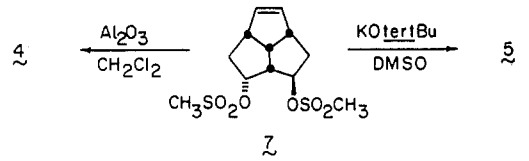
bond. A number of years ago, a facile synthesis of 5[10] was uncovered in this laboratory. This finding, which forms the subject of this note, may serve to stimulate renewed interest in acepentalene (6), the most fully dehydrogenated, strained, and electronically perturbed member of this class of molecules.[5]

As Deslongchamps and co-workers first pointed out,[8] dimesylate 7 in dichloromethane solution readily undergoes twofold elimination when slurried with activated alumina at room temperature to give 4 in moderate yield. We have



observed that substitution of potassium *tert*-butoxide in anhydrous dimethyl sulfoxide leads instead to a product mixture highly enriched in the less thermodynamically stable 5 in 69% crude yield (5:4 = 96:4). Following purification by preparative vapor-phase chromatography, 5 was isolated as a colorless oil, which, while relatively stable in dilute solution or under an inert atmosphere, polymerized on standing in air at room temperature for several hours. Its ^1H and ^{13}C NMR spectra (see Experimental Section) are fully consistent with the unsymmetrical nature of the triene.

In the belief that 5 is formed under kinetically controlled conditions, attempts were made to induce its isomerization to 4 with activated alumina. However, reaction times up to 48 h led to no detectable double-bond isomerization (error limits ±1%). Isotriquinacene was thereby shown not to be a precursor of triquinacene under the Deslongchamps conditions. These results constitute an interesting dichotomy concerning the manner in which the two reagents in question enter into formal E_2 elimination chemistry. Such differences may be more widespread than heretofore appreciated in conformationally rigid systems[11] and may offer insightful opportunities for developing proper synthetic strategies toward strained olefins.

Experimental Section

Tricyclo[5.2.1.0^{4,10}]deca-1,5,8-triene (Isotriquinacene, 5). To a solution of 7[8] (2.0 g, 6.2 mmol) in dry dimethyl sulfoxide (40 mL) was added potassium *tert*-butoxide (2.2 g, 19 mmol) in one portion. The reaction flask was purged with nitrogen and stirred at room temperature for 24 h. The dark reaction mixture was poured into water (150 mL) extracted with ether (3 × 100 mL), dried, and evaporated to leave 560 mg (69%) of triene mixture as a reddish oil. VPC analysis (15% Carbowax 20M on Chromosorb P, 100 °C, 10 ft × $^1/_8$ in) showed the mixture to be comprised of 4% of 4 and 96% of 5 (assuming the same detector response for the isomers). Preparative VPC isolation (5% SE-30 on Chromosorb P, 130 °C, 6 ft × $^1/_4$ in.) afforded 5 as a colorless liquid; ^1H NMR (270 MHz, $CDCl_3$) δ 6.21 (dd, J = 5.7 and 0.5 Hz, H_9), 6.07 (dd, J = 5.7 and 2.8 Hz, H_8), 5.54 (dt, J = 5.4 and 0.6 Hz, H_6), 5.41 (dt, J = 5.4 and 1.9 Hz, H_5), 5.37 (dt, J = 3.7 and 2.2 Hz, H_2), 3.78 (m, H_{10}), 3.45 (m, H_7), 3.16 (dq, J = 5.8 and 2.0 Hz, H_4), 3.00 (m, exo-H_3), 2.55 (ddd, J = 16.6, 3.7, and 2.0 Hz, endo-H_3); ^{13}C NMR ($CDCl_3$) ppm 155.87 (s), 139.16 (d), 136.09 (d), 128.43 (d), 127.91 (d), 117.94 (d), 59.92 (d), 52.01 (d), 47.72 (d), 42.73 (t).

Anal. Calcd for $C_{10}H_{10}$: C, 92.26; H, 7.74. Found: C, 91.84; H, 8.08.

Acknowledgment. We thank the National Institutes of Health (Grant AI-11490) for underwriting the costs of this research.

Registry No. 5, 89032-66-6; 7, 42501-47-3; potassium *tert*-butoxide, 865-47-4.

(9) Wyvratt, M. J.; Paquette, L. A. *Tetrahedron Lett.* **1974**, 433. Paquette, L. A.; Wyvratt, M. J.; Berk, H. C.; Moerck, R. E. *J. Am. Chem. Soc.* **1978**, *100*, 5845. Paquette, L. A.; Kearney, F. R.; Drake, A. F.; Mason, S. F. *Ibid.* **1981**, *103*, 5064.

(10) Tricyclo[5.2.1.0^{4,10}]deca-1,5,8-triene, the proposed colloquial name for which is isotriquinacene.

(11) Compare: Deslongchamps, P.; Cheriyan, U. O.; Lambert, Y.; Mercier, J.-C.; Ruest, L.; Russo, R.; Soucy, P. *Can. J. Chem.* **1978**, *56*, 1687.

Biologically Oriented Organic Sulfur Chemistry. 23. A Hydrodisulfide from a Sulfonamide Derivative of Penicillamine[1]

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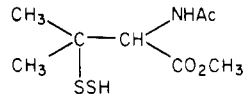
Hydrodisulfides (RSSH) are important intermediates in several biochemical and chemical systems. For example, they play essential roles in enzyme-catalyzed reactions[2] and are formed in the oxidation of phosphorothioates to phosphates (e.g., of parathion, p-$O_2NC_6H_4OPS(OEt)_2$, to paraoxon, p-$O_2NC_6H_4OPO(OEt)_2$) by cytochrome P-450.[3] In previous work,[4] a hydrodisulfide (1) derived from the



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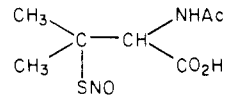

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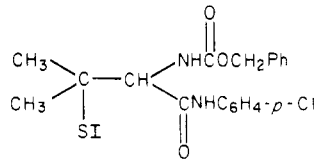

3

methyl ester of *N*-acetylpenicillamine was prepared in the hope that, as had been found with a thionitrite (2)[5] and a sulfenyl iodide (3),[6] the hydrodisulfide would be relatively stable. We hoped that 1 thus might provide a product that would make the corresponding thiol a useful trap for sulfur atoms generated either photochemically from carbonyl sulfide[7] or from the oxidation of phosphorothioates with

(1) For paper 22, see: Bowman, G. T.; Field, L. *J. Org. Chem.* **1982**, *47*, 222.

(2) Ploegmon, J. H.; Drent, G.; Kalk, K. H.; Hol, W. G. J.; Heinrickson, R. L.; Keim, P.; Weng, L.; Russell, J. *Nature (London)* **1978**, *273*, 124. Massey, V.; Edmondson, D. *J. Biol. Chem.* **1970**, *245*, 6595. Edmondson, D.; Massey, V.; Palmer, G.; Beacham, L. M., III; Elion, G. B. *Ibid.* **1972**, *247*, 1597. Branzoli, U.; Massey, V. *Ibid.* **1974**, *249*, 4346. Cavallini, D.; DeMarco, C.; Mondovi, B.; Mori, B. G. *Enzymologia* **1960**, *22*, 161. Flavin, M. *J. Biol. Chem.* **1962**, *237*, 768. Loiselet, J.; Chatagner, F. *Bull. Soc. Chim. Biol.* **1966**, *48*, 595.

(3) Neal, R. A.; Kamataki, T.; Lin, M.; Ptashne, K. A.; Dalvi, R. R.; Poore, R. E. In "Biological Reactive Intermediates"; Jallow, D. J., Kocsis, J. J., Snyder, R., Vainio, H., Eds.; Plenum: New York, 1977; p 320. Neal, R. A. In "Sulfur in Pesticide Action and Metabolism"; Rosen, J. D., Magee, P. S., Casida, J. E., Eds.; American Chemical Society: Washington, DC, 1981; pp 19–34, ACS Symposium Series, No. 158.

(4) Heimer, N. E.; Field, L.; Neal, R. A. *J. Org. Chem.* **1981**, *46*, 1374.

(5) Field, L.; Dilts, R. V.; Ravichandran, R.; Lenhert, P. G.; Carnahan, G. E. *J. Chem. Soc., Chem. Commun.* **1978**, 249.

(6) Field, L.; White, J. E. *Proc. Natl. Acad. Sci. U.S.A.* **1973**, *70*, 328. Field, L.; White, J. E. *Int. J. Sulfur Chem.* **1976**, *8*, 539.

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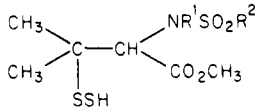
oxidizing agents used as models for P-450 oxidations.[8] Hydrodisulfide **1**, however, did not appear to have a shelf life that compared favorably with *tert*-butyl hydrodisulfide, which can be purified by distillation at 40 °C (120 torr).[9]

In view of the reported ease with which 2-acetamidoethyl hydrodisulfide decomposes,[10] as well as our own conclusion that the *N*-acetyl group was involved in the decomposition of **1**,[4] it seemed that replacement of the *N*-acetyl group with an *N*-alkane- or *N*-arenesulfonyl group might lead to a crystalline hydrodisulfide with a longer lifetime than **1** and thus provide a better trapping product for sulfur atoms. This paper reports the synthesis and characterization of the *N*-tosyl analogue of the *N*-acetylhydrodisulfide **1**, for example, of **4** with R^1 = H and R^2 = *p*-$C_6H_4CH_3$. Efforts to prepare other derivatives of **4** (i.e., with R^1 =



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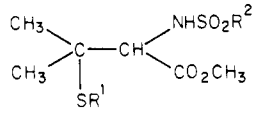

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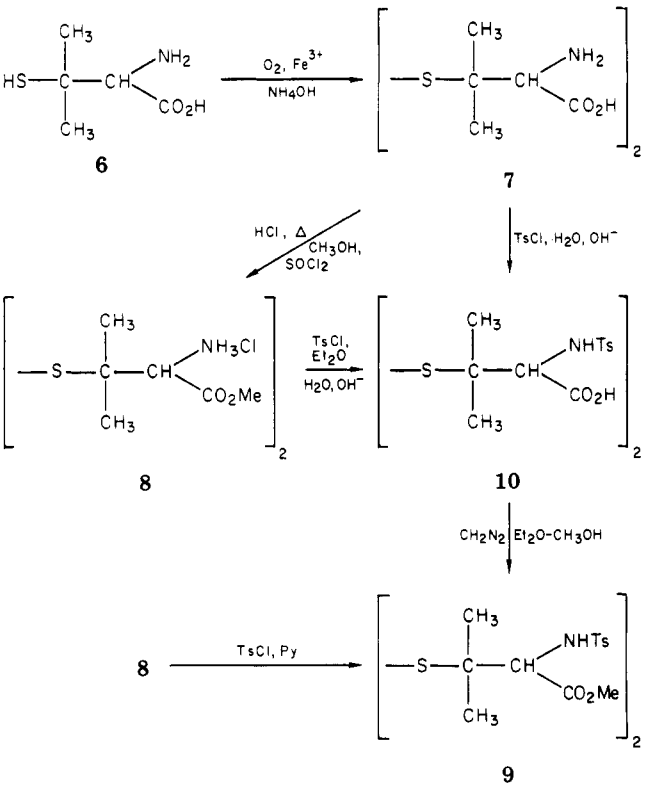
H and R^2 = CH_3 or *p*-BrC_6H_4) gave materials that were very difficult to purify; furthermore, these hydrodisulfide derivatives, on the basis of preliminary studies, did not show solution lifetimes very different than the *p*-toluenesulfonyl derivative, so only it was studied further.

Preparation of hydrodisulfides usually is accomplished by methanolysis of acetyl disulfide derivatives (AcSSR), which often are prepared by the reaction of acetylsulfenyl chloride (AcSCl) with a thiol,[12] although reaction of the thiol with methoxycarbonyl acetyl disulfide[4] or of a sulfenyl chloride with thioacetic acid provide alternate routes. The key intermediate in the preparation of *N*-sulfonyl derivatives of penicillamine of type **4** thus is the corresponding acetyl disulfide derivative **5**, with R^1 = SAc.

When an effort to prepare an *N*-mesyl hydrodisulfide (**4**; R^1 = H, R^2 = CH_3) was thwarted by the reaction of eq 1 (R = $C(CH_3)_2CN(CO_2CH_3)NHSO_2CH_3$), D-penicillamine (**6**) was converted to disulfide **7**, under standard conditions,[13] after which the preparation of the dimethyl ester of *N,N'*-ditosylpenicillamine disulfide (**9**) proceeded as shown by Scheme I. Disulfide **7** was converted to dimethyl ester **8** by reaction with HCl–$SOCl_2$ in MeOH for 24 h at reflux. The hygroscopic dimethyl ester dihydrochloride **8** was used without purification. Reaction of crude **8** with tosyl chloride in pyridine gave **9** as a semisolid. An attempt to prepare **9** from **8** by the Schotten-Baumann procedure yielded, after acidification, only the *N,N'*-ditosyl dicarboxylic acid **10**. Ditosyl dicarboxy disulfide **10** was isolated following crystallization from diethyl ether as a monoetherate (NMR, elemental analysis); recrystallization of the etherate from acetic acid resulted in replacement

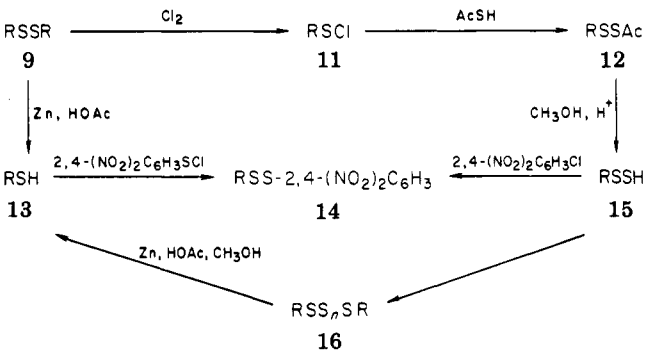
$$RSH + CH_3SO_2Cl \rightarrow RSSO_2CH_3 \xrightarrow{RSH} RSSR \quad (1)$$

Scheme I[a]



[a] Ts = $CH_3C_6H_4SO_2^-$.

Scheme II[a]



[a] R = $-C(CH_3)_2CH(CO_2Me)NHTs$.

of the ether by two molecules of acetic acid. These results suggest inclusion-type possibilities for **10** that warrant further study. The most convenient route to the pure ditosyl diester **9** was by conversion of disulfide **7** to ditosyl diacid **10** with tosyl chloride, followed by esterification with diazomethane to give **9** as a crystalline product with the same IR and NMR spectra as the product prepared from **8** with tosyl chloride in pyridine.

Attempts to reduce disulfide **9** to the thiol **13**, with tin in acetic acid, sodium borohydride in methanol, borane-THF in ether, and sodium dithionite gave only recovered **9**. Attempted reduction with sodium in liquid ammonia gave several reduction products but not the thiol. Reduction of **9** with zinc in MeOH–$HC_2H_3O_2$ gave thiol **13** but only after inconveniently long periods (25 h) and in such low yield (ca. 27%) that an alternate route to **12** other than via **13** was sought.

Conversion of **9** to the acetyl disulfide **12** and hydrodisulfide **15** ultimately was achieved as shown by Scheme II. Chlorinolysis of **9** in chloroform at room temperature gave **11**, which reacted with thioacetic acid to give un-

(7) Field, L.; Ravan, J. V.; Dunkel, J. D.; Waites, J. A.; White, D. W.; Heimer, N. E.; Neal, R. A. *J. Org. Chem.* **1982**, *47*, 4651.
(8) (a) Heimer, N. E.; Field, L.; Neal, R. A. *J. Org. Chem.* **1981**, *46*, 1374. (b) Field, L.; Heimer, N. E.; McNeil, R. I.; Neal, R. A.; Swinson, J.; VanWazer, J. R. *Sulfur Lett.* **1983**, *1*, 135.
(9) Aycock, D. F.; Jurch, G. R. *J. Org. Chem.* **1974**, *44*, 569.
(10) Tsurugi, J.; Yasuo, A.; Kawamura, S. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1890.
(11) Nakabayashi, T.; Tsurugi, J.; Yabuta, T. *J. Org. Chem.* **1964**, *29*, 1236.
(12) Field, L. In "Organic Chemistry of Sulfur"; Oae, S., Ed.; Plenum: New York, 1977; pp 307–309.
(13) Crooks, H. M., Jr. In "The Chemistry of Penicillin"; Clarke, H. T., Johnson, J. R., Robinson, R., Eds.; Princeton University Press: Princeton, NJ, 1949; p 31.

symmetrical disulfide **12**, the desired precursor to the hydrodisulfide. Methanolysis of **12** could be monitored by observing the relative magnitudes in the ^1H NMR spectrum of the methine proton resonances (a doublet at δ 3.83 for **12** and a doublet at δ 3.89 for **15**). The resulting hydrodisulfide **15** was characterized by ^1H and ^{13}C NMR, by IR, and by conversion to the dinitrophenyl disulfide derivative **14** by reaction with 2,4-dinitrochlorobenzene, which also was obtained by reaction of thiol **13** with 2,4-dinitrobenzenesulfenyl chloride.

Upon standing in acidic methanol solution for short periods of time (ca. 2 h), hydrodisulfide **15** decomposes to products presumed to be a mixture of polysulfides (**16**), since the ^1H NMR spectrum of the mixture showed two sets of methine protons and four lines for the *gem*-dimethyl groups. Reduction of this product mixture with Zn–CH_3OH–$HC_2H_3O_2$ produced thiol **13**. In $CHCl_3$ solution, decomposition of hydrodisulfide **15** was quite slow as determined by ^1H NMR; no change was observed after 2 weeks at room temperature although a faint odor of H_2S was detected. Solutions of **15** in $CHCl_3$ that were not gently washed with H_2O decomposed more rapidly. The addition of 1 drop of concentrated aqueous NH_3 to a sample that had been observed for 2 weeks caused it to become yellow immediately, and within 3 min the *gem*-dimethyl and methine ^1H NMR peaks assigned to the hydrodisulfide had disappeared and were replaced by sets of peaks considered to represent a mixture of polysulfide products (^1H NMR peaks at δ 1.26, 1.40, and 1.48 for the *gem*-dimethyl groups and doublets centered at δ 3.85 and 3.96 for the methine proton). The gently washed neat hydrodisulfide kept at −20 °C for 12 h did not appear to have undergone measurable decomposition and after standing at room temperature for 24 h showed only 15% decomposition. The *N*-acetyl derivative **1**, however, completely decomposed in less than 26 h at −10 °C.[4] It therefore appears that the substitution of the *p*-toluenesulfonyl group in **15** for the acetyl group in **1** leads to a product that decomposes significantly less rapidly, thus supporting our earlier conclusion that the acetyl group of **1** played a significant role in its decomposition.[4] On the other hand, comparison of the shelf life of **15** with that deduced for *tert*-butyl hydrosulfide from reports of its preparation and purification by distillation[9] indicates that **15** probably decomposes more rapidly than a simple tertiary hydrodisulfide.

Attempts to prepare *N*-methyl derivatives failed. Reaction of **9** with KOH and CH_3I led only to recovered **9**. Attempted *N*-methylation of **17** gave only acrylate **18** (eq 2).

$$8 \xrightarrow[C_5H_5N]{MeSO_2Cl} [SC(CH_3)_2CH(CO_2Me)NHSO_2Me]2 \xrightarrow[CH_3OH]{CH_3I,\ KOH} \underset{17}{} (CH_3)_2C{=}C(CO_2Me)N(Me)SO_2Me \quad (2)$$
$$\underset{18}{}$$

Experimental Section

Melting points were determined by using a Thomas-Hoover stirred-liquid apparatus and are corrected. NMR spectra were recorded in $CDCl_3$ unless otherwise specific with either a JEOL JNM-MH-100 or a JEOL FX-60Q spectrometer using Me_4Si as an internal standard; chemical shifts are reported in parts per million (δ). IR spectra were obtained on KBr pellets or on $CHCl_3$ solution with a Perkin-Elmer Model 521 spectrophotometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Moist extracts were dried by using $MgSO_4$ or Na_2SO_4, and solvents then were removed under reduced pressure by using a rotary flask evaporator. TLC was done by using Eastman Chromagram sheets of No. 13181 silica gel. D-Penicillamine, 2,4-dinitrobenzenesulfenyl chloride, and thioacetic acid were purchased from Aldrich Chemical Co. D-Penicillamine disulfide (**7**) was prepared by air oxidation of D-penicillamine;[13] mp 202–205 °C dec; lit.[13] mp 204–205 °C.

D-Pencillamine Disulfide Dimethyl Ester Dihydrochloride (8). Enough HCl (g) was added to a suspension of 5.0 g (16.9 mmol) of **7**[13] in 50 mL of MeOH to saturate the solution. The solution then was cooled to 0 °C and 2.63 mL of $SOCl_2$ (28 mmol) was added dropwise. The solution was allowed to warm to room temperature and after 4 h was heated under gentle reflux for an additional 24 h. Evaporation of the MeOH under reduced pressure gave 7.7 g of a very hygroscopic syrup that could not by crystallized and was used without further purification.

Bis(D-1-(*p*-Tolylsulfonamido)-1-carboxy-2-methyl-2-propyl) Disulfide (10). *p*-Toluenesulfonyl chloride, (26 mmol) 5.0 g, was added to a solution of 3.50 g (11.8 mmol) of **7** and 3.0 g (46 mmol) of 85% KOH in 30 mL of H_2O, and the mixture was stirred overnight at room temperature. The resulting mixture was made strongly basic with KOH, washed with 20 mL of Et_2O, acidified with 35% aqueous HCl, and extracted twice with CH_2Cl_2. Evaporation of the CH_2Cl_2 solution yielded 2.70 g (38%) of **10**, which was recrystallized from MeOH and Et_2O to give **10** as a colorless ether solvate: mp 180–181 °C; ^1H NMR ($CDCl_3$) δ 1.12 (t, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3Ar), 3.44 (q, 2 H, CH_2O), 3.94 (d, 1 H, CHN), 6.56 (d, 1 H, NH), 7.3–7.9 (m, 4 H, Ar), 8.50 (s, 1 H, CO_2H).

Anal. Calcd for $C_{24}H_{32}N_2O_8S_4 \cdot (C_2H_5)_2O$: C, 49.53; H, 6.23. Found: C, 49.42; H, 6.53.

Recrystallization of the ether solvate of **10** from acetic acid gave **10** as a colorless diacetic acid solvate: mp 145–152 °C; ^1H NMR (acetone-d_6) δ 1.34 (s, 3 H, CH_3C), 1.38 (s, 3 H, CH_3C), 1.96 (s, 3 H, CH_3CO), 2.40 (s, 3 H, CH_3Ar), 3.90 (d, J = 10.3 Hz, CHN), 6.7 (d, J = 10.3 Hz, NH), 7.2–7.8 (m, 4 H, *p*-C_6H_4), 7.8 (br s, 2 H, OH).

Anal. Calcd for $C_{24}H_{32}N_2O_8S_4 \cdot (HC_2H_3O_2)_2$: C, 46.39; H, 5.56; S, 17.69. Found: C, 46.34; H, 5.66; S, 17.99.

Recrystallization of the acetic acid solvate from Et_2O provided the ether solvate again. The report of the D,L counterpart of D-**10** gives only the melting point (224–229 °C) and neither mentions solvates nor gives other details.[14]

The same material (**10**) was obtained by the reaction of the ester **8** with *p*-toluenesulfonyl chloride under Schotten–Baumann conditions. Thus to a solution of 2.4 g of crude **8** in 20 mL of H_2O was added 2.4 g of *p*-toluenesulfonyl chloride in 30 mL of Et_2O; 3 M NaOH was added at intervals to keep the water layer basic to phenolphthalein. After 3 h, the solution remained basic and the water layer was acidified. A colorless solid that precipitated was removed by filtration: mp 176–178 °C. One recrystallization from MeOH–Et_2O gave 2.4 g (65%) of **10** having mp 179–180 °C, and a second recrystallization gave **10**, again as the etherate, with a constant mp of 180–181 °C.

Bis(D-1-(*p*-Tolylsulfonamido)-1-(methoxycarbonyl)-2-methyl-2-propyl) Disulfide (9). To a solution of 2.05 g of **10** in MeOH (5 mL) and Et_2O (50 mL) was added a solution of CH_2N_2 in Et_2O until the solution of the disulfide just remained yellow. After 0.5 h, the excess CH_2N_2 was decomposed by addition of a small quantity of **10**. Removal of solvent gave 2.10 g (98%) of the methyl ester **9** as a colorless solid. Recrystallization from Et_2O gave material with a melting point of 166–168 °C, and two further recrystallizations from MeOH–Et_2O gave **9** with a constant melting point of 172–174 °C.

Anal. Calcd for $C_{26}H_{36}N_2O_8S_4$: C, 49.34; H, 5.73; S, 20.26. Found: C, 49.51; H, 5.96; S, 20.04.

Material (**9**) with the same ^1H NMR spectrum also could be prepared by the reaction of **8** with *p*-toluenesulfonyl chloride in pyridine; however, this material was very difficult to crystallize and was handled as a semisolid.

D-1-(*p*-Tolylsulfonamido)-1-(methoxycarbonyl)-2-methyl-2-propanethiol (13). To a solution of 300 mg (0.47 mmol) of **9** in 10 mL of MeOH was added 1.5 mL of HOAc and 400 mg of Zn dust. The mixture was heated at reflux with vigorous stirring

(14) A procedure reported for the D,L disulfide **7**: Abraham, E. P.; Baker, W.; Boon, W. R.; Calam, C. T.; Carrington, A. C.; Chain, E.; Florey, H. W.; Freeman, G. G.; Robinson, R.; Sanders, A. G. in ref 13, p 469.

for 24 h. After filtration to remove excess Zn, the solvent was removed, and the resulting oil was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was evaporated to dryness, and the resulting product mixture was purified by preparative TLC on silica gel (25% EtOAc in hexane), yielding 80 mg (27%) of **13** as an oil that crystallized upon standing for a few hours. Two recrystallizations from 50% MeOH–H_2O gave **13** with a constant mp of 105–107 °C: ^1H NMR ($CDCl_3$) δ 1.41 (s, 6 H, $(CH_3)_2C$), 1.94 (s, 1 H, HS), 2.42 (s, 3 H, CH_3Ar, 3.38 (s, 3 H, CH_3O) 3.81 (d, J = 11.4 Hz, CHN), 5.54 (d, J = 11.4 Hz, NH), 7.2–7.8 (m, 4 H, p-C_6H_4).

Anal. Calcd for $C_{13}H_{19}NO_4S_2$: C, 49.18; H, 6.03. Found: C, 48.87; H, 6.06.

Acetyl D-1-(*p*-Tolylsulfonamido)-1-(methoxycarbonyl)-2-methylpropyl Disulfide (12). To a solution of 0.63 g (1.0 mmol) of disulfide **9** in 5 mL of CH_2Cl_2 at room temperature was added 1.0 mL of a 1.05 M solution of Cl_2 in CCl_4. After 10 min, a solution of 0.15 g (2.0 mmol) of freshly distilled thioacetic acid in 1.0 mL of CH_2Cl_2 was added and after 0.5 h the solvent was removed. Purification by chromatography over silica gel in 30% EtOAc in hexanes gave 0.60 g (77%) of **12** that was homogeneous by TLC, but which could not be induced to crystallize: ^1H NMR ($CDCl_3$) δ 1.35 (s, 6 H, $(CH_3)_2C$), 2.44 (s, 6 H, CH_3CO and CH_3Ar), 3.88 (s, 3 H, CH_3O), 3.83 (d, 1 H, J = 10.5 Hz, CHN), 5.79 (d, 1 H, J = 10.5 Hz, NHC), 7.0–7.8 (m, 4 H, C_6H_4). This material was used immediately to obviate problems due to disproportionation.

D-1-(*p*-Tolylsulfonamido)-1-(methoxycarbonyl)-2-methyl-2-propyl Hydrodisulfide (15) and the 2,4-Dinitrophenyl Derivative 14. To a solution of 0.13 g of **12** in 2 mL of MeOH was added 6 drops of 35% aqueous HCl. After 1.5 h the ^1H NMR spectrum of the reaction mixture no longer showed the presence of **12**. The MeOH was removed, the resulting oil was dissolved in $CHCl_3$; washed with a small volume of water, and dried by pouring through dry cotton, and the $CHCl_3$ was removed. Solutions of **15** allowed to stand in acidic methanol showed extensive decomposition in 2 h. Efforts to crystallize the oil **15** were unsuccessful: IR ($CDCl_3$, cm^{-1}) 3340 (NH), 2520 (SSH), 1750 (C=O), 1350 and 1160 (SO_2); ^1H NMR ($CDCl_3$) δ 1.29 (s, 3 H, CH_3C), 1.37 (s, 3 H, CH_3C), 2.42 (s, 3 H, CH_3Ar), 2.93 (s, 1 H, SH), 3.40 (s, 3 H, CH_3O), 3.89 (d, 1 H, CHN), 5.38 (d, 1 H, NH), 7.2–7.9 (m, 4 H, C_6H_4); ^{13}C NMR δ 170.1 (s), 143.8 (s), 136.2 (s), 129.53 (d), 127.4 (d), 61. 1 (q), 52.1 (d), 49.7 (s), 24.0 (q), 23.4 (q), 21.5 (q). After 3 days at 25 °C, the ^1H NMR spectrum was unchanged and the $CDCl_3$ was removed. An 18-mg portion of this sample of **15** was titrated with 0.96 mL of 0.053 N I_2: equiv wt calcd for $C_{13}H_{19}NO_4S_3$ 349, found, 354. The remainder of the material was dissolved in 5 mL of MeOH, and 0.10 g of 2,4-dinitrochlorobenzene was added, followed by the addition of 0.10 g of Et_3N. After 1 h, the solvent was removed, and the residue was taken up in $CHCl_3$, washed with dilute aqueous HCl, dried, and evaporated to dryness. The residue was purified by preparative TLC over silica gel in 25% EtOAc in hexanes, which provided **14** as a yellow oil that crystallized upon trituration with Et_2O. Recrystallization from EtOAc–Et_2O gave **14**, mp 125–130 °C, mmp with authentic **12** described below, 128–130 °C.

2,4-Dinitrophenyl D-1-(*p*-Tolylsulfonamido)-1-(methoxycarbonyl)-2-methyl-2-propyl Disulfide (14). To a solution of 50 mg (0.16 mmol) of **13** in 3 mL of Et_2O was added a solution of 40 mg (0.17 mmol) of 2,4-dinitrobenzenesulfenyl chloride in 2 mL of Et_2O, followed by 16 mg (0.16 mmol) of Et_3N. After 1 h at 25 °C the Et_2O was removed, and the residue was dissolved in CH_2Cl_2, washed with water, and then purified by preparative TLC (silica gel, 25% EtOAc–hexane). Recrystallization from EtOAc–Et_2O gave **14**, mp 132–133 °C, identical by TLC and ^1H NMR spectrum with **14** obtained from the reaction described above **15** with 2,4-dinitrochlorobenzene: ^1H NMR ($CDCl_3$) δ 1.37 (s, 6 H, $(CH_3)_2C$), 2.44 (s, 3 H, CH_3Ar), 3.44 (s, 3 H, CH_3O), 3.93 (d, 1 H, J = 10.5 Hz, CHN), 5.48 (d, 1 H, J = 10.5 Hz, NH), 7.2–9.1 (7 H, Ar).

Anal. Calcd for $C_{19}H_{21}N_3O_8S_3$: C, 44.27; H, 4.10; S, 18.66. Found: C, 44.28; H, 4.33; S, 18.80.

Methyl 2-(Methylsulfonamido)-3-methyl-2-butenoate (18). Crude **8** from 5.00 g (14 mmol) of **7** in 20 mL of pyridine was cooled (5 °C), and 4.6 g (40 mmol) of mesyl chloride was added. After 1 h, solvent was removed and a solution of the residue in $CHCl_3$ was washed with 3 M HCl, H_2O, dried, and evaporated; yield 3.5 g (52%) of crude **17**; ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H, CH_3C), 1.44 (s, 3 H, CH_3C), 2.98 (s, 3 H, CH_3SO_2), 3.83 (s, 3 H, CH_3O), 4.03 (d, 1 H, CHN), 5.49 (d, 1 H, NH). A solution of 0.30 g (0.62 mmol) of **17** in CH_3OH was treated with KOH (2 equiv/mol) and CH_3I. After 16 h, MeOH was removed, and the residue was dissolved in $CHCl_3$, washed with aqueous NaOH, and dried. Evaporation of the solvent yielded **18** as a mobile oil (0.15 g, 54%), which was purified by chromatography (silica gel): ^1H NMR ($CDCl_3$) δ 2.15 (s, 3 H), 2.31 (s, 3 H), 3.12 (s, 3 H), 3.11 (s, 3 H), 3.88 (s, 3 H).

Anal. Calcd for $C_8H_{15}NO_4S$: C, 43.42; H, 6.83; S, 14.49. Found: C, 43.03; H, 6.89; S, 14.64.

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New Intermediates in the Self-Condensation of β-Aminocrotonamide

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The self-condensation of β-aminocrotonamide (**1**) is known to give 2,6-dimethyl-3*H*-4-pyrimidone (**6**) in good yields.[1,2] In an attempt to synthesize 4-pyrimidone derivatives utilizing the reaction, we have isolated new reaction intermediates **2** and **3** from the thermolysis of **1**.

These compounds have been identified as 1,2-dihydro-2,6-dimethyl-4-pyrimidon-2-ylacetamide (**2**) and 1,5-dimethyl-3,7-dioxo-2,6,9-triazabicyclo[3.3.1]nonane (**3**) on the basis of spectral analyses and elemental analysis. Compound **3** is isolated in pure form by recrystallization from methanol of the initially obtained mixture of **2** and **3**, and **2** is obtained pure by silica gel column chromatography of the remaining mother liquor after recrystallization of **3**.

A substituted 2,6,9-triazabicyclo[3.3.1]nonane was previously prepared from crotonaldehyde and methylamine,[3] but the 3,7-dioxo compound **3** has not been reported yet. Chick and Wilsmore[4] reported that the thermolysis of **1** at 110 °C gave 4-amino-3,4-dihydro-4,6-dimethyl-1*H*-2-pyridone-5-carboxamide, but Kato et al.[1,2] reinvestigated the reaction and reported that the self-condensation of **1** proceeds through β-(β′-aminocrotonylamino)crotonamide (**5**) to yield the final product **6** negating the Chick and Wi lsmore's report. Kato et al. claimed the intermediate structure **5** on the basis of an olefinic proton peak at δ 4.25 (only NMR data reported) in dimethyl sulfoxide and UV absorption at 295 nm (log ϵ 3.72). However, **5** has to show two olefinic proton peaks in the NMR spectrum. The elemental analyses of **2**, **3**, and **5** would be identical. Furthermore, **2** shows UV absorption maximum at 295 nm (log ϵ 3.85) and an olefinic proton peak at δ 4.27 in dimethyl sulfoxide. It is evident that Kato et al. worked with a 74:26 mixture of **2** and **3**. We repeated the Kato's work and

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