afforded 75 g. of colorless crystals, m.p. 199–200°, $[\alpha]^{25}D$ −93.2° (*c* 0.8, alcohol).

D-(−)-α-**Benzyloxycarbonylaminophenylacetic Acid.**—The aforementioned diastereomeric salt (75 g., 0.131 mole) was treated with 1 l. of saturated sodium carbonate solution and 2 l. of ether as described for the isolation of (+)-α-phenoxypropionic acid. The acid was isolated by extraction of the aqueous layer at pH 2 with three 500-ml. portions of ether. The ether extracts were combined, washed with water, and dried over anhydrous sodium sulfate. The ether was evaporated to one-fifth its original volume and 1 l. of Skellysolve B (petroleum ether, b.p. 60–71°) was added. The crystals weighed 30 g. after drying *in vacuo* over P_2O_5: m.p. 128–129°, $[\alpha]^{25}D$ −116.5° (*c* 1, absolute alcohol); lit.[6] m.p. 130–130.5°, $[\alpha]^{21}D$ −119° (*c* 4, alcohol).

2-Hydrazino- and 2-(2,2-Dimethylhydrazino)-2-thiazoline[1]

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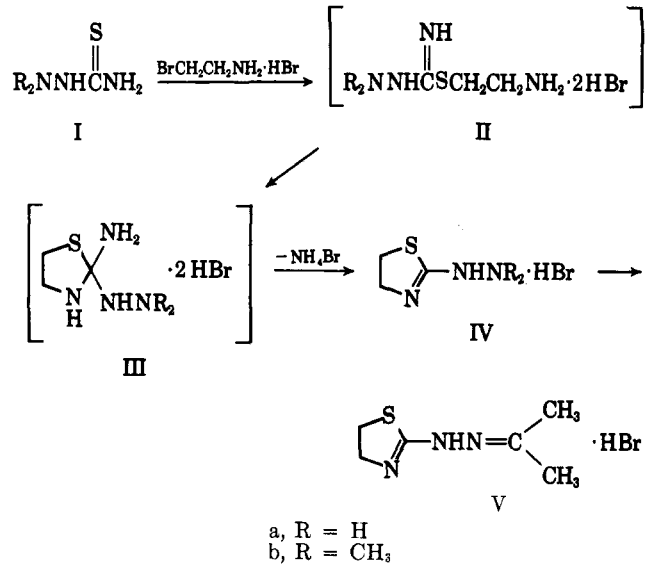
The interaction of equivalent amounts of thiosemicarbazide and 2-bromoethylamine hydrobromide under conditions chosen to minimize thiazoline formation (that is, in refluxing 2-propanol[2] for 45 min.) resulted in the isolation of a small amount of 2-hydrazino-2-thiazoline hydrobromide (IVa), which was characterized as a picrate and also, subsequently, as acetone (2-thiazolin-2-yl)hydrazone hydrobromide (V). The structure of IVa was deduced initially from an infrared spectral comparison with 2-amino-2-thiazoline hydrobromide. The only product that could be isolated from the remaining reaction mixture was additional IVa and not 2-aminoethyl thiocarbazimidate dihydrobromide (IIa), which, being a close structural relative of AET [2-(2-aminoethyl)-2-thiopseudourea dihydrobromide],[3] was desired as a potential antiradiation agent. The yield of pure IVa, which precipitated from the cooled reaction mixture, was eventually increased to 35% by prolonging the reflux period to 5 hr.,[4] ammonium bromide (and not hydrazinium bromide) precipitating from the hot reaction mixture as a result of elimination from the assumed intermediate III.

Similar results were obtained in the attempted conversion of 1,1-dimethyl-3-thiosemicarbazide (Ib) to 2-aminoethyl 3,3-dimethylthiocarbazimidate dihydrobromide (IIb). Unreported until recently,[6] Ib was made available for this work by a convenient displacement of methanethiol from methyl 3,3-dimethyldithiocarbazate[7] by ammonia. Thiazoline formation



occurred in 2-propanol at reflux and in N,N-dimethylformamide at 80–90°; however, unchanged Ib (58%) was recovered after 0.5 hr. in methanol at reflux. 2-(2,2-Dimethylhydrazino)-2-thiazoline hydrobromide (IVb) could not be obtained as a crystalline solid and was first characterized as a picrate.

The attempted basic hydrolysis of IVa under conditions that effected the conversion of 2-amino-2-thiazoline hydrobromide to (2-mercaptoethyl)urea[8] resulted in the isolation of an unstable red oil, which was identified as the free base of IVa by conversion to a stable, characterizable hydrochloride. The same treatment of crude IVb (that is, a 2-hr. reflux period in 2 *N* sodium hydroxide under nitrogen) did not cause appreciable opening of the thiazoline ring as evidenced by an 80% recovery of pure, crystalline 2-(2,2-dimethylhydrazino)-2-thiazoline, the structure of which is supported by the p.m.r. spectrum determined in chloroform: the single signal at τ 7.54 is assigned to the methyl groups, the group of signals centered at about τ 6.65, to the thiazoline methylene groups (an A_2B_2 system), and the single signal at τ 3.54, to the NH of the hydrazino group. When the reaction time was extended to 18 hr., 30% of the starting material precipitated (as the free base) from the reaction mixture saturated at pH 8 with sodium bromide; a nitroprusside-positive reaction mixture attested ring opening, but no characterizable products could be isolated. The stability of these hydrazinothiazolines toward basic hydrolysis relative to 2-aminothiazoline may be attributed to a greater over-all electron density, which makes C-2 more resistant to attack by hydroxyl ion.

Experimental

1,1-Dimethyl-3-thiosemicarbazide (Ib).—A mixture of methyl 3,3-dimethyldithiocarbazate[10] (121 g., 0.803 mole) and concentrated ammonium hydroxide (1.5 l.) was heated gradually to the boiling point and the resulting solution was refluxed for 4 hr. The solution, now yellow, was cooled slightly. More ammonium hydroxide (150 ml.) was added, and refluxing was continued over-

(1) This investigation was supported by the U. S. Army Medical Research and Development Command under Contract No. DA-49-193-MD-2028.

(2) (a) D. G. Doherty, R. Shapira, and W. T. Burnett, Jr., *J. Am. Chem. Soc.*, **79**, 5667 (1957); (b) R. Shapira, D. G. Doherty, and W. T. Burnett, Jr., *Radiation Res.*, **7**, 22 (1957).

(3) The radioprotective properties of AET are comprehensively reviewed by D. G. Doherty ("Radiation Protection and Recovery," A. Hollaender, Ed., Pergamon Press, New York, N. Y., 1960, pp. 56–66).

(4) Hydrazinothiazoline formation in buffered or unbuffered aqueous systems[2a,5] was not investigated.

(5) (a) J. X. Khym, R. Shapira, and D. G. Doherty, *J. Am. Chem. Soc.*, **79**, 5663 (1957); (b) J. X. Khym, D. G. Doherty, and R. Shapira, *ibid.*, **80**, 3342 (1958).

(6) J. Sandstrom and S. Sunner, *Acta Chem. Scand.*, **17**, 731 (1963).

(7) T. P. Johnston and A. Gallagher, *J. Org. Chem.*, **26**, 3780 (1961).

(8) A. Schöberl and G. Hansen, *Chem. Ber.*, **91**, 1055 (1958).

(9) Infrared absorption spectra were determined in pressed potassium bromide disks with a Perkin-Elmer Model 221-G spectrophotometer; melting points are uncorrected.

(10) The published procedure[7] was adapted to the preparation of large amounts only after decomposition was circumvented by removing the solvent, N,N-dimethylformamide, *in vacuo* under 40°.

night. After the addition of still more ammonium hydroxide (150 ml.) followed by a 2-hr. reflux, the solution was concentrated to near dryness under reduced pressure and chilled. The gray crystalline precipitate was collected, washed with water, and dried *in vacuo:* yield 78.3 g. (82%), m.p. 182–184° (lit.[6] m.p. 163°). Recrystallization of a small sample from ethanol provided white crystals (melting point unchanged) for analysis.

Anal. Calcd. for $C_3H_9N_3S$: C, 30.23; H, 7.61; N, 35.25; S, 26.91. Found: C, 30.08; H, 7.40; N, 34.70; S, 26.8.

2-Hydrazino-2-thiazoline Hydrobromide (IVa).—A mixture of thiosemicarbazide (13.7 g., 0.150 mole), 2-bromoethylamine hydrobromide, and 2-propanol (400 ml.) was heated under reflux for 5 hr. The resulting mixture was filtered hot to remove ammonium bromide, and the filtrate was allowed to cool slowly. The solid that precipitated was collected, dried *in vacuo*, and recrystallized from ethanol (220 ml.) to yield IVa as white needles, 10.4 g. (35%), m.p. 167–168°, ν_{max}^{KBr} 1670 cm.$^{-1}$ (s, C=N).

Anal. Calcd. for $C_3H_7N_3S \cdot HBr$: C, 18.18; H, 4.07; N, 21.21. Found: C, 18.37; H, 4.22; N, 21.27.

2-Hydrazino-2-thiazoline picrate was prepared from IVa in ethanol and recrystallized from methanol as fine yellow needles, m.p. 203–204° dec.

Anal. Calcd. for $C_9H_{10}N_6O_7S$: C, 31.24; H, 2.91; N, 24.27; S, 9.24. Found: C, 31.40; H, 3.07; N, 24.00; S, 9.3.

Acetone (0.4 ml.) was added to a solution of IVa (495 mg., 2.50 mmoles) in water (5 ml.). When exothermic reaction ceased, the solution was warmed slightly and then evaporated to dryness under reduced pressure. Recrystallization of the residue from ethanol (10 ml.) gave 383 mg. (64%) of vacuum-dried **acetone (2-thiazolin-2-yl)hydrazone hydrobromide (V)** as a white crystalline solid, m.p. 210–212°.

Anal. Calcd. for $C_6H_{11}N_3S \cdot HBr$: C, 30.25; H, 5.20; N, 17.65. Found: C, 30.57; H, 5.18; N, 17.56.

2-Hydrazino-2-thiazoline hydrochloride was recrystallized from ethanol and melted at 185–187° dec., ν_{max}^{KBr} 1675 cm.$^{-1}$ (s, C=N).

Anal. Calcd. for $C_3H_7N_3S \cdot HCl$: C, 23.45; H, 5.25; Cl, 23.07. Found: C, 23.76; H, 5.29; Cl, 22.5.

2-(2,2-Dimethylhydrazino)-2-thiazoline (IVb Free Base).—A stirred mixture of Ib (11.9 g., 0.100 mole), 2-bromoethylamine hydrobromide (20.5 g., 0.100 mole), and 2-propanol (100 ml.) was heated under reflux for 5 hr. Complete solution resulted as the mixture was gradually heated, but precipitation of ammonium bromide began shortly after reflux temperature was reached. The reaction mixture was filtered hot, ammonium bromide (6.49 g., vacuum dried) being removed. The filtrate was evaporated to dryness under reduced pressure. Extraction of the viscous semisolid residue first with acetonitrile and then with chloroform left additional ammonium bromide (2.15 g.) making the total yield 88%. Evaporation of the combined filtrates *in vacuo* gave crude IVb as a yellow, viscous oil, which eventually solidified to a gummy solid (21.1 g., 93%), ν_{max}^{KBr} 1640 cm.$^{-1}$ (s, C=N). The **picrate** was prepared from crude IVb in ethanol and recrystallized from ethanol as yellow needles, m.p. 205° dec. (Kofler Heizbank).

Anal. Calcd. for $C_{11}H_{14}N_6O_7S$: C, 35.29; H, 3.77; N, 22.45; S, 8.56. Found: C, 35.21; H, 3.89; N, 22.11; S, 8.4.

A solution of crude IVb (3.65 g., 16.2 mmoles) and (ethylenedinitrilo)tetraacetic acid (0.35 g.) in 2 *N* sodium hydroxide (26 ml.) was heated at 90° for 2 hr., cooled, and brought to pH 8 with 48% hydrobromic acid (4 ml.). The solution was then extracted continuously with ether for 3.5 hr. in a liquid–liquid extractor (225-ml. volume). Evaporation of the ether left 1.88 g. (79%, 73% from Ib) of IVb free base as a white crystalline solid.

For analysis a small sample was recrystallized from hexane with 87% recovery, m.p. 113–115°.

Anal. Calcd. for $C_5H_{11}N_3S$: C, 41.34; H, 7.63; S, 22.08. Found: C, 41.35; H, 7.48; S, 22.2.

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Metal Acetylacetonate Catalyzed Epoxidation of Olefins with *t*-Butyl Hydroperoxide

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In the course of efforts to explore the usefulness of *t*-butyl hydroperoxide as an epoxidizing agent for olefins,[1] the effect of small quantities of metal acetylacetonates was noted. Table I sets forth results obtained with 2,4,4-trimethyl-1-pentene. It is noteworthy that the Cr(III), MoO_2(II), VO(II), and V(III) compounds gave quantitative yields of epoxide. In the absence of metal acetylacetonates no reaction occurred under the stated conditions. The metal-catalyzed epoxidation is general for hydrocarbon olefins (see Table II), and appears to be stereospecific

TABLE I

EPOXIDE FORMATION IN THE SYSTEM *t*-BUTYL HYDROPEROXIDE[a]–2,4,4-TRIMETHYL-1-PENTENE–METAL ACETYLACETONATE[b] (at 25° *in vacuo*)

Metal	*n*	Remaining hydroperoxide, %	Epoxide, %[c]
Cr	3	47[d]	100
V	3	60[e]	100
VO	2	56[e]	100
MoO_2	2[f]	83[d]	100
Co	3	75[d]	30
Cu	2	67[d]	25
Co	2	52[d]	20
Mn	3	53[g]	15
Mn	2	56[g]	15
Al	3	100[d]	...
Fe	3	100[d]	...
Mg	2	95[g]	...
Ni	2	100[e]	...
TiO	2	95[e]	...
Zn	2	90[e]	...
Zr	4	90[e]	...

[a] About 2.0 *M*. [b] 4×10^{-4} *M*. [c] Based on reacted hydroperoxide. [d] After 4 days. [e] After 7 days. [f] At 60° in octene-1. [g] After 5 days.

TABLE II

EFFECT OF OLEFIN STRUCTURE ON EPOXIDE YIELD IN *t*-BUTYL HYDROPEROXIDE EPOXIDATION THE IN PRESENCE AND ABSENCE OF CHROMIUM(III) ACETYLACETONATE

Olefin	Uncatalyzed epoxide,[a] %	Catalyzed epoxide,[a] %
Octene-1	5–10	5–53
4-Vinylcyclohexene	10–20[b]	13–60[b]
Octene-2	25–40	42–78
2,4,4-Trimethyl-1-pentene	40–50	28–100

[a] Based on reacted hydroperoxide. Lower values represent yields at 60° or higher, long reaction times, high metal chelate concentration. See ref. 1. [b] Mono ring epoxide only.

(1) W. F. Brill and N. Indictor, *J. Org. Chem.*, **29**, 710 (1964). See also references cited therein.