chloroform yielded pale yellow crystals of 3,5-dimethyl-1,2,4-triazol-4-amine (3; 60.3 mg, 0.538 mmol, 66.4%). After a second sublimation and a second recrystallization from chloroform, this material melted at 196.5–198.0 °C (lit.[13] mp 196.5–197.5 °C) and was identical by NMR with an authentic sample.[13]

B. Isolation of Glyoxal Dihydrazone (4) and Ethanolammonium Nitrite (5). The distillate obtained at 100 °C (0.60 torr) was extracted with dichloromethane (20 mL). Evaporation of solvent from the extract left a colorless, crystalline residue of glyoxal dihydrazone (4; 75.1 mg, 0.872 mmol, 53.8%), which was identical by IR, NMR, and melting point with an authentic sample.[14]

The insoluble fraction, a colorless liquid that could not be crystallized, was ethanolammonium nitrite (5; 81.2 mg, 0.751 mmol, 46.4%): IR (liquid film) 1605, 1500, 1325, 1210, 1060, 1000 cm^{-1}; ^1H NMR (90 MHz, Me_2SO-d_6) δ 2.80 (t, 2 H, J = 6 Hz), 3.54 (t, 2 H, J = 6 Hz); mass spectrum (EI), 61, 47. This material was identical by IR and NMR with a sample prepared independently from ethanolammonium chloride by ion exchange (Dowex 1-X8, NO_2^- form), and it gave a positive ferrous sulfate ring test for nitrite.[25] Addition of a solution of oxalic acid dihydrate (70.3 mg, 0.558 mmol) in absolute ethanol (2.0 mL) to a solution of nitrite 5 (76.0 mg, 0.703 mmol) in absolute ethanol (3.0 mL) caused the precipitation of ethanolammonium oxalate (56.0 mg, 0.264 mmol, 75.1%). Recrystallization from aqueous ethanol provided material melting at 197–198 °C dec (lit.[26] mp 199–200 °C dec), which was identical by IR and mixture melting point with an authentic sample.[26]

Hydrazinolysis of 2-Methyl-4-nitro-1*H*-imidazole-1-ethanol (7). A solution of 2-methyl-4-nitro-1*H*-imidazole-1-ethanol (7; 100 mg, 0.584 mmol) in hydrazine (6.3 mL, 95%) was heated under Ar for 6 days at 60 °C. Volatile compounds were then removed by evaporation under reduced pressure. By the procedure described in the previous experiment, the following three products were isolated from the residue: 3,5-dimethyl-1,2,4-triazol-4-amine (3; 19.9 mg, 0.177 mmol, 60.6%); glyoxal dihydrazone (4; 24.5 mg, 0.285 mmol, 48.8%); and ethanolammonium nitrite (5; 38.4 mg, 0.355 mmol, 60.8%).

Reduction of α-(Methoxymethyl)-2-nitro-1*H*-imidazole-1-ethanol (2, Misonidazole) by Hydrazine. A solution of α-(methoxymethyl)-2-nitro-1*H*-imidazole-1-ethanol (2; 62.1 mg, 0.309 mmol) in a mixture of tetrahydrofuran (1.0 mL) and absolute ethanol (1.0 mL) was treated at 30 °C with 5% palladium on charcoal (7.4 mg) and hydrazine (70 μL, 95%). After an initially vigorous evolution of gas had subsided, the mixture was stirred under N_2 for 3.5 h at 52 °C. The catalyst was then removed by filtration, and volatile compounds were removed by evaporation under reduced pressure. Molecular distillation of the residue at 125 °C (0.11 torr) yielded α-(methoxymethyl)-2-amino-1*H*-imidazole-1-ethanol (13; 50.0 mg, 0.292 mmol, 94.5%)[20] as a colorless liquid: IR (liquid film) 1615, 1535, 1490, 1260, 1185, 1100 cm^{-1}; ^1H NMR (90 MHz, D_2O) δ 3.38 (s, 3 H), 3.4 (m, 2 H), 3.8 (m, 2 H), 4.0 (m, 1 H), 6.58 (d, 1 H, J = 2 Hz), 6.70 (d, 1 H, J = 2 Hz); mass spectrum (EI) (relative intensity), 171 (81), 156 (51), 97 (100), 96 (71), 84 (49), 71 (60), 69 (72), 55 (76). This substance was identical by NMR with material independently prepared by the normal catalytic hydrogenation of misonidazole (2).[20]

Treatment of compound 13 with an equimolar amount of picric acid produced a monopicrate, which was purified by crystallization from water: mp 149.0–150.0 °C (lit.[20b] mp 145–146 °C). Anal. Calcd for $C_{13}H_{16}N_6O_9$: C, 39.01; H, 4.03; N, 20.99. Found: C, 38.93; H, 4.11; N, 20.94.

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Registry No. 1, 443-48-1; 2, 13551-87-6; 3, 3530-15-2; 4, 3327-62-6; 5, 31086-83-6; 7, 705-19-1; 13, 76620-73-0; 13·picrate, 88454-11-9; Pd, 7440-05-3; hydrazine, 302-01-2.

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Mechanistic Studies of 2-Lithio-1,3-dithiane Reactions with Radical Probes[1]

Sung Kee Chung* and Larson B. Dunn, Jr.

Department of Chemistry, Texas A&M University, College Station, Texas 77843

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The reaction of α,β-unsaturated carbonyls with a variety of organometallic nucleophiles can lead to either [1,2] or [1,4] addition products. The regiochemical control of [1,2] vs. [1,4] addition has important consequences in the synthetic design. The ratio of the regioisomers for a given α,β-unsaturated carbonyl has been found to be dependent on the nature of the carbon nucleophile (hard or soft), the counterion (ion association vs. carbonyl activation control), and the reaction conditions such as solvent and temperature (kinetic vs. thermodynamic control).[2] For example, in reversible reactions, the [1,2] and [1,4] adducts are usually the results of kinetic and thermodynamic control, respectively.[3] Reversible additions are normally observed with carbanions that are well stabilized or highly delocalized (i.e., high level of HOMO),[4] and the reversibility is often promoted by high reaction temperature[3,5] or high solvent polarity.[5,6] Even for kinetically controlled reactions, the nature of the solvent, e.g., the addition of HMPA, has been found to have a crucial effect in determining regioselectivity.[7]

The reasons for the change in regioselectivity caused by the addition of HMPA in these reactions are not clear, although a number of possible explanations may be offered. HMPA perhaps makes the addition process reversible by virtue of its cation-solvating ability.[8] It is also possible that the carbonyl activation by the counterion becomes insignificant in the presence of HMPA, thus making [1,4] addition more favorable.[4] Another possibility is that HMPA perturbs the highest occupied molecular orbital (HOMO) of the nucleophile in some manner favoring conjugate addition over [1,2] addition.[9] Eliel et al. have observed that HMPA causes upfield shifts of the phenyl proton and carbon resonances in their NMR study of 2-lithio-2-phenyl-1,3-dithiane.[10] They have suggested that the observed shifts are due to the ion-pairing change, namely, a contact ion pair in THF vs. a solvent-separated ion pair in the presence of HMPA. A most significant consequence of this type of perturbation by addition of HMPA is the likelihood of electron transfer between the nucleophile and the electrophile, since the higher level of the nucleophile's HOMO makes an electron donation easier.[11] In other words, the nucleophile can act as a reducing agent under the HOMO-raising perturbation, and the electrophiles such as α,β-unsaturated carbonyl can behave as electron acceptors.[12]

* Address correspondence to SmithKline & French Laboratories, Analytical, Physical, and Structural Chemistry, F-90, 1500 Spring Garden Street, Philadelphia, PA 19101.

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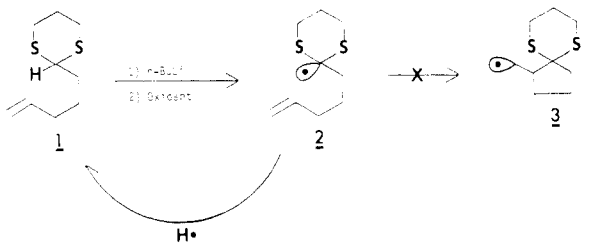
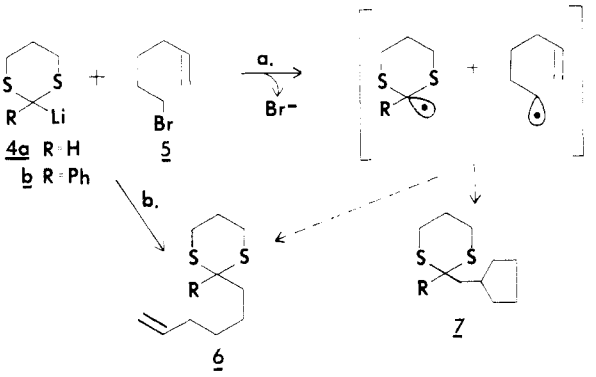
Scheme I



Scheme II



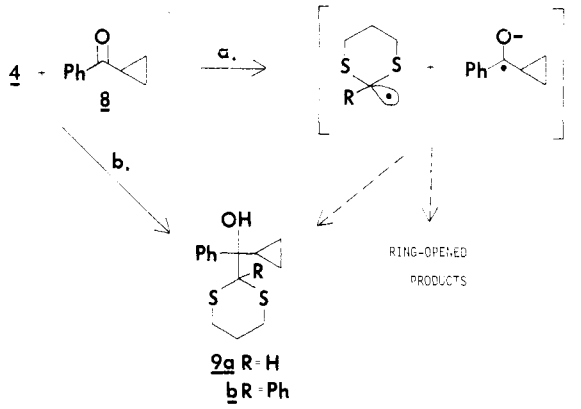
Metallated dithianes are synthetically versatile as acylcarbanion equivalents and react with a variety of electrophiles, e.g., alkyl halides and carbonyls.[13] Lithiodithianes generally react with α,β-unsaturated carbonyls to give only the [1,2] adducts, although some limited exceptions have been noted.[3,14] Recently, it has been reported that HMPA induces the conjugate addition of dithianes to α,β-unsaturated carbonyls.[7,15] Thus, we have investigated the possibility that reactions of lithiodithianes with such electrophiles as alkyl halides, ketones, and enones may involve an electron-transfer process in their reaction mechanisms, in particular in the presence of HMPA. In our study, we employed the well-established chemical probes for the detection of radicals, e.g., the cyclization of the hexenyl radical,[16] the ring opening of the cyclopropylcarbinyl radicals,[16] and the radical isomerization of *cis*-2,2,6,6-tetramethyl-4-hepten-3-one.[17]

Table I. Reactions of Lithiodithianes (4) with Phenyl Cyclopropyl Ketone (8) in THF

run	dithiane	conditions	additive	product (% yield)[a]
1	4a	−78 °C, 10 min		9a (99)
2	4a	−78 °C, 10 min	HMPA	9a (99)
3	4b	−78 °C, 10 min		9b (99)
4	4b	−78 °C, 10 min	HMPA	
5	4b	−78 °C, 1 h	HMPA	9b (50)
6	4b	−78 °C to RT[b]		
7	4b	−78 °C to RT	HMPA	

[a] Determined by ^{1}H NMR analysis. [b] RT = room temperature.

Scheme III



Results and Discussion

In mechanistic probe design it is possible in theory to incorporate the chemically based radical probe into the structure of either the nucleophile (dithiane) or the electrophile. Previous studies in the literature indicated that a cyclopropylcarbinyl probe at the 2-position of 1,3-dithiane would be problematic because of the competing ring opening of both the radical and the carbanion,[18] although the distinction between these two reactive intermediates may be possible on the basis of the nature of the hydrogen ultimately incorporated into the ring-opened product. We, therefore, opted for the hexenyl cyclization probe as a part of the dithiane nucleophile. The probe molecule 1 was prepared by alkylation of 2-lithio-1,3-dithiane with 1-bromo-4-pentene. However, this probe unfortunately failed to cyclize even under the conditions known to produce radicals, e.g., *p*-dinitrobenzene[19] and cupric chloride.[20] This may be due to the high stability of radical **2**[21] and reasonably fast hydrogen atom abstraction by **2** from the solvent, THF (Scheme I).

Next, we examined the reactions of 2-lithio-1,3-dithianes **4** with various electrophiles in which a potential radical probe is incorporated. When the lithiodithianes **4a** and

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Table II. Reactions of Lithiodithianes (4) with 10a in THF

run	dithiane	time, min	additives	unreacted enones (cis/trans ratio)[a]	product (% yield)[b]
1	4a	10		96:4	11 (71)
2	4a	10	HMPA	0:100	11 (50)
3	4a	10	HMPA, *p*-DNB	100:0	11 (47)
4	4b	10		56:44	
5	4b	120		0:100	12 (78)
6	4b	10	HMPA	0:100	
7	4b	120	HMPA	0:100	12 (30)
8	4b	10	HMPA, *p*-DNB	100:0	

[a] Determined by GC analysis. [b] Determined by ^{1}H NMR analysis.

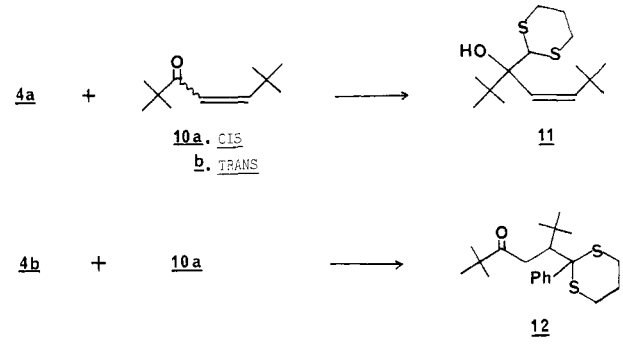
4b were reacted with 1-bromo-5-hexene in THF, only simple alkylated products (**6a** and **6b**, respectively) were obtained in excellent yields. The addition of HMPA did not have any discernible effect on either the product formation or the yield (Scheme II). Neither the reduction product (hexene or methylcyclopentane) nor the cyclized-coupled product **7** could be detected in these reactions by careful GC and TLC analyses. Although electron transfer from **4** to **5**, followed by a fast radical coupling to form **6**, cannot be rigorously ruled out by these results, this possibility appears rather unlikely.

The reactions of the lithiodithianes **4** with phenyl cyclopropyl ketone (**8**), a radical ring-opening probe, were also examined, and the results are summarized in Table I. In all cases, the simple addition products, alcohols **9**, have been obtained as the sole products. No ring-opened products of any kind could be detected in these reactions (Scheme III). Although no evidence of electron transfer from **4** to **8** was found, the addition of HMPA showed an interesting effect on the reaction of **4b** with **8**. While an excellent yield of alcohol **9b** was achieved in run 3, the same reaction in the presence of HMPA produced no alcoholic product (run 4). It was found that when the reaction in run 4 was quenched with D_2O, the 2-position of **4b** was almost completely deuterated. This finding indicates that the carbanion was still intact and HMPA was somehow slowing down the product formation.[22] No such effect was noted in the reactions of **4a** and **8** or of **4a** and **4b** with 1-bromo-5-hexene.

A possible cause for the observed retarding effect of HMPA on the reaction of **4b** and **8** may be that HMPA prevents the complexation of the lithium ion of **4b** with the carbonyl of **8**, thereby reducing the reactivity of **8** toward nucleophilic attack. However, this explanation is in conflict with the lack of such an effect on the reaction of **4a** with **8**. A more likely explanation is that since HMPA induces a greater delocalization of the carbanionic charge by increasing the electron density in the phenyl ring of **4b**,[10] the addition reactivity of **4b** is fundamentally changed and lowered. No such effect is expected with **4a**, which does not have a phenyl substituent.[24]

Another noteworthy observation from Table I is the absence of any alcohol product when the reaction was allowed to warm to room temperature before quenching (runs 6 and 7). It has been found that when these reactions were quenched with D_2O, the deuterium was exclusively located at the α-position of phenyl cyclopropyl ketone. It seems likely that as the temperature increases, the addition of **4b** to **8** becomes reversible and the deprotonation of **8** by the lithiodithiane predominates.[25] This suggestion is further supported by the following observation. When the alcohol **9b** was treated with *n*-BuLi at 78 °C and allowed to warm up to room temperature, phenyldithiane and phenyl cyclopropyl ketone were quantitatively obtained after the acidic quenching. In a similar experiment, the alcohol **9a** was recovered unchanged.

Scheme IV



Finally, we have studied the reactions of the lithiodithianes **4** with a twofold excess of the radical isomerization probe, *cis*-2,2,6,6-tetramethyl-4-hepten-3-one (**10a**), and the results are listed in Table II. Several features from the table are worthy of discussion. First, the enone **10a** reacts with **4a** and **4b** to produce exclusively the [1,2] adduct **11** and the [1,4] adduct **12**, respectively, regardless of whether the HMPA additive is present or not (Scheme IV). Second, good evidence for the HMPA-promoted electron transfer from **4** to **10a** could be obtained in terms of the geometric isomerization of the unreacted enone. As can be seen in Table II, when **4a** was reacted with the cis enone **10a** without HMPA, very little (ca. 4%) isomerization was observed and the only product was the cis alcohol **11** (run 1). In contrast, the presence of HMPA accelerated the isomerization of the enone and reduced the yield of the alcohol **11** (run 2). When the latter reaction was repeated in the presence of *p*-dinitrobenzene, an electron scavenger, the enone isomerization was completely suppressed (run 3). These results indicate that the enone isomerization is clearly HMPA promoted and a result of an electron-transfer process. It is very informative to note that despite the facile isomerization of the enone **10a** in the presence of HMPA, the reaction product **11** exclusively possesses the cis geometry.

When **4b** was reacted with a twofold excess of the cis enone without HMPA, a partial isomerization was detected in 10 min, but no addition product was formed (run 4). When a longer reaction time (2 h) was allowed, complete isomerization and the [1,4]-adduct formation were observed even in the absence of HMPA (run 5). Addition

(22) Similar rate retardations have been reported with lithioacetonitrile[11] and lithium dimethylcuprate.[23]
(23) Hallnemo, G.; Ullenius, C. *Tetrahedron* **1983**, *39*, 1621.
(24) We have obtained essentially identical results in the reactions of **4** with 1,1-dimethyl-2-benzocyclopropane and 1-benzoyl-2-phenylcyclopropane.
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of 2 equiv of HMPA to the reaction caused accelerated isomerization and the decreased yield of the [1,4] adduct (runs 6 and 7). The enone isomerization with HMPA could again be suppressed by use of *p*-dinitrobenzene. The reason for the reduced yield of the [1,4]-addition product in the presence of HMPA may be similar to that described for the reaction of **4b** with phenyl cyclopropyl ketone (**8**) (vide supra).

In summary, no evidence has been found to indicate that the reactions of **4** with alkyl halides or ketones proceed via an electron-transfer process. In the [1,2] addition of **4a** to the cis enone **10a**, HMPA clearly promotes electron transfer between the reactants, but this process is not mechanistically related to the [1,2]-addition process. The [1,4] addition of **4b** to the enone **10a** shows an appreciable degree of the electron transfer both in the presence and absence of HMPA. Although no definitive evidence has yet been obtained, electron transfer may be possible in some [1,4]-addition reactions of enones, in particular with soft nucleophiles and in the presence of HMPA.

Experimental Section

General Information. The following compounds were purchased from Aldrich Chemical Co. and used as received: methylcyclopentane, 1-hexene, pinacolone, pivalaldehyde, phenyl cyclopropyl ketone. *p*-Dinitrobenzene was purchased from Easman Chemical Co., and 1-bromo-4-pentene and 1-bromo-5-hexene were purchased from Pfaltz and Bauer, Inc. 1,3-Dithiane (**4a**),[27] 2-phenyl-1,4-dithiane (**4b**),[28] and *cis*-2,2,6,6-tetramethyl-4-hepten-3-one (**10a**)[17] were prepared according to literature procedures. A solution of *n*-BuLi in hexane (Aldrich) was occasionally titrated with 1,10-phenanthroline in 2-butanol to determine the precise concentration.[29] N_2 gas was passed through Drierite before use, and THF was freshly distilled from Na and benzophenone. Diisopropylamine and HMPA were distilled under N_2 from CaH_2 and stored in serum-capped bottles over molecular sieves. $CuCl_2$ was pulverized, dried in an oven at 130 °C, and stored in a dessicator over $CaSO_4$.

All reactions involving air-sensitive material were carried out under N_2 in flame-dried glassware equipped with septums by using the standard syringe technique. The low temperatures of −78 °C and −22 °C were obtained by CO_2/acetone and CO_2/CCl_4 mixtures, respectively. Unless indicated otherwise, all reactions were worked up by the following standard extractive procedure. The reaction mixture was quenched by being poured into a separatory funnel containing saturated NH_4Cl and diethyl ether. The organic products were extracted with ether several times. The combined extracts were washed with brine until neutral, dried over $MgSO_4$, filtered, and evaporated.

Dithianes were lithiated by the following two procedures. (A) A stirred solution of 1 equiv of 1,3-dithiane or 2-(4-pentenyl)-1,3-dithiane in 2 mL of THF at −22 °C was treated with 1.1 equiv of *n*-BuLi. After 1.5 h at −22 °C, the slightly cloudy solution was brought to the desired temperature. (B) To a stirred solution of 2-phenyl-1,3-dithiane in 2 mL of THF at −78 °C was added 1.1 equiv of *n*-BuLi dropwise. After the addition, the temperature was raised to −22 °C, kept there for 30 min, and brought to the desired temperature.

Gas chromatographic analyses were performed on an Antek 300 GC chromatograph equipped with a flame ionization detector and a Hewlett-Packard 3390A integrator. ^1H NMR spectra were obtained on Varian T-60 or EM-390 spectrometers in $CDCl_3$ containing Me_4Si as an internal reference. Fully decoupled ^{13}C NMR spectra were obtained on a JEOL PFT-100 spectrometer in the FT mode using $CDCl_3$ as solvent and reference. IR spectra were obtained on a Sargent-Welch Pye-Unicam 2-300 or a Perkin-Elmer 297 spectrometer. Mass spectra were obtained on a Hewlett-Packard 5980A spectrometer. Elemental analyses were done on a Perkin-Elmer 240 elemental analyzer. Melting points were measured on a Büchi 510 melting point apparatus and are uncorrected.

2-(4-Pentenyl)-1,3-dithiane (1). A solution of 1,3-dithiane[27] (2.5g, 21 mmol) in 20 mL of THF at −22 °C was treated with *n*-BuLi (15.6 mL of a 1.6 M solution in hexane, 25 mmol). After 1.5 h at −22 °C, the temperature was lowered to −78 °C, and 1-bromo-4-pentene (3.73 g, 25 mmol) was added all at once. The reaction mixture was allowed to slowly warm to room temperature overnight. An extractive workup followed by column chromatography on SiO_2 (diethyl ether and hexane) provided the product (3.42 g, 87%): liquid; IR (CCl_4) 3080, 2900, 1680, 1420, 1280, 1240, 1185, 995 cm^{-1}; ^1H NMR δ 1.70 (m, 4 H), 2.07 (m, 4 H), 2.80 (m, 2 H), 4.02 (t, 1 H), 4.95 (m, 2 H), 5.70 (m, 1 H); ^{13}C NMR δ 25.6, 25.8, 29.2, 33.0, 34.6, 47.2, 114.7, 137.7; MS, *m/z* (relative intensity) 188 (M^+, 59.1), 145 (16.4), 119 (100), 106 (44.5), 80 (25), 69 (8.0).

Attempted Radical Cyclization of 1. To a solution of 2-lithio-2-(4-pentenyl)-1,3-dithiane prepared from **1** (80 mg, 0.426 mmol) and *n*-BuLi (0.29 mL of a 1.6 M solution in hexane, 0.469 mmol) in 8 mL of THF at −22 °C was added *p*-dinitrobenzene (107 mg, 0.639 mmol) in 2 mL of THF. The reaction mixture, which turned black immediately, was allowed to warm to room temperature overnight. After an extractive workup, the crude reaction mixture was analyzed by TLC and ^1H NMR and found to contain only starting material. The use of 1.5 equiv of $CuCl_2$ instead of *p*-dinitrobenzene gave identical results.

Reaction of 4 with 1-Bromo-5-hexene (5). To a solution of 2-lithio-1,3-dithiane (**4a**), prepared from 1,3-dithiane (51.2 mg, 0.426 mmol) and *n*-BuLi, in 2 mL of THF at −78 °C was added **5** (6.95 mg, 0.426 mmol) in 2 mL of THF. (In the reactions involving HMPA, 2 equiv of HMPA was added before the addition of **5**.) The reaction mixture was allowed to slowly warm to room temperature overnight. Aliquots were taken and quenched with aqueous NH_4Cl and checked by GC for reduction produts, i.e., methylcyclopentane or 1-hexene. After the extractive workup, the crude reaction mixture was analyzed by ^1H NMR and TLC and was found to have only one product, which was purified by preparative TLC (10% diethyl ether in hexane on SiO_2) to give **6a** as yellow oil: IR ($CHCl_3$) 3080, 2920, 2860, 1635, 1420, 1270 cm^{-1}; ^{13}C NMR δ 138.6, 114.5, 47.6, 35.3, 33.5, 30.5, 28.5, 26.1, 26.0; MS, *m/z* (relative intensity) 202 (M^+, 22.2), 119 (100), 106 (43.4), 95 (22.6), 83 (5.6). Anal. Calcd for $C_{10}H_{18}S_2$: C, 59.41; H, 8.91. Found: C, 59.30; H, 8.54.

The reaction of 2-lithio-2-phenyl-1,3-dithiane (**4b**) with **5** similarly gave **6b** as yellow oil: IR ($CHCl_3$) 3060, 2920, 2900, 1635, 1590, 1435, 1275, 1030, 990 cm^{-1}, ^1H NMR δ 1.20 (m, 4 H), 1.90 (m, 6 H), 2.60 (m, 4 H), 4.85 (m, 2 H), 5.72 (m, 1 H), 7.25 (m, 3 H), 7.85 (m, 2 H); ^{13}C NMR δ 141.8, 138.5, 128.7, 128.3, 126.7, 114.3, 59.1, 45.0, 33.3, 28.8, 27.6, 25.3, 23.3; MS, *m/z* (relative intensity) 278 (M^+, 4.2), 195 (100), 106 (18.8), 83 (3.0), 77 (6.0). Anal. Calcd for $C_{16}H_{22}S_2$: C, 69.06; H, 7.91. Found: C, 69.16; H, 7.47.

Reaction of 4 with Phenyl Cyclopropyl Ketone (8) (Representative Procedure). To a solution of **4a**, prepared from 1,3-dithiane (51.6 mg, 0.429 mmol) and *n*-BuLi (0.462 mmol), in 2 mL of THF at −78 °C was added **8** (62.7 mg, 0.429 mmol) in 2 mL of THF. (In the reactions involving HMPA, 2 equiv of HMPA were added immediately before the addition of **8**.) The reaction was quenched after 10 min at −78 °C. An extractive workup followed by preparative TLC gave **9a** as yellow oil: IR ($CHCl_3$) 3540, 3080, 3060, 3010, 2900, 1670, 1600, 1490, 1420, 1325, 1270, 1170, 1030 cm^{-1}; ^1H NMR δ 0.51 (m, 4 H), 1.85 (m, 3 H), 2.80 (m, 5 H), 4.68 (s, 1 H), 7.30 (m, 3 H), 7.85 (m, 2 H); ^{13}C NMR δ 143.8, 127.6, 127.2, 125.9, 75.7, 61.0, 30.3, 30.2, 25.5, 19.0, 3.2, 0.9; MS, *m/z* (relative intensity) 266 (M^+, 0.2), 249 (0.9), 225 (0.5), 189 (0.2), 147 (91.6), 120 (90.8), 119 (58.7), 106 (10.6), 105 (100), 91 (17.2), 77 (26.3). Anal. Calcd for $C_{14}H_{18}OS_2$: C, 63.16; H,6.77. Found: C, 63.60; H, 6.56.

The reaction of **4b** with **8** similarly produced **9b**: mp 90–92 °C; IR ($CHCl_3$) 3510, 3060, 3010, 2910, 1660, 1595, 1480, 1440, 1325, 1225, 1150, 1030 cm^{-1}; ^1H NMR δ 0.20 (m, 2 H), 0.82 (m, 2 H), 1.27 (m, 1 H), 1.75 (m, 2 H), 2.56 (m, 4 H), 3.10 (s, 1 H), 7.18 (m, 8 H), 7.61 (m, 2 H); ^{13}C NMR δ 141.5, 136.9, 132.2, 128.3, 127.6, 127.3, 127.0, 126.1, 79.2, 74.0, 27.7, 27.4, 24.7, 17.3, 5.4, 0.90; MS, *m/z* (relative intensity) 342 (M^+, not present), 301 (0.5), 195 (100), 147 (95.7), 121 (77.5), 105 (92.3), 91 (16.6), 77 (33.8). Anal. Calcd for $C_{20}H_{22}OS_2$: C, 70.18; H, 6.43. Found: C, 69.60; H, 6.56.

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Deuterium Oxide Quenching Experiments. The previously described procedures were used, except that after 10 min at −78 °C from run 4, Table I, or warming to room temperature overnight for runs 6 and 7, Table I, the reactions were quenched with 0.5 mL of D_2O. After extractive workup, the reaction mixtures were analyzed by ^1H NMR. The spectrum of run 4 showed no singlet at δ 5.18, indicating almost complete deuterium incorporation into the 2-position of phenyldithiane. The ^1H NMR of runs 6 and 7 showed a singlet at δ 5.18, but the multiplet at δ 2.50 was missing, indicating almost complete deuteration of the α-position of **8**.

Equilibration Experiments of 9a and 9b. Two alcohols (**9a** and **9b**) were separately treated with 1.1 equiv of *n*-BuLi in 2 mL of THF at −78 °C and allowed to warm to room temperature overnight. The ^1H NMR of the reaction mixture involving **9a** showed no change, whereas the ^1H NMR spectrum of the reaction mixture involving **9b** showed the presence of 2-phenyl-1,3-dithiane and phenyl cyclopropyl ketone, but none of **9b**.

Reaction of 4 with *cis*-2,2,6,6-Tetramethyl-4-hepten-3-one (10a) (Representative Procedure). To a solution of **4a** prepared from 1,3-dithiane (49.8 mg, 0.414 mmol) and *n*-BuLi (0.456 mmol) in 2 mL of THF at −22 °C was added 2.0 equiv of **10a** (140 mg, 0.829 mmol) in 2 mL of THF. (In reactions involving HMPA or *p*-dinitrobenzene, the additive was added immediately before the addition of **10a**.) After extractive workup, the product yield was estimated by ^1H NMR and the composition of the enone isomers was determined by GC analysis. The pure product **11** was obtained by preparative TLC (10% diethyl ether in hexane on SiO_2): oil; IR ($CHCl_3$) 3510, 3350, 2950, 2900, 1640, 1460, 1420, 1350, 1195, 1095, 1005 cm^{-1}; ^1H NMR δ 1.12 (s, 9 H), 1.22 (s, 9 H), 2.00 (m, 2 H), 2.87 (m, 5 H), 4.29 (s, 1 H), 5.45 (q, 2 H, J = 13.5 Hz); ^{13}C NMR δ 142.7, 127.5, 81.8, 59.5, 39.8, 32.6, 31.7, 29.7,26.7, 25.6; MS, m/z (relative intensity) 288 (M^+, not present), 231 (1.4), 202 (0.2), 182 (43.3), 169 (12.8), 151 (2.0), 120 (19.1), 119 (43.3), 105 (5.3), 95 (13.6), 83 (34.2), 57 (100). Anal. Calcd for $C_{15}H_{28}OS_2$: C, 62.50; H, 9.72. Found: C, 61.99; H, 10.00.

The reaction of **4b** with **10a** similarly produced **12**: mp 40–41 °C; IR ($CHCl_3$) 3050, 2960, 2900, 1700, 1590, 1480, 1420, 1360, 1275, 1215, 1060 cm^{-1}; ^1H NMR δ 0.62 (s, 9 H), 1.25 (s, 9 H), 1.83 (m, 2 H), 2.35–3.0 (m, 6 H), 3.85 (m, 1 H), 7.30 (m, 3 H), 8.10 (m, 2 H); ^{13}C NMR δ 214.0, 142.7, 131.0, 127.9, 126.8, 67.6, 53.1, 44.1, 39.3, 36.9, 30.1, 27.7, 27.4, 27.1, 25.1; MS, m/z (relative intensity) 364 (M^+, 1.2), 258 (47.2), 201 (49.0), 195 (43.0), 145 (32.3), 121 (27.3), 115 (28.9), 91 (6.1) 77 (9.3), 57 (100). Anal. Calcd for $C_{21}H_{32}OS_2$: C, 69.23; H, 8.79. Found: C, 68.73; H, 8.51.

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Registry No. 1, 88180-26-1; **4a**, 36049-90-8; **4b**, 53178-41-9; **5**, 2695-47-8; **6a**, 88563-40-0; **6b**, 88563-41-1; **8**, 3481-02-5; **9a**, 88563-42-2; **9b**, 88563-43-3; **10a**, 29569-89-9; **11**, 88563-44-4; **12**, 88563-45-5.

Intramolecular Hydrogen Bonding and Acidity of Some γ-Hydroxy- and γ-Methoxy-α,β-unsaturated Carboxylic Acids

Layton L. McCoy* and Dipakranjan Mal

Department of Chemistry, University of Missouri—Kansas City, Kansas City, Missouri 64110

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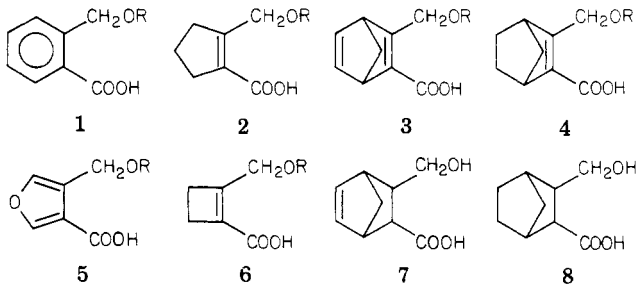
In earlier work, the effect of intramolecular hydrogen bonding on acidity as a function of the distance between the carboxyl groups in dicarboxylic acids was examined.[1] An obvious extension of that work is the determination in a similar manner the effect of intramolecular hydrogen bonding on the acidity of γ-hydroxy and γ-methoxy carboxylic acids—in effect analogues of the dicarboxylic acids and their half methyl esters in which a carbonyl has been replaced by methylene. For comparison with the previous study,[1] the requisite compounds are various cyclic and bicyclic γ-hydroxy- and γ-methoxy-α,β-unsaturated acids. The present paper describes the preparation and acidities of a set of such compounds (**1–6**).



1 **2** **3** **4**

5 **6** **7** **8**

a, R = H; b = CH_3

Of these, **1a**,[2] **1b**,[2] **2a**,[3] and **2b**[4] have been reported, but in each case the synthesis was not of a general character. Since the corresponding dicarboxylic acids are known and readily available, it seemed possible that a general approach could be used. Thus, either the diacid (c) or the diester (d) could be converted to the half-ester, half-acid (e), reduced to the hydroxymethyl ester (f), saponified to the hydroxy acid (a), and subsequently converted to the methoxy acid (b). This sequence worked satisfactorily for **2**, **5**, and **6**.

Although **1e** was examined briefly in this sequence, the much simpler hydrolysis of readily available phthalide was used to prepare **1a**[5] and subsequently **1b**.

The bicyclic systems **3** and **4** presented many problems. Compounds of the **3** series (dienes) were prepared, and in appropriate cases these were partially reduced to the **4** series (monoenes). Several procedures for half-saponification of **3d** were tried, but all gave less than 10% yield of **3e**. However, **3e** (R = ethyl) was prepared in 58% yield by Diels–Alder reaction between cyclopentadiene and the ethyl half-ester of acetylenedicarboxylic acid. After the attempted conversion of **3e** to **3f**, the crude product "**3f**" was saponified directly. Instead of **3a**, only a compound believed to be **7** was isolated. Similarly, **4e** gave a product presumed to be **8**.

In an attempt to circumvent this difficulty, the acetate of **3a** was prepared by Diels–Alder reaction between cyclopentadiene and 4-acetoxytetrolic acid;[6] the acetate of **4a** was prepared by partial reduction of **3a** acetate. Hydrolysis of these acetates produced materials that appeared by NMR and IR spectra to contain the desired compounds **3a** and **4a**. Unfortunately, the crude products on standing for a few hours were transformed into insoluble, possibly polymeric substances; earlier attempted purification by chromatography resulted in gross structural changes and a complex mixture, e.g., IR spectra and qualitative tests indicated the presence of aldehyde.

Compound **3b** was obtained by reaction of cyclopentadiene and 4-methoxytetrolic acid.[7] This acid also appeared to be somewhat unstable, but clearly more stable than **3a**. Partial reduction of **3b** did not lead to any material identifiable as **4b**.

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