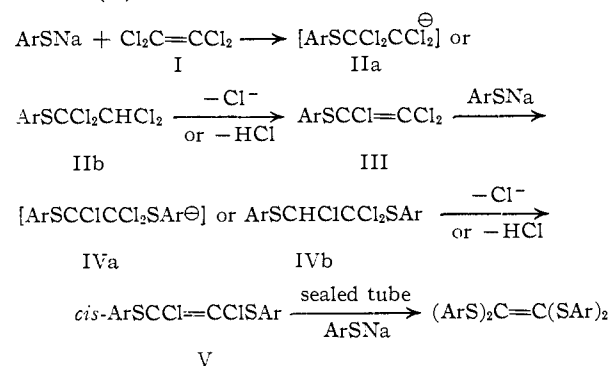
RECEIVED JUNE 2, 1958

Sodium *p*-toluenethiolate reacts with tetrachloroethylene (I) in refluxing ethanol to give *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V); the intermediate 1-(*p*-tolylmercapto)-1,2,2-trichloroethane may be isolated. Under forcing conditions, tetra-(*p*-tolylmercapto)-ethene is obtained. Mechanistic interpretations, based on concepts developed with di- and trichloroethylenes, are discussed.

The mechanisms of the reactions of thiolate reagents with 1,2-dichloroethylenes,<sup>2</sup> vinylidene chloride<sup>3</sup> and trichloroethylene<sup>4a</sup> were reported in recent papers.<sup>4b</sup> These studies have now been extended to the last compound in this series, tetrachloroethylene.

Although the reaction of tetrachloroethylene with thiolates has been known for some time,<sup>5</sup> its stereochemical and mechanistic course was unknown. It was observed in this Laboratory that tetrachloroethylene undergoes a stereospecific reaction with sodium *p*-toluenethiolate, the product being *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene. Previously we had demonstrated that the reaction of vinylidene chloride with sodium *p*-toluenethiolate proceeded by an initial addition,<sup>3</sup> whereas with *cis*-dichloroethylene<sup>2</sup> and trichloro-

ethylene,<sup>4a</sup> initial dehydrohalogenation occurred.<sup>6</sup> Since tetrachloroethylene is incapable of dehydrohalogenation, the initial step in the reaction with thiolate reagent must be nucleophilic "addition" forming either an incipient carbanion (IIa) or a saturated intermediate (IIb), which produces 1-(*p*-tolylmercapto)-1,2,2-trichloroethene (III) by loss of Cl<sup>-</sup> or HCl, respectively. By a repetition of this sequence of steps, further treatment with alcoholic sodium *p*-toluenethiolate produces the product, *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V) as outlined.



(1) For preceding paper see ref. 4a. Taken from Mr. Kassinger's Ph.D. thesis.

(2) W. E. Truce, M. M. Boudakian, R. F. Heine and R. J. McManis. *THIS JOURNAL*, **78**, 2743 (1956).

(3) W. E. Truce and M. M. Boudakian, *ibid.*, **78**, 2748 (1956).

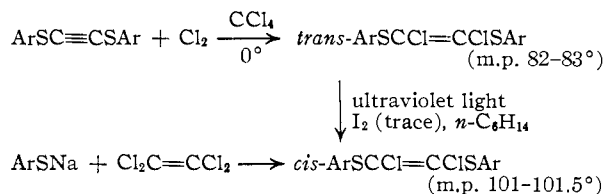
(4) (a) W. E. Truce and R. Kassinger, *ibid.*, **80**, 1916 (1958). (b) Furthermore, in the formation of vinyl *p*-tolyl sulfide from vinyl chloride and sodium *p*-toluenethiolate [Truce, Hill and Boudakian, *ibid.*, **78**, 2760 (1956)], an elimination-addition mechanism is suggested for at least part of the reaction product by the facts that (1) the strong base, sodium ethoxide, has an accelerating influence, (2) the presence of acetylene in the reaction mixture was noted and (3) acetylene is known to react with thiolate reagent under similar conditions to form the vinyl sulfide.

(5) N. W. Cusa and H. McCombie, *J. Chem. Soc.*, 767 (1937).

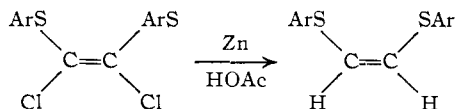
(6) For a further discussion of some of the factors determining whether initial elimination or nucleophilic "addition" occurs in such over-all displacements see paper VII of this series (ref. 4).

The reaction of tetrachloroethylene with a mixture of *p*-toluenethiol and a catalytic amount of sodium *p*-toluenethiolate was observed to give a product which, after removal of unreacted thiol by alkaline extraction, was identified by its crystalline sulfone as 1-(*p*-tolylmercapto)-1,2,2-trichloroethene (III). Treatment of this intermediate (III) with an excess of sodium *p*-toluenethiolate gave V in 82% yield. However, treatment of III with a mixture of thiol and a catalytic amount of thiolate gave no reaction. This suggests that the reaction to product V proceeds *via* the incipient carbanion IVa rather than the saturated intermediate IVb. Although V does not react further with excess sodium *p*-toluenethiolate in refluxing ethanol, it may be converted to tetra-(*p*-tolylmercapto)-ethene in 97% yield by treating it with thiolate reagent in a sealed tube at an elevated temperature.

The configuration of V was assigned on the following basis. Halogenation of 1,2-bis-(*p*-tolylmercapto)-ethyne with an equivalent amount of chlorine in carbon tetrachloride gave an isomer which had a different configuration from that obtained by the thiolate-tetrachloroethylene reaction (additive halogenations of alkynes frequently have been reported to give predominantly the *trans* isomer<sup>7</sup>). Treatment of this halogen addition product in *n*-hexane (containing a trace of iodine) with ultraviolet light for 24 hours converts it into the "*cis*" isomer. It has been reported that "the usual action of light on geometrical isomers is to transform the more absorptive *trans* form into the less absorptive *cis* form."<sup>8</sup> Furthermore it was



observed that the reduction of V with zinc in glacial acetic acid gave as the only isolated product *cis*-bis-(*p*-tolylmercapto)-ethene. Although the mechanism of this reduction is not known, it does proceed to form the less stable of the isomeric 1,2-bis-(*p*-tolylmercapto)-ethenes.<sup>2</sup> Finally, the



dipole moment<sup>9</sup> of V is relatively large ( $\mu = 2.34$  D.). Since this is a symmetrically substituted olefin system, this is consistent with a *cis* configuration; the *trans* isomer should have a vanishingly small dipole moment.<sup>10</sup>

(7) (a) E. Bergmann, *J. Chem. Soc.*, 402 (1936); (b) A. T. Morse and L. Leitch, *Can. J. Chem.*, **33**, 6 (1955); (c) A. Leitch, *ibid.*, **31**, 385 (1953); (d) G. F. Hennion and C. E. Welsh, *THIS JOURNAL*, **62**, 1367 (1940); (e) G. F. Hennion and G. M. Wolf, *ibid.*, **62**, 1368 (1940); (f) H. Sinn, *Angew. Chem.*, **69**, 754 (1957); (g) R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworths Scientific Publications, London, 1955, p. 35.

(8) E. P. Carr, *THIS JOURNAL*, **51**, 3048 (1929).

(9) The dipole moment was determined by the method of Brown and DeVries, *ibid.*, **73**, 1811 (1951).

(10) W. H. King and H. A. Smith, *ibid.*, **72**, 3450 (1950); see also reference 7a.

Although complete addition was observed as a step in the over-all reaction of vinylidene chloride with thiolate reagent, an analogous saturated intermediate IIb was not isolated in the present system. It is conceivable that such a product, if formed, would dehydrohalogenate very readily.<sup>11</sup> On the other hand, the reaction of I with thiolate to produce III may proceed by an incipient carbanion IIa. A similar situation is seen to exist in the formation of the final product from III. For this latter case it was pointed out that an incipient carbanion seemed more probable since treatment of III with *p*-toluenethiol in the presence of a catalytic amount of thiolate gave no reaction. The formation of an unstable intermediate analogous to anions IIa or IVa (drawn in the Newman notation<sup>12</sup> in Fig. 1) having  $sp^3$ -hybridization was previously suggested by a number of workers.<sup>13,14</sup> Loss of  $\text{Cl}^-$  from IV (assuming an intermediate carbanion is indeed involved) must occur in a stereospecific manner to give the *cis* product. This may be

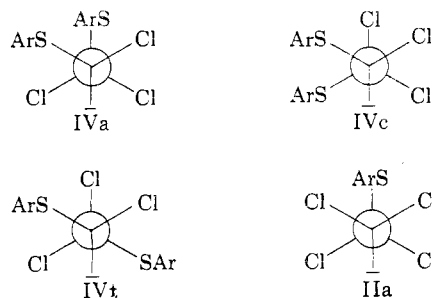


Fig. 1.

accounted for by assuming that the unstable intermediate IVa, which is in equilibrium with such other conformations as IVc and IVt, will react by the path most energetically favorable. This path is *via* the transition state (IVc<sup>+</sup>) formed from IVc rather than IVt, which leads to the formation of the thermodynamically more stable isomer (thermodynamic control) on the loss of chloride ion.<sup>15</sup> This of course requires that the *cis* isomer be the thermodynamically more stable of the pair. This

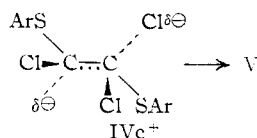
(11) Cusa and McCombie<sup>4</sup> reported that  $\text{C}_6\text{H}_5\text{SCCl}_2\text{CHCl}_2$ , which was formed by the chlorination of  $\text{C}_6\text{H}_5\text{SCCl}=\text{CClH}$ , rapidly lost HCl on standing. They speculated that the product formed was  $\text{C}_6\text{H}_5\text{SCCl}=\text{CCl}_2$ .

(12) M. S. Newman, *J. Chem. Ed.*, **32**, 344 (1955).

(13) V. Gold, *J. Chem. Soc.*, 1430 (1951).

(14) J. F. Bunnett and D. E. Zahler, *Chem. Revs.*, **49**, 273 (1951).

(15) A transition state ("activated complex") which accounts for retention of configuration in the displacement reaction of haloalkenes was suggested recently by Miller and Yonan [*THIS JOURNAL*, **79**, 5931 (1957)]. It was pictured as a "stage in the formation of" a carbanion having  $sp^3$  hybridization as depicted in IVa. Several references cited therein report that the main process in the nucleophilic displacement at an alkene carbon results in retention of configuration. In fact Montanari [*Gazz. chim. ital.*, **87**, 1073 (1957)] suggests a Rule of Retention of Configuration (but offers no mechanism to account for it). However we have encountered at least two exceptions to this notion. For example, vinylidene chloride reacts with an equivalent amount of sodium *p*-toluenethiolate to form *trans*-1-chloro-2-(*p*-tolylmercapto)-ethene<sup>3</sup> and with excess reagent to form *cis*-di-(*p*-tolylmercapto)-ethene. In addition, *trans*-1,2-dichloro-1-(*p*-tolylmercapto)-ethene reacts with a thiol-thiolate mixture to form *trans*-1-chloro-1,2-di-(*p*-tolylmercapto)-ethene.<sup>4a</sup> These results have been explained on an "addition"-elimination, elimination-addition sequence of steps, the geometry of the products being controlled by the Rule of *trans*-Nucleophilic Addition and the *cis*-Effect. It should be emphasized that these considerations explain the retention of configuration observed.



phenomenon is not unusual since it has been observed in a number of other 1,2-dichloroolefins.<sup>16</sup>

### Experimental<sup>17</sup>

**Preparation of 1,2-Dichloro-1,2-di-(*p*-tolylmercapto)-ethene.**—To a solution of sodium ethoxide prepared from 200 ml. of absolute ethanol and 2.53 g. (0.11 g. atom) of sodium was added 12.4 g. (0.10 mole) of *p*-toluenethiol and 16.6 g. (0.10 mole) of freshly distilled tetrachloroethylene. The resulting mixture was refluxed under a dry, oxygen-free, nitrogen atmosphere for 24 hours and then filtered while hot to remove the sodium chloride which formed. On cooling the filtrate a crystalline solid separated. A second crop of crystals was obtained by concentrating the filtrate, cooling, and filtering the resulting product. The combined product was recrystallized from absolute ethanol to give 11.7 g. (0.034 mole) of 1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V), m.p. 101–101.5°.

Unreacted *p*-toluenethiol was recovered from the filtrate by diluting with water, acidifying the aqueous solution with concd. HCl, and extracting the resulting thiol with petroleum ether (35–37°). The petroleum ether solution was dried over magnesium sulfate and upon evaporation of the solvent, 1.6 g. of *p*-toluenethiol was recovered.

*Anal.*<sup>18</sup> Calcd. for C<sub>16</sub>H<sub>14</sub>S<sub>2</sub>Cl<sub>2</sub>: C, 56.30; H, 4.13; S, 18.78; Cl, 20.77. Found: C, 56.04; H, 4.61; S, 18.76; Cl, 20.52.

**Preparation of 1,2-Dichloro-1,2-di-(*p*-tolylsulfonyl)-ethene.**—To 100 ml. of glacial acetic acid was added 2.23 g. (0.0065 mole) of *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V) and 10 ml. of 30% hydrogen peroxide. The solution was refluxed for 2 hours and then allowed to stand overnight at room temperature. The solid which formed was filtered, the filtrate in turn was evaporated to dryness and triturated with cold ethanol to give an additional crop of sulfone crystals. The combined yield of sulfone was 1.57 g. (67%). After one recrystallization from 1:1 benzene–95% ethanol and a second recrystallization from absolute ethanol the m.p. was 190–191°.

*Anal.* Calcd. for C<sub>16</sub>H<sub>14</sub>S<sub>2</sub>Cl<sub>2</sub>O<sub>4</sub>: C, 47.41; H, 3.48; Cl, 17.50; S, 15.82. Found: C, 47.38; H, 3.83; Cl, 17.68; S, 15.59.

**Preparation of Tetra-(*p*-tolylmercapto)-ethene.**—A Carius tube was charged with a solution prepared from 5.26 g. (0.015 mole) of *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V), 4.10 g. (0.033 mole) of *p*-toluenethiol, 0.81 g. (0.035 g. atom) of sodium and 50 ml. of absolute ethanol. The reaction was heated for 36 hours at 160° giving a product which was very insoluble in hot ethanol, slightly soluble in hot benzene but relatively soluble in hot trichloroethylene. After extracting the product with water to remove the salt, it was recrystallized from trichloroethylene to give 7.5 g. of tetra-(*p*-tolylmercapto)-ethene (97%). The molecular weight of the product determined by the freezing point depression method was 530 (calculated 516).

*Anal.* Calcd. for C<sub>30</sub>H<sub>24</sub>S<sub>4</sub>: C, 69.70; H, 5.42. Found: C, 69.59; H, 5.18.

**Isolation of 1-(*p*-Tolylmercapto)-1,2,2-trichloroethene (III).**—A solution prepared from 24.8 g. (0.20 mole) of *p*-toluenethiol, 2.3 g. (0.10 g. atom) of sodium and 150 ml. of absolute ethanol was added dropwise over a one-hour period to a refluxing solution (under a nitrogen atmosphere) containing 49.8 g. (0.30 mole) of tetrachloroethylene in 50 ml. of absolute ethanol. After refluxing an additional 1.5 hours

the solution was diluted with 400 ml. of 0.5 *N* sodium hydroxide, extracted with ether to remove the product and the ether extracts were dried over magnesium sulfate. The remaining aqueous solution was acidified with concd. HCl and extracted with ether. The ether extracts were dried over magnesium sulfate and evaporated to give 16.0 g. (0.13 mole) of unreacted *p*-toluenethiol, m.p. 41–42.5°. Evaporation of solvent from the organic extract gave an oil which was dissolved in petroleum ether (60–70°) and chromatographed through a column (20 cm. × 2.5 cm.) containing silica gel (Davison, 200 mesh) using petroleum ether (60–70°) as the eluent. The chromatographic separation yielded 2.85 g. of 1-(*p*-tolylmercapto)-1,2,2-trichloroethene (III), 3.94 g. of *p*-tolyl disulfide and 3.45 g. of *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene. A fraction containing intermediate III (1.0 g.) was dissolved in a solution containing 20 ml. of glacial acetic acid and 6 ml. of 30% hydrogen peroxide. After 1 hour of refluxing on a steam-bath the solution was poured onto crushed ice and the crude sulfone obtained was recrystallized from absolute ethanol to give 0.8 g. of a crystalline product, m.p. 74–77°. This was recrystallized four times from absolute ethanol; m.p. 80.5–82°.

*Anal.* Calcd. for C<sub>9</sub>H<sub>8</sub>SO<sub>2</sub>Cl<sub>3</sub>: C, 37.85; H, 2.47; Cl, 37.25. Found: C, 37.93; H, 2.58; Cl, 37.30.

**Reaction of 1-(*p*-Tolylmercapto)-1,2,2-trichloroethene (III) with Sodium *p*-Toluenethiolate.**—A solution prepared from 0.75 g. (0.006 mole) of *p*-toluenethiol, 0.18 g. (0.008 g. atom) of sodium and 20 ml. of absolute ethanol was added dropwise to a refluxing solution of 1.1 g. (0.0043 mole) of III in 20 ml. of absolute ethanol. After 5 hours of reflux under a nitrogen atmosphere, the solution was cooled yielding 1.2 g. (82%) of product. One recrystallization from ethanol gave a product, m.p. 100–101°, which did not depress the melting point of an authentic sample of *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V).<sup>5</sup>

**Reaction of 1-(*p*-Tolylmercapto)-1,2,2-trichloroethene (III) with *p*-Toluenethiol and a Catalytic Amount of Sodium *p*-Toluenethiolate.**—A solution prepared from 1.24 g. (0.01 mole) of *p*-toluenethiol and 20 ml. of absolute ethanol (containing 0.001 mole of sodium ethoxide) was added dropwise to 20 ml. of a refluxing ethanol solution containing 2.26 g. (0.009 mole) of III. The solution was allowed to reflux for 6 hours under a nitrogen atmosphere before quenching with 300 ml. of 0.1 *N* sodium hydroxide. The organic material was extracted with ether and these extractions were dried over magnesium sulfate. Upon evaporation 2.02 g. (9.6%) of 1-(*p*-tolylmercapto)-1,2,2-trichloroethene was obtained.

**Chlorination of Bis-(*p*-tolylmercapto)-ethyne.**—A solution of 150 ml. of carbon tetrachloride containing 5.0 g. (0.019 mole) of bis-(*p*-tolylmercapto)-ethyne, maintained at 0°, was chlorinated by slowly passing in a preweighed amount of chlorine (1.6 g., 0.02 mole) through a glass dispersion tube. Upon complete addition of chlorine, the solution was stirred for an additional 30 minutes. On evaporating the solution to dryness a solid was obtained which subsequently was chromatographed, using carbon tetrachloride as the eluent, through a column (24 cm. × 2.5 cm.) containing silica gel (Davison, 200 mesh) to give 2.4 g. of *trans*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V).

*Anal.* Calcd. for C<sub>16</sub>H<sub>14</sub>S<sub>2</sub>Cl<sub>2</sub>: C, 56.30; H, 4.13; Cl, 20.77. Found: C, 56.41; H, 4.30; Cl, 20.80.

**Isomerization of *trans*-1,2-Dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V).**—A sample (0.30 g.) of *trans*-V was dissolved in 50 ml. of *n*-hexane containing a trace of iodine, placed in a quartz flask and irradiated with a mercury vapor lamp (100 watt) for 24 hours. Upon completion of the illumination period, the solvent was evaporated and the resulting material was decolorized with Norite and recrystallized from ethanol. A second recrystallization from ethanol gave a product (0.1 g.) which did not depress the melting point of an authentic sample of *cis*-1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene (V).

**Reduction of 1,2-Dichloro-1,2-di-(*p*-tolylmercapto)-ethene.**—A mixture of 1.95 g. (0.0057 mole) of V, 5.0 g. of zinc dust and 75 ml. of glacial acetic acid was refluxed for four hours and filtered while hot. After evaporating the filtrate to near dryness and recrystallizing the product from ethanol, 0.32 g. of material (21%) was obtained which did not depress the melting point of an authentic sample of *cis*-bis-(*p*-tolylmercapto)-ethene, m.p. 92°.<sup>2</sup>

(16) T. W. J. Taylor and A. R. Murray, *J. Chem. Soc.*, 2078 (1938); G. Chavanne, *Bull. soc. chim. Belg.*, 26, 287 (1912); H. A. Stuart, *Physik. Z.*, 32, 793 (1931); H. van de Walle and A. Henne, *Akad. Roy. Belg.*, 11, 360 (1925); *C. A.*, 20, 1050 (1926).

(17) All boiling and melting points are uncorrected.

(18) Microanalyses were performed by Dr. C. S. Yeh and Mrs. S. L. Margerom in this department.

**Reduction of 1,2-Dichloro-1,2-di-(*p*-tolylsulfonyl)-ethene.**<sup>19</sup>—A mixture of 0.65 g. (0.0016 mole) of 1,2-dichloro-1,2-di-(*p*-tolylmercapto)-ethene, 5.0 g. of zinc dust and 45 ml. of glacial acetic acid was stirred at reflux for 5 hours, and filtered while hot. The zinc residue was extracted with hot benzene and combined with the original filtrate before evaporating to dryness. The residues were combined, washed with water, filtered and dried to give 0.34 g. (63%)

(19) This and the preceding experiment were performed by R. J. McManimie.

of crude product. This did not depress the melting point of an authentic sample of bis-(*p*-tolylsulfonyl)-ethene, m.p. 204–205°,<sup>20</sup> after one recrystallization from ethanol.

**Acknowledgment.**—The authors gratefully acknowledge support of this work by the Office of Ordnance Research, Department of the Army, under Contract No. DA-33-008-ORD 983.

(20) E. Fromm and E. Seibert, *Ber.*, **55B**, 1014 (1922).  
LAFAYETTE, IND.

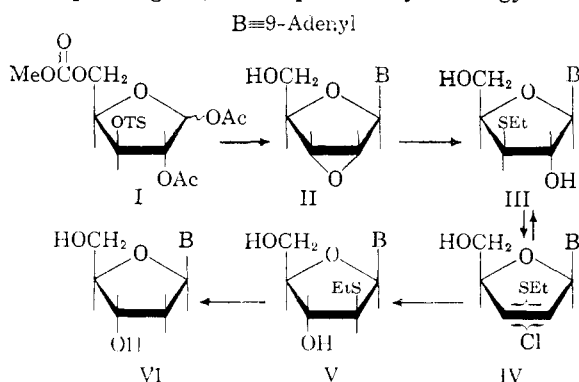
## COMMUNICATIONS TO THE EDITOR

### POTENTIAL ANTICANCER AGENTS.<sup>1</sup> SYNTHESIS OF 2'-DEOXYADENOSINE

Sir:

The first syntheses of pyrimidine 2'-deoxyribonucleosides have been announced within the past year.<sup>2,3</sup> This Communication reports the first synthesis of a purine 2'-deoxyribonucleoside, 2'-deoxyadenosine (VI). The method employed is independent of the nature of the substituent at C.1' in contrast to the earlier pyrimidine 2'-deoxyribonucleoside syntheses, all of which involve participation of a 2-oxo- or 2-thiopyrimidine moiety.

1,2-Di-*O*-acetyl-5-*O*-(methoxycarbonyl)-3-*O*-tosyl-D-xylofuranose<sup>4</sup> (I) was converted to the corresponding chloro sugar by treatment with ethereal hydrogen chloride and coupled with chloromercuri-6-benzamidopurine. The crude blocked nucleoside was converted to 6-amino-9-(2',3'-anhydro- $\beta$ -D-ribofuranosyl)-purine (II) [8.9% yield over-all from I; m.p. 200–203° dec.;  $[\alpha]^{25D} -3^\circ$  (0.6%<sup>5</sup>); C, 48.2; H, 4.72; N, 28.0]<sup>6</sup> by treatment with methanolic sodium methoxide. Reaction of II with refluxing methanolic ethylmercaptide gave, as expected by analogy with



(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center of the National Cancer Institute, Contract No. SA-43-ph-1892.

(2) D. M. Brown, D. B. Parihar, C. B. Reese and A. Todd, *Proc. Chem. Soc.*, 321 (1957); *J. Chem. Soc.*, 3035 (1958).

(3) G. Shaw and R. N. Warrener, *Proc. Chem. Soc.*, 81 (1958).

(4) C. D. Anderson, L. Goodman and B. R. Baker, *THIS JOURNAL*, **80**, 5247 (1958).

(5) Unless otherwise stated, rotations were measured in 20% aqueous pyridine.

(6) The ultraviolet spectra of all the nucleosides described were compatible with their designation as 9-substituted adenines.

methyl 2,3-anhydro- $\beta$ -D-ribofuranoside,<sup>7</sup> predominantly 6-amino-9-(3'-deoxy-3'-ethylthio- $\beta$ -D-xylofuranosyl)-purine (III) [66% yield (or 6.8% over-all from I without isolation of II); m.p. 135–155° and 181–182°;  $[\alpha]^{27D} -76^\circ$  (0.8%); C, 46.2; H, 5.77; N, 22.2; S, 10.0].

The isomer 6-amino-9-(2'-deoxy-2'-ethylthio- $\beta$ -D-arabinofuranosyl)-purine (V) was obtained by a two-step procedure utilizing the powerful anchimeric effect of a neighboring sulfide group: (a) conversion of III to 6-amino-9-[3'(2')-chloro-2',-3'-dideoxy-2'(3')-ethylthio- $\beta$ -D-arabino-(xylo)furanosyl]purine (IV) [86% yield; m.p. 188–192° dec.;  $[\alpha]^{26D} -60^\circ$  (1.0% in chloroform); C, 43.2; H, 4.97; Cl, 10.9, 10.8; S, 9.74] by treatment with thionyl chloride at room temperature and (b) hydrolysis of IV with sodium acetate in refluxing 95% aqueous methyl Cellosolve. This afforded a mixture of III and V from which V [m.p. 211–213°;  $[\alpha]^{25D} -65^\circ$  (0.9%); C, 46.3; H, 5.12; N, 22.4; S, 10.6] could be separated in 58% yield.<sup>8</sup> Desulfurization of the triacetate of V with Raney nickel and deacetylation gave a 13% yield (based on unrecovered V) of synthetic 2'-deoxyadenosine (VI) [m.p. 184–186°;  $[\alpha]^{25D} -25^\circ$  (1.2% in water)]. Its identity with natural 2'-deoxyadenosine<sup>9</sup> was established by determination of the mixed m.p. (183–186°) and by the complete coincidence of the paper chromatographic behavior (in four solvent systems), X-ray diffraction patterns, and infrared and ultraviolet spectra of the two samples.

The preparation of two classes of fraudulent 2'-deoxyribonucleosides that may be of interest as antimetabolites should be possible. Use of this sequence with unnatural bases can give one class. Reaction of IV (where B = a natural base) with nucleophiles other than hydroxide ion could afford a second class of deoxynucleosides with a fraudulent 2'-deoxyribose moiety.

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(7) C. D. Anderson, L. Goodman and B. R. Baker, *THIS JOURNAL*, **81**, in press (1959).

(8) Analogous reactions had first been studied on the corresponding methyl furanosides, see reference 7.

(9) The sample employed (m.p. 183–186°) was obtained from the California Corporation for Biochemical Research, Los Angeles 63, California.