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A Photochemical Route to the Thieno[*c*]cyclobutene System

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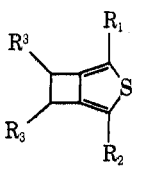
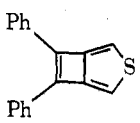
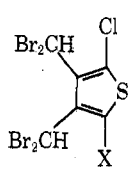
Photolysis of either of the cis or trans dihydrothienothiophene sulfones **15** and **16** affords primarily the thienocyclobutene **6**; similarly, the methoxy sulfone isomers **18** yield the methoxythienocyclobutene **19**. Both **6** and **19** undergo ready thermolysis to naphtho[*c*]thiophene derivatives. Evidence is presented which indicates that the thermolysis of **6** does not proceed *via* a tetravalent sulfur quinodimethane-type intermediate.

The first thieno[*c*]cyclobutenes have been reported only recently. These include the parent heterocycle **1**[1] and the tetrahalo derivatives **2** and **3**,[2] as well as the stable thienocyclobutadiene **4**.[3] Compounds **1** and **4** were prepared by constructing the thiophene nucleus by a Wittig synthesis; compounds **2** and **3** were prepared by a Finkelstein-type dehalogenation of an appropriate halo thiophene (**5**).



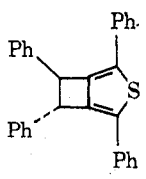


1, $R_1 = R_2 = R_3 = H$
2, $R_1 = R_2 = Cl$; $R_3 = Br$ (cis and trans)
3, $R_1 = Cl$; $R_2 = R_3 = Br$ (cis and trans)



5

We now report the synthesis and properties of several 3,4-diphenylthieno[*c*]cyclobutenes (**6**, **7** and **8**), employing the photochemical decomposition of a sulfone precursor as the key synthetic step.



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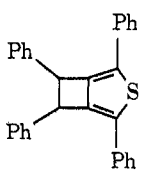

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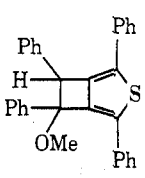
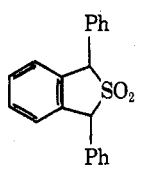


8

Results

The photochemical decomposition of the cyclic benzylic sulfones **9** and **10** affords a direct synthesis of the condensed cyclobutane aromatic hydrocarbons **11** and **12**.[4] Consequently, we decided to investigate the applicability of this type of reaction in the thiophene series. Thus, peracid oxidation of the known dihydrothienothiophenes **13** and **14**[5] gave the corresponding sulfone isomers **15** and **16**.

Both **15** and **16** lost sulfur dioxide cleanly upon irradiation in benzene–methanol in the presence of barium oxide



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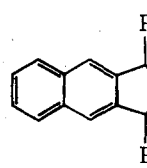

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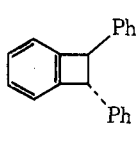

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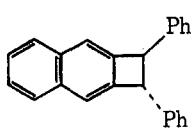

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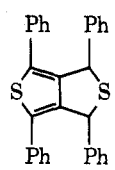
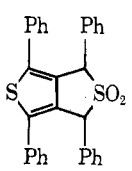


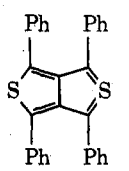
13, cis isomer
14, trans isomer



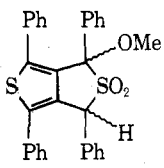
15, cis isomer
16, trans isomer

to give, in good yield, the crystalline trans thienocyclobutene **6**. Careful chromatography of the photolysis residues afforded a very small amount of the corresponding cis isomer **7**. The nmr spectra of **6** and **7** showed benzylic singlets at δ 4.47 and 5.20, respectively; the corresponding reported values for *trans*-1,2-diphenylbenzocyclobutene (**11**) and its cis isomer are δ 4.42 and 5.20, respectively.[6]

A two-step conversion of tetraphenylthieno[3,4-*c*]thiophene (**17**) to the methoxy sulfone **18** has been reported.[5] We have now found that sulfone **18** can be separated into two stereoisomers, A and B (mp 234° dec and 210° dec, respectively), both of which lose sulfur dioxide upon irradiation to give the same methoxycyclobutene **19**. The nmr spectrum of **19**, which is probably the trans isomer, shows a single benzylic hydrogen at δ 4.72 as well as a methoxyl signal at δ 3.00.



17



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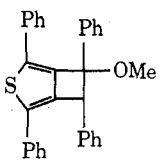
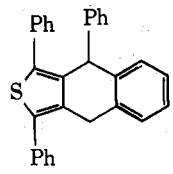


19

The thienocyclobutene **6** is quite stable in solution at temperatures up to about 60°. At 75°, however, an nmr study showed that it rearranged completely in hexachlorobutadiene solution within 45 min. The product, which was isomeric with **6** and which showed a one-proton singlet at δ 5.42 and a two-proton singlet at δ 3.98, was assigned structure **20**. Compound **20** was also obtained directly by the pyrolysis of sulfones **15** and **16** at their melt-

ing points (>200°). Palladium dehydrogenation of **20** afforded the bright red naphtho[c]thiophene derivative **21**.



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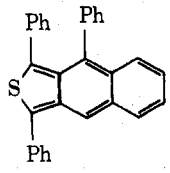
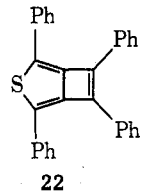


21

A number of unsuccessful attempts were made to carry out an acid-catalyzed elimination of methanol from the methoxy cyclobutene **19**, a reaction which we hoped would yield the thienocyclobutadiene **22**. The failure to achieve this conversion appears to be due to the thermal lability of **19**, which was completely converted to a complex mixture of products in a neutral deuteriobenzene solution in 30 min at 45°. Preparative decomposition of **19** in refluxing benzene, or in benzene containing *p*-toluenesulfonic acid at 25°, gave, after chromatographic separation, three isolable products. The major product was the red naphtho[c]thiophene **21**. The second product was also red and had spectral properties similar to those of **21**, although it contained a methoxyl group. It was therefore assigned structure **23**. The third product was colorless and contained a carbonyl group, and was assigned structure **24**, which is the expected acid hydrolysis product of **23**. It has been shown[7] that the parent ketone of **24**, namely **25**,



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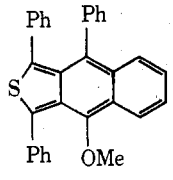
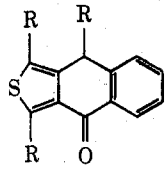


23



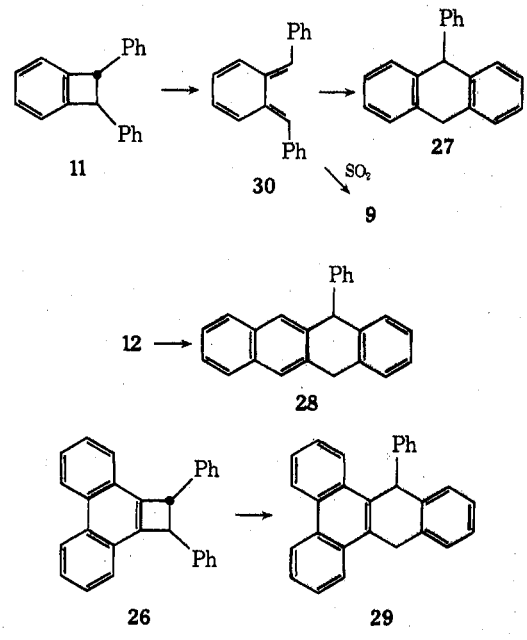
24, R = Ph
25, R = H

exists in the keto form rather than in the phenolic form. The pyrolysis of either of the stereoisomers of methoxy sulfone **18** also gave the naphtho[c]thiophene **21**.

Discussion

The thermal isomerization of the thienocyclobutene **6** to the isomeric dihydronaphtho[c]thiophene **20** is quite analogous to the thermolysis of the benzocyclobutene **11**,[8] the naphtho[*b*]cyclobutene **12**,[9] and the phenanthro[*l*]cyclobutene **26**[10] to give the corresponding rearrangement products **27**, **28**, and **29**. The rearrangements of **11**, **12**, and **26** all proceed by way of reactive *o*-quinodimethane intermediates (*i.e.*, **30**), which can be trapped either by olefinic dienophiles or by sulfur dioxide.[9,10,11] For example, the intermediate **30** from **11** is intercepted quantitatively by sulfur dioxide in boiling carbon tetrachloride,[11] or even in ether,[12] to give the sulfone **9**.

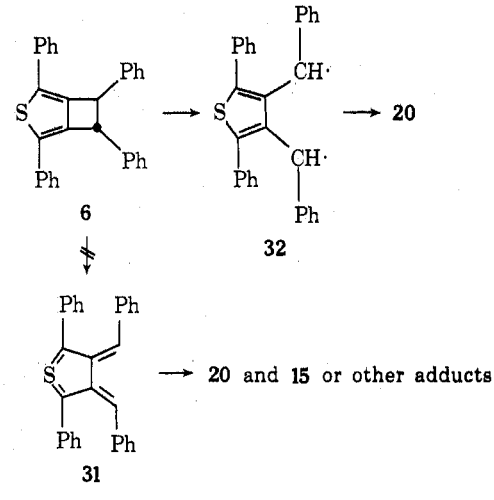
If the isomerization of **6** to **20** were to follow a similar pathway, the *o*-quinodimethane intermediate **31** would be an example of a new type of tetracovalent sulfur structure.[13] Attempts to intercept **31** during the thermolysis of **6** with either sulfur dioxide or *N*-phenylmaleimide were completely unsuccessful; only the isomer **20** was formed in the presence of these reagents. We conclude, therefore, that the tetravalent nature of the sulfur in quinomethane **31** destabilizes this species to a considerable extent relative to the diradical **32**, and that **32** is the actual intermediate in the conversion of **6** to **20**. Concerted addition of sulfur dioxide or a dienophile to **32** would not be expected on the basis of electrocyclic reaction theory.[14] Finally, it may be pointed out that the conversion of **6** to **20** represents the first case of *any* condensed cyclobutane aromatic compound which decomposes thermally without the generation of an *o*-quinonoid intermediate.



11 **30** **9** **27**

12 **28**

26 **29**



6 **32** **20**

31 → **20** and **15** or other adducts

The ultraviolet spectra of both benzocyclobutene and naphtho[*b*]cyclobutene show practically no effect of ring strain on the positions of the aromatic maxima.[15,16] In contrast, a β,β-fused four-membered ring causes a considerable bathochromic shift in the thiophene series. Thus, the thieno[c]cyclobutene **6** has as its band of longest wavelength a triplet of maxima centered at 343 nm. Its thermal rearrangement product **20**, in which an unconjugated six-membered ring has replaced the cyclobutene ring, has a corresponding unresolved band centered at 310 nm. Since the analogous band of sulfide **13** is observed at 317 nm, it is clear that the major electronic distortion of the 2,5-diphenylthiophene chromophore occurs only when a four-membered ring is condensed to the heterocyclic nucleus.

Experimental Section

General. Melting points are uncorrected. Infrared spectra were determined in KBr, on a Perkin-Elmer Model 137 spectrophotometer. Ultraviolet and visible spectra were determined in cyclohexane solution, unless otherwise noted, using a Perkin-Elmer Model 202 instrument. Nmr spectra were recorded on a Varian HA-100 MHz machine. Photolyses were carried out under nitrogen using a Hanovia medium-pressure lamp with a Vycor filter.

Oxidation of Sulfide 13 to Sulfone 15. A solution of 1.6 g of *cis*-1,3-dihydro-1,3,4,6-tetraphenylthieno[3,4-*c*]thiophene (**13**)[5] in 180 ml of benzene–methanol (2:1) was treated with 50 ml of 40%

peracetic acid. The mixture was refluxed for 1 hr. The crystalline cis sulfone **15** was filtered. The filtrate was cooled, cautiously treated with ammonia, and extracted (chloroform) to yield additional **15**. Recrystallization of the total crude **15** from chloroform–ethanol afforded 1.3 g (76%) of pure **15**: mp 290° dec; nmr ($CDCl_3$–DMSO) δ 5.86 (s); ir 7.55, 8.80 μ (SO_2); uv spectrum λ_{max} (EtOH) 310 nm (log ϵ 4.20); mass spectrum m/e (rel intensity) 478 (M^+, 5), 414 (M − 64, 100).

Anal. Calcd for $C_{30}H_{22}S_2O_2$: C, 75.31; H, 4.63. Found: C, 74.82; H, 4.87.

Oxidation of Sulfide 14 to Sulfone 16. The corresponding trans-dihydrothieno[3,4-*c*]thiophene (**14**),[5] upon peracetic acid oxidation in a similar manner, yielded sulfone **16**, mp 225° dec, in 71% yield: nmr ($CDCl_3$–DMSO) δ 5.67 (s); ir 7.55, 8.65 μ (SO_2); uv spectrum λ_{max} (EtOH) 312 nm (log ϵ 4.20); mass spectrum m/e (rel intensity) 478 (M^+, 6), 414 (M − 64, 100).

Anal. Calcd for $C_{30}H_{22}S_2O_2$: C, 75.31; H, 4.63. Found: C, 74.62; H, 4.86.

Photolysis of Sulfone 15 to the Thienocyclobutenes 6 and 7. A solution of 140 mg of **15** in 450 ml of benzene and 100 ml of methanol containing 100 mg of barium oxide was irradiated for 4 hr. The pale yellow solution was concentrated under reduced pressure (<40°). Extraction of the residue with benzene, followed by chromatography (Woelm I alumina, benzene–hexane 1:1 eluent) and crystallization from methanol–ether gave 75 mg (62%) of **6**: mp 145°; nmr ($CDCl_3$) δ 4.47 (s); mass spectrum m/e (rel intensity) 414 (M^+ 98); uv spectrum λ_{max} 245 nm (log ϵ 4.28), 328 (4.41), 343 (4.52), 360 (4.39).

Anal. Calcd for $C_{30}H_{22}S$: C, 86.93; H, 5.35. Found: C, 87.37; H, 5.53.

Elution of the alumina column with benzene gave traces of the isomeric cis cyclobutene **7**. Accumulation of material from several such runs, followed by crystallization from methanol, gave pure **7**: mp 155° dec; nmr ($CDCl_3$) δ 5.20; mass spectrum m/e (rel intensity) 414 (M^+, 77); uv spectrum λ_{max} 245 nm (log ϵ 4.18), 327 (4.34), 343 (4.44), 360 (4.37).

Photolysis of Sulfone 16. Photolysis of 100 mg of **16** in benzene–methanol solution containing 100 mg of barium oxide was carried out as described above for isomer **15** to give 60 mg of **6** (70%), mp 145° dec.

The absence of methanol and barium oxide in the reaction mixture led to a 54% yield of **6**, with recovery of 34% of **16**. No interconversion of sulfones **15** and **16** was observed under the reaction conditions.

Separation of the Isomers of Methoxy Sulfone 18. The methoxy sulfone **18** (908 mg), prepared as described earlier,[5] was boiled with chloroform (120 ml). After cooling, the insoluble crystalline material was filtered to give isomer A (514 mg): mp 234° dec; nmr (DMSO-d_6) δ 6.27 (s, 1 Hz), 3.63 (s, 3 H); ir 7.60, 8.75 μ (SO_2).

Anal. Calcd for $C_{31}H_{24}S_2O_3$: C, 73.23; H, 4.72. Found: C, 73.03; H, 5.13.

Chromatography (silica, benzene eluent) of the residue followed by crystallization gave 290 mg of isomer B: mp 210° dec; nmr (DMSO-d_6) δ 6.26 (s, 1 H), 3.35 (s, 3 H); ir 7.60, 8.75 μ (SO_2).

Anal. Calcd for $C_{31}H_{24}S_2O_3$: C, 73.23; H, 4.72. Found: C, 73.09; H, 5.00.

Photolysis of Isomeric Methoxy Sulfones 18. Photolysis of 100 mg of sulfone **18A** was carried out as described for sulfone **15**. Direct crystallization of the crude product from ether–hexane led to the isolation of 30 mg (33%) of **19**: mp 137° dec; nmr ($CDCl_3$) δ 4.72 (s, 1 H), 3.00 (s, 3 H); mass spectrum m/e (rel intensity) 444 (M^+, 100); uv spectrum λ_{max} 230 nm (sh, log ϵ 4.40), 245 (sh, 4.25), 330 (4.40), 345 (4.45), 364 (4.31).

Anal. Calcd for $C_{31}H_{24}SO$: C, 83.76; H, 5.44. Found: C, 83.59; H, 5.17.

Photolysis of the isomeric sulfone **18B** gave **19** in similar yield. When **18A** was photolyzed at 0–10°, the yield of **19** rose to 69%.

Thermal Rearrangement of 6. The nmr spectrum of a solution of 17 mg of **6** in 0.3 ml of hexachlorobutadiene was unchanged after 30 min at 25, 30, 40, 50, and 60°, no aliphatic proton being observed in addition to the singlet at δ 4.47. At 75° new signals at δ 5.42 and 3.98 (1:2 ratio) soon appeared and within 45 min the signal at δ 4.47 had vanished completely.

A solution of 30 mg of **6** in 10 ml of carbon tetrachloride was refluxed for 1 hr. Evaporation of the solvent and crystallization of the residue (ether–hexane) yielded 20 mg of **20**: mp 178°; nmr ($CDCl_3$) δ 5.42 (s, 1 H), 3.98 (s, 2 H); mass spectrum m/e (rel intensity) 414 (M^+ 100); uv spectrum λ_{max} 254 nm (log ϵ 4.15), 310 (4.29).

Anal. Calcd for $C_{30}H_{22}S$: C, 86.93; H, 5.35. Found: C, 87.35; H, 5.77.

Thermal Decomposition of Sulfone 15. The sulfone **15** (100 mg) was heated in a tube at 290–295° until gas evolution ceased. Chromatography (Woelm neutral I alumina, hexane eluent) of the residue followed by crystallization (benzene–hexane) gave 45 mg (52%) of **20**, mp 178°.

From 48 mg of sulfone **16**, proceeding in a similar fashion, 20 mg (45%) of **20** was obtained.

Pyrolysis of Methoxy Sulfone 18A. The sulfone **18A** (100 mg) was heated at 235° until gas evolution ceased. Chromatography (Woelm neutral I alumina, hexane eluent) of the melt followed by crystallization gave 25 mg (31%) of **21** as red needles: mp 222°; uv-visible spectrum λ_{max} 255 nm (log ϵ 4.53), 270 (sh, 4.45), 287 (sh, 4.32), 315 (sh, 4.13), 485 (3.90), 505 (3.95); mass spectrum m/e (rel intensity) 412 (M^+, 100).

Anal. Calcd for $C_{30}H_{20}S$: C, 87.35; H, 4.89. Found: C, 86.70; H, 5.07.

Dehydrogenation of 20 to 21. An intimate mixture of **20** (20 mg) and 5% Pd/C (20 mg) was heated for 5 min over a free flame. The melt was dissolved in benzene, freed from catalyst, and chromatographed [silica, benzene–hexane (1:1) eluent] to yield 5 mg (25%) of **21**, mp 220° (from ether–hexane).

Attempted Elimination of Methanol from 19. A solution of 20 mg of **19** in 10 ml of benzene was heated on the steam bath. Within a few minutes all of the starting material had disappeared. The solvent was evaporated and the residue was subjected to plc [silica gel, benzene–hexane (1:1)] to give two red compounds A and B and a colorless compound C. Compound A, mp 220°, was identical with **21** as shown by comparison of melting point and ir and uv spectra with an authentic sample.

Compound B (**23**), mp 152° (from ether–hexane), was orange: nmr ($CDCl_3$) δ 3.44 (s, 3 H); uv-visible spectrum λ_{max} 235 nm (log ϵ 4.92), 278 (sh, 4.15), 287 (sh, 4.13), 476 (3.37), 510 (3.45); mass spectrum m/e (rel intensity) 442 (M^+, 20).

A satisfactory elemental analysis of this compound could not be obtained, probably because of the ease with which it undergoes photooxidation.

Compound C (**24**) had mp 178° (ether–hexane); nmr δ 5.52 (1 H, s); uv spectrum λ_{max} 220 nm (sh, log ϵ 4.58), 262 (sh, 4.37), 279 (4.40), 340 (3.84); ir 6.0 μ (C=O); mass spectrum m/e (rel intensity) 428 (M^+, 100).

Anal. Calcd for $C_{30}H_{20}SO$: C, 84.11; H, 4.67. Found: C, 84.11; H, 4.85.

Conversion of 23 to 24. A solution of **23** (5 mg) in moist benzene (10 ml) was refluxed for 1 hr after the addition of a trace of *p*-toluenesulfonic acid. The solution was evaporated to dryness. The residue was worked up by plc (silica–benzene) to yield **24** (3 mg, 61%), mp 178°.

Rearrangement of 6 to 20 in the Presence of Trapping Agents. A. In the Presence of Sulfur Dioxide. Sulfur dioxide was bubbled through a solution of 10 mg of **6** in 20 ml of ether at room temperature, taking care to maintain the solvent level. After 3 hr, evaporation of the ether gave unchanged **6** (7 mg). No trace of either sulfone **15** or **16** could be detected. The use of benzene or dimethylformamide at room temperature also led to recovery of **6**. The sulfur dioxide addition was then attempted in boiling solvents, such as carbon tetrachloride, benzene, and xylene. Again no trace of **15** or **16** was detected, the only product isolated being **20**, formed in good yield.

B. In the Presence of *N*-Phenylmaleimide. Solutions of **6** (10 mg) and *N*-phenylmaleimide (10 mg) in (a) benzene and (b) chloroform were stirred at room temperature for 24 hr. Evaporation followed by purification of the residue led to recovery of **6**.

When a solution of **6** (20 mg) and *N*-phenylmaleimide (20 mg) in benzene (10 mg) was refluxed for 4 hr, the product obtained was **20** (13 mg). No other product could be detected.

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Registry No. **6**, 42962-82-3; **7**, 42962-83-4; **13**, 40953-23-9; **14**, 40953-24-0; **15**, 42880-82-0; **16**, 42880-83-1; *cis*-**18**, 42880-84-2; *trans*-**18**, 42962-84-5; **19**, 42880-85-3; **20**, 42893-99-2; **21**, 42894-00-8; **23**, 42894-01-9; **24**, 42894-02-0.

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Urylenediphosphonates. A General Method for the Synthesis of α-Ureidophosphonates and Related Structures

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Urea and many mono- and disubstituted ureas and their thio analogs react with aldehydes and certain esters of trivalent phosphorus acids, providing a route to numerous new α-ureidophosphonates, $(RO)_2P(O)CHR'NHCONH_2$, and related products. Surprisingly, triphenyl phosphite is more readily converted to phosphonates in this process than are trialkyl phosphites, a reversal of the normal order of reactivity of phosphite esters. Acid catalysis is beneficial in some cases. Urylenediphosphonates, $(RO)_2P(O)CHR'NHCONHCHR'P(O)(OR)_2$, as well as monophosphonates are obtained when unsubstituted urea is used, whereas mono- and disubstituted ureas give only monophosphonates. Phosphonite and phosphinite esters react similarly, giving ureaphosphinates and -phosphine oxides, respectively. Cyclic 1,4,2-diazaphospholidins are the major products when 1,3-dimethylurea is used. Many of the products can be readily hydrolyzed to the corresponding ureidophosphonic and -phosphinic acids.

While the synthesis and properties of many types of nitrogen-containing organophosphorus compounds have been widely investigated,[1] for example, aminophosphonates in biochemical[2] and in chelation[3,4] studies, ureaphosphonates have received little attention. In connection with our interests in new biologically active structures and in permanent fire retardancy of polymers,[5] a search was made for routes to urea derivatives having organophosphorus substituents. The resulting investigation led to the discovery that urea and many mono- and disubstituted ureas and their thio analogs will react with certain esters of trivalent phosphorus acids and aldehydes to give α-ureidophosphonates and related products. Numerous compounds can be synthesized by this process, since the structures of all three reactants are subject to broad variation.

The application of this new reaction to the preparation of urylenediphosphonates (**1a-d**) from urea, phosphite esters, and aldehydes is represented by the following equation.

$$2(RO)_3P + H_2NCONH_2 + 2R'CHO \longrightarrow (RO)_2P(O)CHR'NHC(O)NHCHR'P(O)(OR)_2 + 2ROH$$

1a, R = C_6H_5; R' = CH_3
b, R = C_6H_5; R' = C_6H_5
c, R = CH_2CH_2Cl; R' = CH_3
d, R = CH_2CH_2Cl; R' = $CH(CH_3)_2$

Generally, the reaction is initiated when a mixture of the three reactants is warmed to about 60–70°; it is usually complete after 10–15 min at 70–100°. Alternatively, the aldehyde may be added gradually to a mixture of urea and the phosphite ester at this temperature. Since the crude products are mixtures of isomers, resulting from formation of two asymmetric centers in each diphosphonate molecule, crystallization is usually slow. Yields of crystalline diphosphonates isolated have consequently been limited to 60% or less even though ^{31}P nmr measurements have indicated that some of the crude reaction mixtures contained considerably more material.

Although thiourea is less reactive than urea in this process, results are satisfactory when it is used with triphenyl phosphite and an alkyl aldehyde. Tetraphenyl (thiourylenedibutyl)diphosphonate (**2**) was obtained from thiourea, triphenyl phosphite and *n*-butyraldehyde in nearly a quantitative yield according to ^{31}P nmr measurements.

$$2(C_6H_5O)_3P + H_2NCSNH_2 + 2CH_3CH_2CH_2CHO \longrightarrow (C_6H_5O)_2P(O)CH(CH_2CH_2CH_3)NHC(S)NHCH(CH_2CH_2CH_3)P(O)(OC_6H_5)_2 + 2C_6H_5OH$$

2

In a few cases two fractions, presumably *dl* and meso forms, were isolated. Tetraphenyl (urylenedibenzyl)diphosphonate (**1b**), for example, was separated into fractions I and II.

The observed ^{31}P and ^1H nmr multiplets for I and II were consistent with the expected phosphorus–hydrogen and hydrogen–hydrogen spin couplings for structure **1b**. Conversion of the ^1H nmr doublet of doublets for each fraction to a simple doublet, J_{CHNH} = 10 Hz, by heteronuclear ^{31}P spin decoupling provided further evidence of the