

meso-2,5-Dimercapto-*N,N,N',N'*-tetramethyladipamide: A Readily Available, Kinetically Rapid Reagent for the Reduction of Disulfides in Aqueous Solution¹

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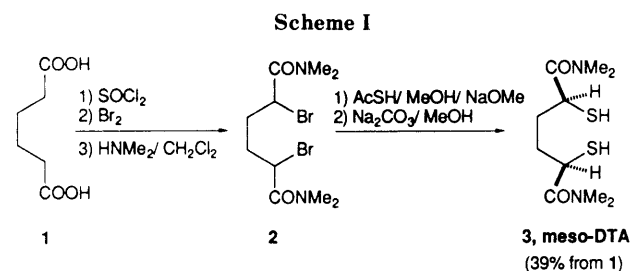
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meso-2,5-Dimercapto-*N,N,N',N'*-tetramethyladipamide (*meso*-DTA) reduces disulfide bonds up to 8 times faster (kinetic) than does dithiothreitol (DTT) in aqueous solution at pH 7.0. *meso*-DTA is easily synthesized in five steps (39% overall yield) from adipic acid. *meso*-DTA, which forms a cyclic disulfide, is less reducing than DTT by approximately 56 mV, but is much more reducing than mercaptoethanol.

Introduction

This paper reports the reduction of small organic disulfides and protein disulfides in water at pH 7.0 using a new reagent, *meso*-2,5-dimercapto-*N,N,N',N'*-tetramethyladipamide (*meso*-DTA). Disulfide-reducing reagents are used in biochemistry to inhibit the oxidation of thiol groups and to reduce disulfide groups in proteins.³⁻⁵ A useful thiol reducing reagent for disulfides should have $pK_a \sim 7.0$ for the SH group, a high reduction potential, ready availability, an unobjectionable odor, high solubility in water, kinetic stability at room temperature, and low toxicity.^{6,7}

We have previously examined *N,N'*-dimethyl-*N,N'*-bis(mercaptoacetyl)hydrazine (DMH),⁸ a reagent that reduces disulfides faster than dithiothreitol (DTT), but is more expensive to synthesize. Mercaptoethanol (ME) and dithiothreitol (DTT)⁶ are the most commonly used di-



sulfide-reducing reagents in biochemistry.³ The principal advantage of ME is its low cost. ME has, however, the disadvantage of a low reduction potential and a relatively high pK_a , 9.6. The primary advantage of DTT is that it is strongly reducing. DTT also has several disadvantages: oxidation of DTT by O₂ in the presence of transition-metal ions can generate hydrogen peroxide;⁹ it is a strong chelating agent and can sequester essential ions (especially transition metals); it is not a fast reductant (the lower pK_a of the thiol groups in DTT is 9.2;¹⁰ thus only about 1% of DTT exists as the thiolate at pH 7.0); it is expensive.¹¹ (For nomenclature, we indicate the oxidized form of a thiol, the disulfide, by the superscript "ox" and leave the reduced

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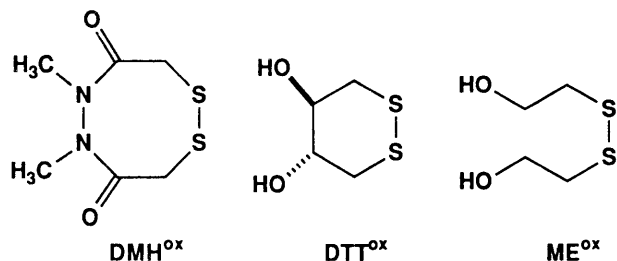
(11) The present price of DTT is \$870/mol from Aldrich.

Table I. Rates of Reduction of Disulfides with *meso*-DTA and DTT

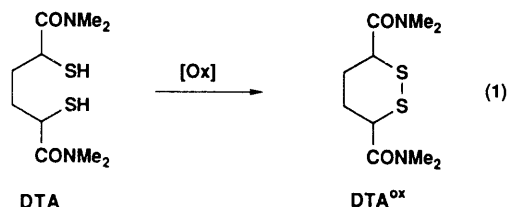
disulfide	k_{app}^{DTA} $M^{-1} s^{-1}$ ^a	k_{app}^{DTT} $M^{-1} s^{-1}$ ^a	$\frac{k_{app}^{DTA}}{k_{app}^{DTT}}$	$\frac{k_{app}^{DTA}}{k_{app}^{DMH}}$ ^b
mercaptoethanol disulfide	0.50	0.065	7.7	1.1
glutathione disulfide	0.31	0.056	5.5	
papain-S-S-Me	260	58	4.5	0.15
creatine kinase-S-S-glutathione	78	23	3.4	0.5
DNase	0.34	0.19	1.8	0.4

^a The rate constants are for aqueous solutions at pH 7.0 and 298 K. ^b Data taken from ref 8.

form, the thiol, unsuperscripted: e.g., DTT (dithiol) vs DTT^{ox} (disulfide).



On the basis of earlier studies of thiol-disulfide interchange,^{8,12} we hypothesized that *meso*-2,5-dimercapto-*N,N,N',N'*-tetramethyladipamide (*meso*-DTA, eq 1) would have many properties desirable for a disulfide-reducing reagent. This paper describes the synthesis and properties of *meso*-DTA and compares this reagent to DTT and DMH.



Results

meso-DTA (3) was synthesized in 39% overall yield on a 100-mmol scale according to Scheme I. The only purification step (excluding extractions) is the final recrystallization. The bromination of adipoyl chloride leads to two products in a 1.6:1.0 ratio (probably *meso:dl* isomer; see below) as determined by integration of the ¹H NMR spectrum. Addition of dimethylamine to the crude mixture results in two products, 2, again in about a 1.6:1.0 ratio. If 2 is recrystallized, then only one product (probably *meso*; see below) is obtained in greater than 50% overall yield based on 1. Reaction of crude 2 (1.6:1.0) with thiolacetic acid and sodium methoxide in methanol at reflux produces only one stereoisomer, in high yield. We believe that the production of only one stereoisomer reflects isomerization under the reaction conditions. Deacetylation of the thiolacetate produces only one stereoisomer, *meso*-DTA. Oxidation of the dithiol, *meso*-DTA, to the disulfide, *meso*-DTA^{ox}, and subsequent analysis of the ¹H NMR coupling constants at 20 and -60 °C established that the dithiol was the *meso* isomer. The *dl* isomer of DTA (*dl*-DTA) could be isolated as a minor product by following a similar route except that the addition of thiolacetic acid

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Table II. Physical Properties of DTA, DTT, and DMH^a

physical property	<i>meso</i> -DTA	<i>dl</i> -DTA	DTT	DMH
ϵ° , ^b V	-0.300	-0.328	-0.356	-0.300
pK _a	7.8, 8.9		9.2, 10.1	7.6, 8.9
mp, ^a °C	118 (137)		42 (132)	38 (155)
k_{app} , ^c M ⁻¹ s ⁻¹	0.50		0.065	0.52
K, ^d M	10 ³	10 ⁴	10 ⁵	10 ³
solubility, ^{a,e} mM	80 (80)		high	250 (23)
odor ^a	weak (none)		weak (none)	weak (none)

^a Data in parentheses are for the oxidized form containing a disulfide group. ^b All values of ϵ° are relative to mercaptoethanol (-0.209 V). ^c The apparent rate constant (k_{app}) is for the reduction of mercaptoethanol disulfide (ME^{ox}) at pH 7.0 in aqueous phosphate buffer (50 mM). ^d The values of equilibrium constant (K) are for the reduction of ME^{ox} with the dithiol in water, pH 7.0, 100 mM phosphate buffer, $K_{eq} = ([ME^{red}]^2[cyclic\ disulfide]/[ME^{ox}][dithiol])$. ^e The solubilities were determined in phosphate buffer (pH 7.0, 100 mM phosphate, 25 °C).

and sodium methoxide to crude 2 was performed at 0 °C. Isolation of the *dl* isomer required several chromatographic steps.¹³

The rates of reduction of various disulfides with *meso*-DTA and DTT were compared (Table I). *meso*-DTA reduces the disulfide linkage of small organic disulfides and dipeptides 5-8 times faster than DTT in water at pH 7.0, and the disulfide bond in proteins 2-5 times faster. In papain and creatine kinase, the disulfide being reduced is derived from an essential active site cysteine,¹⁴ and the rate measured is the rate of reactivation of the modified protein.¹⁵ DNase is deactivated by the reduction of an internal disulfide.^{15,16}

meso-DTA completely reduces noncyclic disulfides (mercaptoethanol disulfide or glutathione disulfide) as determined by ¹H NMR spectroscopy. *meso*-DTA only partially reduces DTT^{ox} in 50 mM phosphate buffer at pH 7.0 ($K_{eq} = [meso-DTA^{ox}][DTT]/[meso-DTA][DTT^{ox}] = 0.010$). *dl*-DTA is more reducing than *meso*-DTA by a factor of 10 in 100 mM phosphate buffer at pH 7.0 ($K_{eq} = [meso-DTA^{ox}][dl-DTA]/[meso-DTA][dl-DTA^{ox}] = 0.10$). We used the equilibrium constant between *meso*-DTA and DTT to determine the values of ϵ° and $K(ME)$ of *meso*-DTA. Some other useful physical properties of *meso*-DTA, DTT, and DMH are listed in Table II.

Discussion

The pK_a of the first thiol in *meso*-DTA is 7.8 ± 0.2; therefore, at pH 7.0 approximately 15% of *meso*-DTA exists as the thiolate. On the basis of this pK_a, we calculate¹⁰ that *meso*-DTA should reduce disulfides 4.4 times faster than DTT at pH 7.0.¹⁷ The relative rate of reduction of disulfides by *meso*-DTA compared to DTT is approximately 6 for small peptides and small organic disulfides (Table I), a value that is slightly above that calculated. For proteins, the relative rate of *meso*-DTA vs DTT (2-5-fold faster) is less than or equal to the calculated value (4.4-fold faster). The difference between the calculated and the actual value for proteins could be due to

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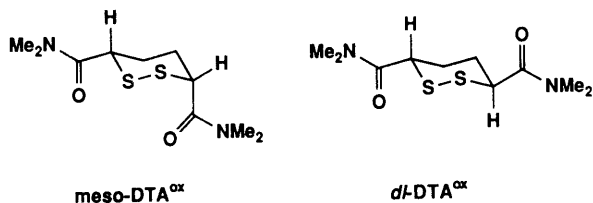
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(17) Using the Bronsted¹⁰ equation $\log k = 7.0 + 0.5 pK_a^{nuc} - 0.27 pK_a^c - 0.73 pK_a^{lk}$ and the equation $k = k_{app}(1 + 10^{pK_a - pH})$, we calculate $k_{app}^{meso-DTA}/k_{app}^{DTT} = 4.4$.

steric interactions, because *meso*-DTA is a secondary thiol and DTT is a primary thiol. The difference in rates could also be due to the relative difference in hydrophobicities of the two compounds.

The equilibrium constant for reduction of ME^{ox} by *meso*-DTA is less than that of DTT by a factor of 10^2 , probably due to the 1,3-diaxial interaction in *meso*-DTA^{ox}. In *meso*-DTA^{ox}, the 1,3-diaxial interaction between the axial hydrogen and axial dimethylamido group will destabilize the cyclic disulfide (*meso*-DTA^{ox}) relative to the noncyclic dithiol (*meso*-DTA). This inference is supported by the fact that *dl*-DTA is 10 times more reducing than *meso*-DTA. In DTT^{ox} there are no 1,3-diaxial interactions to destabilize the oxidized form relative to the unoxidized form (DTT).



meso-DTA and DMH have similar reduction potentials and $\text{p}K_a$'s, but DMH reduces hindered disulfides more rapidly than does *meso*-DTA. This increased rate of reduction of hindered disulfides is probably due to differences in steric interactions and hydrophobicities since DMH contains a primary thiol while *meso*-DTA contains a secondary thiol.

meso-DTA is less soluble in water than DTT. Since nearly all applications in protein chemistry require a concentration of reducing agent less than 50 mM, the lower solubility of *meso*-DTA should not be disadvantageous. In fact, the lower solubility of *meso*-DTA in water permits its extraction from water with organic solvents.

In conclusion, none of the reagents mentioned—ME, DTT, DMH, and *meso*-DTA—is clearly superior as a reducing agent for biochemical applications. ME is inexpensive and commercially available, but is weakly reducing and kinetically slow. DTT is commercially available and strongly reducing, but is reasonably expensive and kinetically slow. DMH is strongly reducing and kinetically fast, but is not commercially available and is expensive to synthesize (primarily because 1,2-dimethylhydrazine, the starting material, is expensive). *meso*-DTA is strongly reducing, relatively inexpensive to synthesize, and kinetically fast, but is not commercially available. We believe that for most applications *meso*-DTA would be superior or equal to DTT.

Experimental Section

General. Starting materials were commercial products: Thionyl chloride, bromine, and thioacetic acid (Fluka); dimethylamine and adipic acid (Aldrich); papain (Boehringer Mannheim); creatine phosphokinase, deoxyribonuclease I, DNA, and *N*-benzoyl-L-arginine *p*-nitroanilide (Sigma). NMR spectra were recorded in CDCl_3 . Chemical shifts are reported in δ (ppm) using CHCl_3 (7.24) as an internal standard. Elemental analyses were performed by Oneida Research Services.

***meso*-2,5-Dimercapto-*N,N,N',N'*-tetramethyladipamide (*meso*-DTA) (3).**¹⁸ Adipic acid (1, 832 mmol, 120.0 g) and thionyl chloride (2.33 mol, 170 mL) were heated at reflux for 90 min with no solvent in a three-necked 1-L flask equipped with a reflux condenser and an addition funnel. The exhaust gases from the reflux condenser were neutralized by bubbling through a 5 M NaOH solution. The ^{13}C NMR (75 MHz) spectrum of the re-

sulting oil showed peaks at δ 173.1, 46.2, and 23.5. Bromine (1.88 mol, 97 mL) was added over 5 h at 95 °C and the reaction mixture kept at 95 °C for another 3 h before being cooled at 25 °C. The ^1H NMR spectrum of the product showed two major components: *meso*- and *dl*-2,5-dibromoadipoyl chloride in a 1.6:1.0 ratio. The solution was dissolved in CH_2Cl_2 (70 mL) and added over 2 h to a biphasic mixture of CH_2Cl_2 (1 L) and dimethylamine (600 mL of a 40% w/w aqueous solution) in a 3-L flask cooled by an ice/salt bath. The temperature of the reaction mixture was kept at 18 °C or less. The resulting biphasic mixture was acidified to pH 4.0 with concentrated hydrochloric acid (ca. 30 mL). The organic layer was separated and extracted with saturated aqueous sodium bicarbonate (150 mL), dried with MgSO_4 , and concentrated under aspirator pressure to provide 197 g of a crude mixture of *meso* and *dl* product 2 (1.6:1.0 ratio). A small portion (ca. 50 mg) was separated by chromatography on silica gel (eluant: 1:1 ethyl acetate/hexane going to ethyl acetate). Major product: ^1H NMR (400 MHz) δ 4.42–4.36 (m, 2 H), 3.04 (s, 3 H), 2.94 (s, 3 H), 2.29–2.20 (m, 2 H), 2.00–1.92 (m, 2 H); ^{13}C NMR (100 MHz) δ 168.2, 42.4, 37.4, 36.2, 33.0. Minor product: ^1H NMR (400 MHz) δ 4.42–4.36 (m, 2 H), 3.04 (s, 3 H), 2.92 (s, 3 H), 2.19–2.08 (m, 4 H); ^{13}C NMR (100 MHz) δ 168.3, 42.7, 37.4, 36.2, 32.9. The crude product was divided into two portions: 97.5 g and 100 g.

The first portion was recrystallized from CH_2Cl_2 (ca. 500 mL) and ether (ca. 500 mL) to provide 74.8 g (51% overall yield) of a single diastereomer 2 (which we presume to be the *meso* isomer; see below). Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{N}_2\text{O}_2\text{Br}_2$: C, 33.54; H, 5.07; N, 7.82. Found: C, 33.27; H, 4.91; N, 7.73. A second recrystallization from a mixture of ether (200 mL) and CH_2Cl_2 (100 mL) produced 14.0 g of a mixture of *meso* and *dl* product (5:1 ratio, the major product being the same as the product from the first recrystallization).

The second portion of crude dibromide mentioned above (279 mmol, 100 g) and thioacetic acid (923 mmol, 66 mL) were dissolved in methanol (500 mL). Sodium methoxide (700 mmol, 37.8 g) was added at a rate that maintained reflux (over 30 min). The solution was stirred for 1 h as it cooled to 25 °C. The solution was concentrated under aspirator pressure and partitioned between CH_2Cl_2 (500 mL) and 300 mL of 5% aqueous sodium bicarbonate solution. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×100 mL). The combined organic layers were dried (MgSO_4) and concentrated under aspirator pressure to provide a crude yellow solid (the diacetate of *meso*-DTA; 99.6 g). Only one stereoisomer was observed by ^1H NMR: ^1H NMR (400 MHz) δ 4.44–4.40 (m, 2 H), 3.02 (s, 3 H), 2.92 (s, 3 H), 2.30 (s, 3 H), 2.07–2.00 (m, 2 H), 1.72–1.66 (m, 2 H); ^{13}C NMR (100 MHz) δ 194.6, 170.2, 42.2, 37.4, 36.1, 30.2, 30.1.

The yellow solid and potassium carbonate (655 mmol, 90.5 g) were added to methanol (400 mL) that had been purged with argon. The mixture was stirred for 14 h under argon. CH_2Cl_2 (200 mL) was added and the solution acidified to pH 3.0 with concentrated sulfuric acid (ca. 35 mL) over 1 h. The solution was partitioned between ethyl acetate (1000 mL) and water (600 mL). The layers were separated, and the water layer was extracted with ethyl acetate (2×300 mL). The combined organic layers were dried (MgSO_4) and concentrated under reduced pressure to provide 77.6 g of crude product, which was recrystallized from THF (ca. 100 mL) to provide 37.9 g of *meso*-DTA. The mother liquor was dissolved in CH_2Cl_2 (200 mL) and extracted with 100 mL of 0.2 N HCl. The organic layer was concentrated in vacuo and recrystallized from THF to provide a further 5.7 g of *meso*-DTA (39% total overall yield from adipic acid): ^1H NMR (500 MHz) δ 3.43–3.35 (m, 2 H), 3.02 (s, 3 H), 2.92 (s, 3 H), 2.07–1.98 (m, 2 H), 1.92 (d, $J = 10.5$ Hz, 2 H), 1.68–1.58 (m, 2 H); ^{13}C NMR (125 MHz) δ 172.0, 37.4, 37.2, 35.0, 34.9. Anal. Calcd for $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2\text{S}_2$: C, 45.43; H, 7.62; N, 10.59. Found: C, 45.32; H, 7.41; N, 10.39.

Oxidized *meso*-DTA. Ellman's reagent (2.0 g, 6.45 mmol) was added to water (75 mL), and the pH was adjusted to 7.0 with saturated aqueous NaHCO_3 solution. *meso*-DTA (1.03 g, 3.89 mmol) was added, and the solution was stirred for 15 min. CH_2Cl_2 (25 mL) was added, and the layers were separated. The water layer was back-extracted with CH_2Cl_2 (2×50 mL). The combined organics were dried (MgSO_4) and concentrated at aspirator pressure to provide 981 mg (96%) of product: ^1H NMR (400 MHz,

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293 K) δ 3.69 (br dd, $J = 6.7, 2.2$ Hz, 2 H), 3.04 (s, 6 H), 2.92 (s, 6 H), 2.81–2.74 (m, 2 H), 2.00–1.92 (m, 2 H); ^{13}C NMR (100 MHz, 293 K) δ 169.8, 43.8 (br), 37.7, 35.9, 27.7; ^1H NMR (400 MHz, 213 K) δ 4.00 (br d, $J = 12.0$ Hz, 1 H), 3.46 (br s, 1 H), 3.06 (br s, 3 H), 3.01 (br s, 3 H), 3.09–3.00 (br, 1 H), 2.95 (br s, 3 H), 2.88 (br s, 3 H), 2.43 (br d, $J = 12.3$ Hz, 1 H), 2.06–1.94 (br, 2 H); ^{13}C NMR (100 MHz, 213 K) δ 170.0, 169.5, 51.5, 37.9, 37.3, 35.8, 35.4, 35.2, 29.3, 25.7. Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{N}_2\text{O}_2\text{S}_2$: C, 45.78; H, 6.91; N, 10.68. Found: C, 45.53; H, 6.97; N, 10.54.

***dl*-DTA.** The product of the secondary recrystallization of 2 (5:1 ratio of meso to *dl*, 2.50 g) was chromatographed on silica gel (ethyl acetate/hexane, 3:1 going to 5:1) to provide 448 mg of a 1:1 (meso:*dl*) mixture. This mixture was dissolved in 30 mL of methanol and cooled to 0 °C. Sodium methoxide (160 mg) and thiolacetic acid (300 μL) were added. After 15 min at 0 °C, the solution was warmed to room temperature, concentrated in vacuo, and partitioned between water (10 mL) and CH_2Cl_2 (20 mL). The organic layer was dried (MgSO_4), concentrated in vacuo, and chromatographed on silica gel (ethyl acetate going to ethyl acetate/methanol, 10:1) to provide 169 mg of the *dl*-dithiolacetate of DTA. The *dl*-dithiolacetate of DTA was dissolved in 10 mL of methanol. After addition of sodium methoxide (48 mg), the solution was stirred for 20 min, acidified with Dowex 50X8 ion-exchange resin (H^+ form), filtered, and partially concentrated under aspirator pressure (2 mL). The methanolic solution was added to an aqueous solution of Ellman's reagent (210 mg, adjusted to pH 7.0 with saturated NaHCO_3). After 10 min, the solution was extracted with CH_2Cl_2 (2×20 mL). The combined organics were dried (MgSO_4), concentrated under aspirator pressure, and chromatographed on silica gel (ethyl acetate going to ethyl acetate/methanol, 10:1) to provide 58 mg of *dl*-DTA $^{\text{ox}}$: ^1H NMR (500 MHz) δ 3.94 (br, 2 H), 3.12 (s, 6 H), 2.92 (s, 6 H), 2.27 (br, 4 H).

Equilibration of *dl*-DTA and meso-DTA. *dl*-DTA $^{\text{ox}}$ (2 mg in 0.5 mL of buffered D_2O (100 mM NaPO_4 , pD 7.0)) and meso-DTA (6 mg in 1.5 mL of buffered D_2O (100 mM NaPO_4 , pD 7.0)) were mixed in an NMR tube, and ^1H NMR spectra were taken at various times. The value of K_{eq} was calculated from the ^1H NMR integrals.

Determination of the pK_a of meso-DTA.¹⁹ The absorbance at 238 nm of meso-DTA (100 μL of an 8 mM ethanolic solution of meso-DTA) in various aqueous buffers (3 mL, 50 mM: 2,2-dimethylsuccinate, pH 6.0, 6.4, 6.8; Tris, pH 7.0, 7.3, 7.7, 8.0, 8.3, 8.7; glycine, pH 9.0, 9.5, 10.0) was plotted against pH. This curve was then compared with plots derived from theory. The best fit was obtained when the first pK_a was 7.8 ± 0.2 and the second was 8.9 ± 0.2 .

Kinetics of Reduction of Glutathione Disulfide by meso-DTA and DTT Using ^1H NMR Spectroscopy. The following solutions were prepared using a 50 mM phosphate buffer solution (pD 7.0 in D_2O) that had been deoxygenated by bubbling argon through it for 30 min: 10 mM glutathione disulfide solution

(15.9 mg in 2.5 mL of buffer); 10 mM DTT solution (3.1 mg in 2 mL of buffer); 10 mM meso-DTA solution (5.3 mg in 2 mL of buffer). Three NMR tubes containing 250 μL of the DTT solution and 250 μL of the glutathione disulfide solution were prepared. The thiol-disulfide interchange reaction was quenched by addition of 25 μL of a DCl solution (12 wt % in D_2O) in one tube after 2 min, in another tube after 4 min, and in another tube after 6 min. The same series of experiments was carried out with the meso-DTA solution instead of the DTT solution. The second-order rate constant was calculated from the integrals of the ^1H NMR spectra. A similar procedure was used for studying the kinetics of reduction of mercaptoethanol disulfide by meso-DTA and DTT.

Equilibrium Experiments. A 10 mM DTT $^{\text{ox}}$ solution (3.0 mg in 2.0 mL of buffer) and a 10 mM meso-DTA solution (5.3 mg in 2 mL of buffer) were made up in D_2O buffer (50 mM phosphate, pD 7.0). The DTT $^{\text{ox}}$ solution (250 μL) and the meso-DTA solution (250 μL) were mixed in an NMR tube. After 4 h, a ^1H NMR spectrum was obtained. The equilibrium constant between meso-DTA and DTT was calculated using the integrals obtained from the ^1H NMR spectrum. When meso-DTA was equilibrated with a 1.5-fold excess of mercaptoethanol disulfide (6 mM) or glutathione disulfide (6 mM), meso-DTA was oxidized completely, and no mixed disulfide or reduced meso-DTA was observed by ^1H NMR spectroscopy.

Kinetics of Reactivation of Creatine Kinase-S-S-Glutathione. The solution of creatine kinase-S-S-glutathione²⁰ (10 μL) was diluted with deoxygenated aqueous buffer (pH 7.0, 0.1 M imidazole, 2 mM EDTA, 2.5 mL). The diluted solution was added to two flasks (1.0 mL each). DTT or meso-DTA (5 μL of a 5 mM solution in pH 6.0 aqueous imidazole buffer) was added to the flask containing enzyme ($t = 0$). At various times, a 50- μL aliquot was withdrawn and added to an assay solution (950 μL , pH 6.0, 0.1 M imidazole, 2 mM EDTA, 10 mM MgCl_2 , 2 mM ADP, 20 mM D-glucose, 2 mM NADP, 30 mM phosphocreatine, hexokinase (50 units/mL), glucose-6-phosphate dehydrogenase (35 units/mL)). The rate of increase in absorbance at 340 nm was recorded.²¹

Kinetics of Reactivation of Papain-S-S-Me. The papain-S-S-Me was prepared as described previously.¹⁵ To assay²² for the rate of reactivation of papain disulfide with DTT and meso-DTA, we used a procedure similar to that described in ref 8.

Registry No. 1, 124-04-9; meso-2, 137300-51-7; *dl*-2, 137300-52-8; meso-DTA dithioacetate, 137300-53-9; *dl*-DTA dithioacetate, 137300-56-2; meso-DTA, 137300-54-0; meso-DTA $^{\text{ox}}$, 137300-55-1; *dl*-DTA $^{\text{ox}}$, 137300-57-3; ME $^{\text{ox}}$, 1892-29-1; meso-2,5-dibromoadipoyl, 137300-49-3; *dl*-2,5-dibromoadipoyl, 137300-50-6; glutathione disulfide, 27025-41-8.

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