JOC Article

Dimethyl Sulfoxide Mediated Elimination Reactions in 3-Aryl 2,3-Dihalopropanoates: Scope and Mechanistic Insights

Wei Li,*,† Jianchang Li,† Melissa Lin,‡ Sumrit Wacharasindhu,‡ Keiko Tabei,‡ and Tarek S. Mansour‡

Chemical and Screening Sciences, Wyeth Research, 200 Cambridge Park Drive, Cambridge, Massachusetts 02140, and Chemical and Screening Sciences, Wyeth Research, 401 North Middletown Road, Pearl River, New York 10965

weili@wyeth.com

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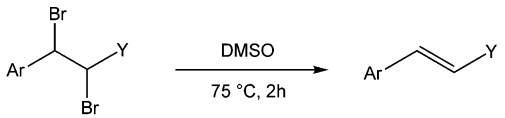


Y=CO_2H, CO_2Et, COPh, $CONH_2$, NO_2
Ar = phenyl, pyridyl, thiophene

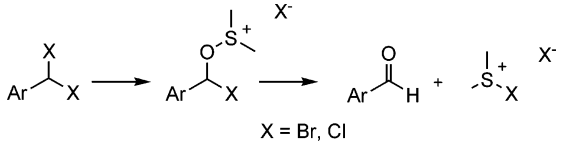
Dimethyl sulfoxide (DMSO) efficiently causes the reductive elimination of 3-aryl 2,3-dibromopropanoates to cinnamates with good yield. With 3-phenyl 2,3-dihalopropanoates, debromination is the major pathway providing 3-phenylacrylate derivatives in high yields, whereas dehydrobromination is a competing pathway with thiophene derivatives. ^{1}H NMR, ^{81}Br NMR, and MS techniques indicated the formation of brominated-DMSO, MeBr, and HBr as byproducts in this transformation with no evidence for the formation of Br_2. The dual role of DMSO as a nucleophile and bromine scavenger accounts for the products formed in this reaction.

Introduction

Recently, we reported the synthesis of aromatic aldehydes from dihalomethylarenes via an oxygen-transfer reaction involving dialkylsulfoxides (Scheme 1).[1] Unlike well-known oxidation reactions such as the Swern oxidation and its numerous variants,[2−3] the oxygen-transfer reaction does not require activation of the sulfoxide and proceeds via an alkoxysulfonium intermediate in a non-oxidative manner.

While oxygen-transfer reactions of sulfoxides catalyzed by metal complexes are well-established,[3] the scope of these reactions has been useful mainly with phosphines and carbenes.[4] In a recent work Khenkin and Neumann demonstrated that polyoxomolybdates can activate sulfoxides leading to the oxidation of alkylarenes[5] and benzylic alcohols[6] catalytically

SCHEME 1



X = Br, Cl

via a Keggin type complex. A crystal structure of a heterobimetallic Zr−Ru complex with DMSO has been reported, indicating oxygen transfer from DMSO to a carbonyl ligand.[7] Remarkably in biological systems dimethyl sulfoxide reductase is a molybdenum containing enzyme that catalyzes the oxygen atom transfer from its substrate DMSO in a two-stage reaction involving oxygen atom transfer and electron transfer.[8] Expanding on our initial report that oxygen-transfer reactions involving DMSO can occur chemically without activation or the involvement of metal complexes, we further explored such reactions with 1,2-dihalo compounds. Herein, we communicate our preliminary results on this reaction which demonstrate that reductive debromination is the predominant pathway in a series

† Wyeth Research, Cambridge.
‡ Wyeth Research, Pearl River.

(1) Li, W.; Li, J.; DeVincentis, D.; Mansour, T. S. *Tetrahedron Lett.* **2004**, *45*, 1071.
(2) (a) Tidwell, T. T. *Org. React.* **1990**, *39*, 2970. (b) Fang, X.; Bandarage, U. K.; Wange, T.; Schroeder, J. D.; Garvey, D. S. *J. Org. Chem.* **2001**, *66*, 4019.
(3) Choi, M. K. W.; Toy, P. H. *Tetrahedron Lett.* **2003**, *59*, 7171.
(4) (a) Kukushkin, Coord, V. Y. *Chem. Rev.* **1995**, *139*, 375. (b) Lim, B. S.; Holm, R. H. *J. Am. Chem. Soc.* **2004**, *123*, 1920.
(5) Khenkin, A. M.; Neumann, R. *J. Am. Chem. Soc.* **2002**, *124*, 4198.
(6) Khenkin, A. M.; Neumann, R. *J. Org. Chem.* **2002**, *67*, 7075.
(7) McAlpine, A. S.; McEwan, A. G.; Bailey, S. *J. Mol. Biol.* **1998**, *275*, 613.
(8) Fabre, S.; Findeis, B.; Trosch, D. J. M.; Gade, L. H.; Scowen, I. J.; McPartlin, M. *Chem. Commun. (Cambridge)* **1999**, 577.

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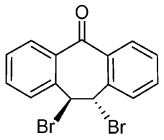
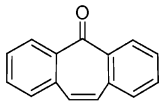
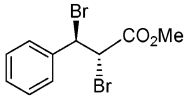
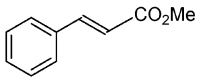
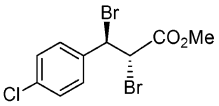
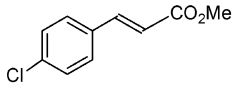
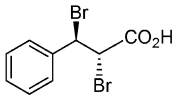
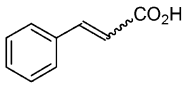
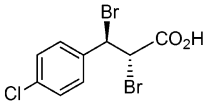
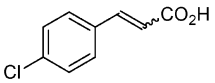
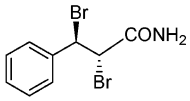
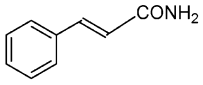
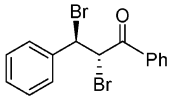
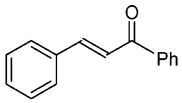
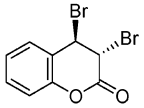
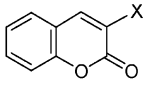
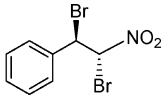
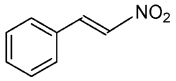
TABLE 1. Reductive Debromination of *vic*-Dibromo Compounds

Entry	S.M.	Product	Conditions	Yield (%)
1			75 °C 2h	98
2			75 °C 2h	97
3			75 °C 2h	97
4			100 °C 1h	62 *trans/cis* 5:1
5			100 °C 1h	62 *trans/cis* 3:1
6			100 °C 6h	80
7			75 °C 3h	95
8		 8A: X = H, 8B: X = Br	25 °C 12h	93 8A:8B 3:1
9			25 °C 18h	51

SCHEME 2

Y=CO_2H, CO_2Et, COPh, $CONH_2$, NO_2
Ar = phenyl, pyridyl, thiophene.

of substituted 2,3-dibromo-3-phenylpropanoates with dehydrobromination as the competitive reaction in some cases.

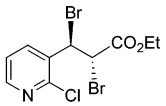
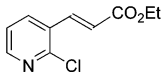
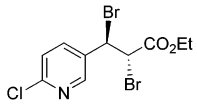
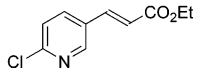
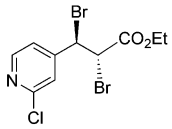
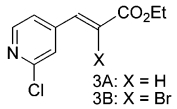
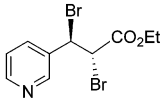
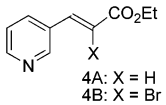
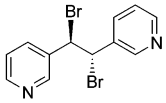
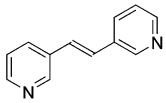
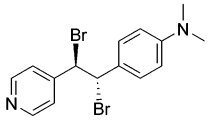
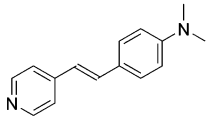
Results and Discussion

Our initial objective was focused on exploring the scope of the reaction of DMSO with various 1,2-dihaloethanes. To this end, we reasoned that at least one activating aryl moiety α to a halogen would be desirable since in our earlier report dihalomethylarenes were suitable substrates for reaction with DMSO. Additionally, we hypothesized further that the incorporation of an electron withdrawing group *β* to the aryl moiety should expand further the scope of the proposed reaction. Thus, we selected 3-phenyl-, 3-pyridyl-, and 3-thiophene-based propionic acid derivatives as useful substrates for investigation.

Scheme 2 illustrates reductive elimination of various phenethyl 1,2-dibromo compounds. A diverse set of substituents at the two carbons bearing the bromo atoms has been investigated. Representative examples in the reaction of DMSO with phenylethyl compounds as shown in Table 1 include dibenzosuberone and coumarin (entries 1 and 8 for cyclic structures), 3-phenylpropionic acids, esters and amides (entries 2−6), and (*E*)-chalcone and phenylnitroethane (entries 7 and 9). In these reactions, reductive debromination could be easily accomplished within 1−6 h of reaction time at 75−100 °C or after longer times at room temperature (entries 8 and 9). The DL-2,3-dibromo-3-phenylpropionic ester (entry 2 and 3) afforded the corresponding cinnamate in excellent yield as indicated by the large coupling constant of the vinyl protons in the ^{1}H NMR spectrum. The trans stereochemistry was also obtained with amide (entry 6) and ketone (entry 7) derivatives in excellent yields. Carboxylic acids (entries 4 and 5) produced a mixture of *trans*- and *cis*-α,*β*-unsaturated acids in 5:1 and 3:1 ratio, respectively. Clearly, a broad range of functional groups (esters, acids, amides, nitro, and keto) was tolerated under the reaction conditions. We also noted that the reductive debromination is accelerated in the presence of water (∼3% in DMSO) and affords better yields and purity. The reaction has been scaled up to multigram quantities with similar outcome.

It is interesting to point out that reductive debromination of the substrates in Table 1 has been the subject of many

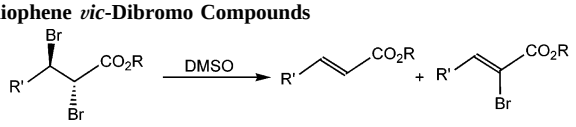
TABLE 2. Reductive Debromination of Pyridine *vic*-Dibromo Compounds

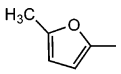
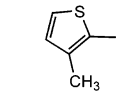
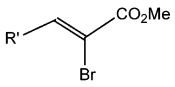
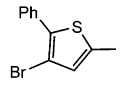
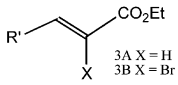
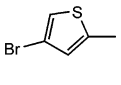
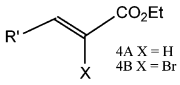
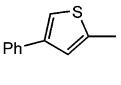
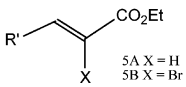
Entry	S.M.	Product	Conditions	Yield (%)
1			75°C 9h	72
2			75°C 9h	74
3		 3A: X = H 3B: X = Br	75°C 9h	68 3A:3B 9:1
4		 4A: X = H 4B: X = Br	75°C 4h	60 4A:4B 6:1
5			75°C 24h	72
6			75°C 2h	19

publications. For example, preparation of the cinnamates from the dibromo precursor (entry 2 of Table 1) has been frequently reported through reductive debromination under a variety of harsh reaction conditions, such as metal reducing agents,[9] dissolving metal chemistry,[10] or using tertiary amines under irradiation conditions.[11] Clearly, this DMSO mediated debromination procedure is the most convenient and practical procedure for the preparation of these compounds.

We next examined extension of the scope of reductive elimination to *vic*-dibromoethylpyridine analogues (Table 2). In these cases, 2,3- and 2,5-disubstituted pyridine propanoates (entries 1, 2) gave the *trans*-α,*β*-unsaturated esters exclusively in good yield. When the ester group is replaced with another pyridine or phenyl ring (entries 5 and 6), *trans*-olefins are also obtained. The 4-dimethylamino moiety at the pyridine ring seemed to have adverse effect on the reaction as indicated by the low yield (entry 6, Table 2). In the case of 2,4-disubstituted pyridine or 3-substituted pyridine (entries 3 and 4), the α,*β*-unsaturated esters were formed as the major products but were accompanied by the dehydrobromination byproducts (<15%).

TABLE 3. Debromination/Dehydrobromination of Furan and Thiophene *vic*-Dibromo Compounds



Entry	R'	Product	Conditions	Yield (%)
1		decomposition	75°C	
2			75°C 7h	37
3		 3A X = H 3B X = Br	85 °C 45 min.	75 3A:3B 1:1
4		 4A X = H 4B X = Br	75°C 6h	52 4A:4B 2:1
5		 5A X = H 5B X = Br	75°C 6h	74 5A:5B 1:3.5

Having established that phenyl and pyridyl acid derivatives showed a consistent reductive elimination outcome, we investigated a series of thiophene and furan 1,2-dibromo compounds (Table 3). The furan dibromo analogue was not stable under the reaction conditions and resulted in decomposition of the starting material. In all the other examples shown in Table 3, competitive pathways leading to both products appear to have occurred and in some cases (entries 2 and 5) dehydrobromination appears to be the major pathway. To confirm the outcome of the dehydrobromination, the structure and configuration of the vinyl bromide in entry 2 of Table 3 was established by mass spectroscopy and NMR techniques. The regiochemistry was assigned on the basis of the results of HMBC studies, as well as the chemical shifts of its ^{1}H and ^{13}C NMR spectra. The olefin configuration was determined on the basis of NOE results and the ^{3}J(C,H) coupling constant obtained from a HSQMBC experiment.[12]

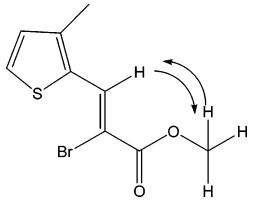
Mechanistic insights into this transformation were unraveled by following the conversion of *trans*-(10,11-dibromo)dibenzosuberone (20 mg) to dibenzosuberone (entry 1 of Table 1) in 0.6 mL of DMSO-d_6 with 3% D_2O by NMR techniques. ^{1}H (400 MHz) and ^{81}Br NMR (108 MHz) spectra were immediately acquired at 25 °C with little changes noted. The sample was then heated to 70 °C, and NMR data were collected over the course of the reaction.

(9) (a) Xu, X.; Lu, P.; Zhang, Y. *Synth. Commun*. **2000**, *30*, 1917. (b) Ranu, B. C.; Guchhait, S. K.; Sarkar, A. *Chem. Commun. (Cambridge)* **1998**, 2113. (c) Adam, W.; Arce, J. *J. Org. Chem*. **1972**, *37*, 507. (d) Schubert, W. M.; Rabinovitch, B. S.; Larson, N. R.; Sims, V. A. *J. Am. Chem. Soc*. **1952**, *74*. 4590. (e) Buckles, B. E.; Bader, J. M.; Thurmaier, R. J. *J. Org. Chem*. **1962**, *27*, 4523. (f) Prince, M.; Bremer, B. W.; Brenner, W. *J. Org. Chem*. **1966**, *31*, 4292. (g) King, J. E.; Pews, R. C. *Can. J. Chem*. **1964**, *42*, 1294.

(10) (a) Olah, G. A.; Prakash, G. K. S. *Synthesis* **1976**, 607. (b) ltalpem, J.; Maher, J. P. *J. Am. Chem. Soc*. **1965**, *87*, 5361. (c) Yanada, R.; Negoro, N.; Yanada, K.; Fujita, T. *Tetrahedron Lett.* **1996**, *37*, 9313. (d) Wang, L.; Zhang, Y. *Tetrahedron* **1999**, *55*, 10695.

(11) Izawa, Y.; Takeuchi, M.; Tomioka, H. *Chem. Lett.* **1983**, 1297.

(12) A NOE correlation was observed from the vinyl proton to the methoxy protons, indicating the cis-relationship of these two groups. In addition, ^{3}J(C,H) between the vinyl proton and the carbonyl carbon is small (4.3 Hz). These results suggest the double bond configuration is *Z*. For reference, see: Williamson, R. T.; Márquez, B. L. Gerwick, W. H.; Kövér, K. *Magn. Reson. Chem.* **2000**, *38*, 265.



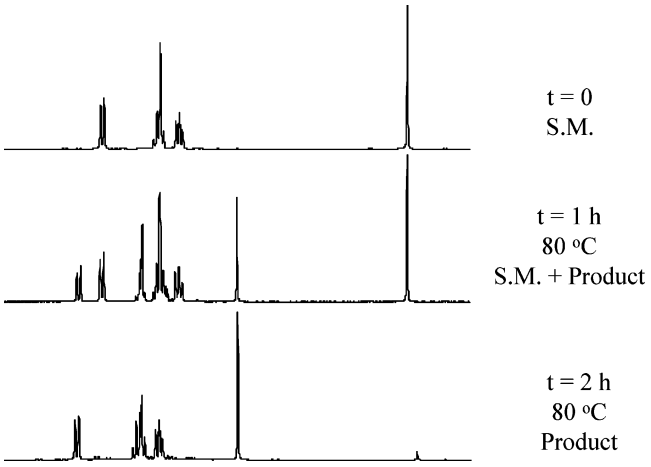


FIGURE 1. Reaction time course monitored by ^{1}H NMR.

The ^{1}H NMR spectra of the starting material, interim reaction mixture, and the final product are shown below (Figure 1). The data suggested that the DMSO mediated reductive debromination is a smooth and clean reaction. Upon heating, the dibromo starting material is continuously converted to the desired product. No major byproducts were detected during the course of the reaction by NMR. The fact that no byproduct arising from aromatic bromination suggests the absence of free elemental bromine in the reaction mixture.

It became clear that looking for the brominated products in the reaction mixture is necessary to get a better understanding of the reaction mechanism. It was noted that the HOD signal of the final solution shifted downfield, suggesting possible pH changes. Therefore, a small amount of KOH solution was added into the reaction mixture. ^{1}H and ^{81}Br NMR spectra were then acquired. While no changes occurred in the ^{1}H spectrum of the product after the addition of KOH (except the HOD signal), the ^{81}Br NMR spectrum (Figure 2) showed a Br^- signal suggesting the presence of HBr or DBr since covalently bound bromine nuclei are usually undetectable in ^{81}Br NMR due to unfavorable quadrupolar relaxation.

We then investigated the composition of the reaction mixture further in a time course study correlating NMR and GC-MS techniques together. Bromomethyl methylsulfoxide (CD_3SOCD_2Br), CD_3Br, and Br^- were observed in GC-MS after ca. 15 min and increased over the course of 2 h. The latter was also confirmed by electrospray MS analysis. Careful analyses by MS techniques revealed the formation of trace amounts of 10-bromo-11-hydroxyldibenzoseberone, 10-bromodibenzoseberone, and 10,11-dioxodibenzoseberone (Figure 3). All of these byproducts might arise from a common intermediate—the alkoxysulfonium species (Figure 4). These techniques were also applied to confirm that the reaction of DMSO with 4-phenylthiophene analogue (entry 5 of Table 3) at 85 °C for 2 h gave a mixture of dehydrobromination and debromination products in 3.5:1 ratio, respectively. CD_3SOCD_2Br, CD_3Br, and Br^- were also observed in GC-MS analyses, as in the previous case.

Since the amount of bromomethyl methylsulfoxide increased with time, it was of interest to study the reductive elimination of dibromo−dibenzosuberone in this sulfoxide[13] instead of DMSO. Under identical reaction conditions or even longer reaction time, formation of dibenzosuberone from the dibromo derivative did not occur, indicating the specific preference of DMSO versus its monobromo derivative in effecting this reaction.

On the basis of the above observations, the DMSO mediated reductive debromination appears to follow a complex pathway as indicated by the composition of the reaction mixture. However, on the basis of the selective transformation of the dibromo precursor to the *trans*-olefin, the following reaction pathway seems plausible. The DMSO oxygen moiety displaces the first bromine atom at the carbon α to the aromatic ring to form the alkoxysulfonium intermediate, which is followed by *syn* elimination of the second bromine to complete the reductive debromination leading to the *trans*-olefin (pathway a, Figure 4). The *syn* elimination pathway is especially favored in the medium-sized ring system (entries 1 and 7, Table 1). The fact that no rearranged byproducts were detected from entry 1 (Table 1) also suggests that an open carbocation intermediate is less likely. The active alkoxysulfonium intermediate could also lose its acidic proton α to the carbonyl to undergo dehydrobromination and form the *Z*-vinyl bromide (pathway b, Figure 4), which was observed as a competitive process in some examples. Although the *syn* elimination pathway has been found in open-chain systems less frequently,[14] the lack of reactivity of the bromomethyl methylsulfoxide toward reductive debromination may also support the proposed pathway due to its weak nucleophilicity. Our results indicate that the debromination pathway is enhanced with 2,3-dibromopropaonates having a more acidic benzylic-type proton.[15]

The fact that no elemental bromine was detected in the reaction system suggested that the role of DMSO here not only serves as a nucleophile but also as a scavenger to remove the bromine *in situ* by formation of the brominated derivatives, such as bromomethyl methylsulfoxide and HBr, or by fragmentation to bromomethane and methanesulfonic acid, a known DMSO/Br_2/HBr reaction outcome in the literature.[16] Therefore, the DMSO mediated reductive debromination undergoes a pathway different from all of the classical mechanisms due to the unique multifunction of the DMSO molecule. This finding highlights the unique reactivity of DMSO in these systems and offers the possibility to expand the scope of these reactions further. Our findings also call attention to careful analysis of halo−aryl compounds stored in DMSO for long times, such as the high-throughput screening (HTS) samples in the pharmaceutical industry, where all the compounds are stored as DMSO stock solution.

As to the limitations, the reaction did not occur if the *vic*-carbons are not activated. For example, 1,2-dibromobutane, or 2,3-dibromobutane did not react with DMSO to generate the corresponding 1-butene or 2-butenes, respectively. However, preliminary investigations indicate that DMSO reacts with mono-activated *vic*-dibromo compounds under similar condition—but does not provide the reductive debromination products. The scope of these reactions is currently under further investigation, and the results will be reported shortly.

(13) Iiuchijima, S.; Tsuchihashi, G. *Synthesis* **1970**, *1*, 58.

(14) Smith, B. M.; March, J. *Advanced Organic Chemistry*, 5th ed.; John Wiley & Sons, Inc.: New York, 2001; p 1305.

(15) (a) Fraser, R. R.; Mansour, T. S.; Savard, S. *J. Org. Chem.* **1985**, *50*, 3232. (b) Fraser, R. R.; Mansour, T. S.; Savard, S. *Can. J. Chem.* **1985**, *63*, 3505. (c) Fraser, R. R.; Mansour, T. S. *J. Organomet. Chem.* **1986**, *310*, C60.

(16) Aida, T.; Akasaka, T.; Furukawa, N.; Oae, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1117.

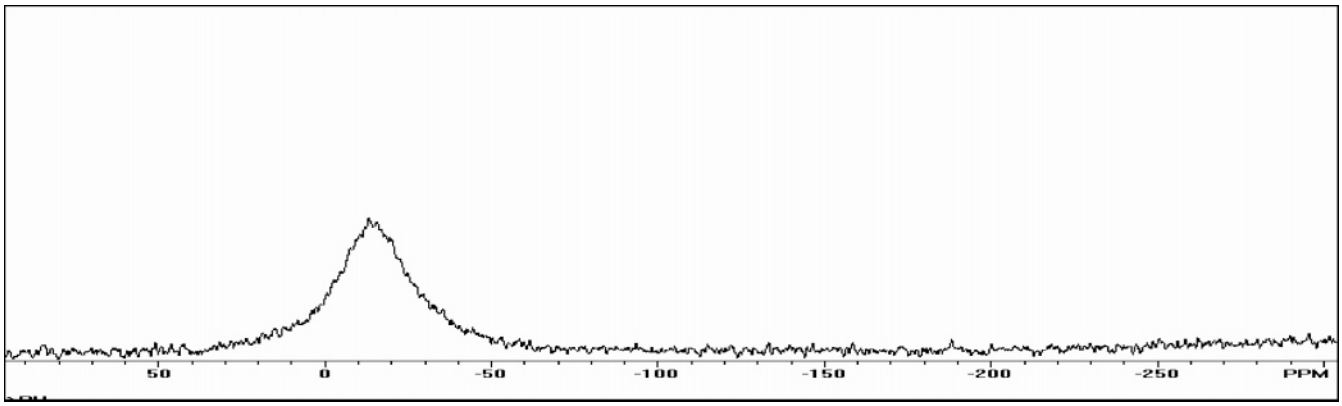


FIGURE 2. ^{81}Br NMR spectrum of the rection mixture (externally referenced to a 10 mM NaBr solution).

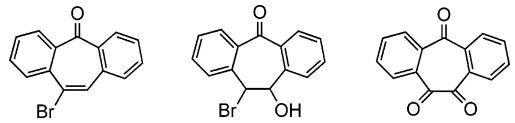


FIGURE 3. Byproducts (trace amounts in entry 1 of Table 1) detected by LC-MS.

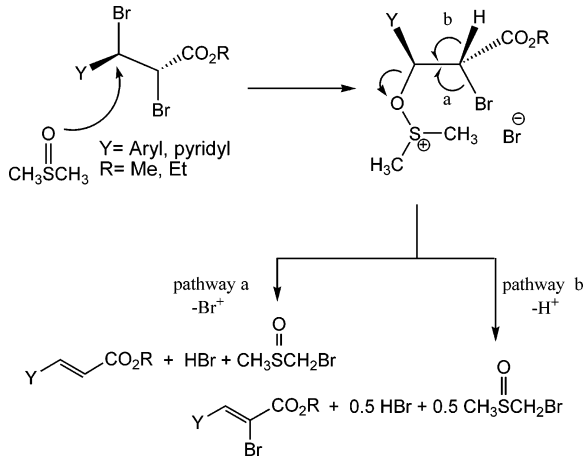


FIGURE 4. Proposed reaction pathway.

The 1,2-dibromo compounds used in these studies were prepared by addition of bromine in either carbon tetrachloride or carbon disulfide according to literature procedures.[17]

In conclusion, we have demonstrated that DMSO alone without a metal or an oxidant efficiently effects reductive debromination pathways in a variety of substrates. The combination of halogenation and reductive dehalogenation has been used to temporarily protect double bonds,[18] to purify olefins,[19] and to introduce a new double bond in organic synthesis.[20] Although reductive dehalogenation of 1,2-dihalo compounds with other agents has been the subject of many reports,[21] our novel DMSO procedure reported here is the most facile, mild, and convenient method for such a transformation.

Experimental Section

(*E*)-Ethyl 3-(2-Chloropyridin-3-yl)acrylate (Entry 1 in Table 2). ^{1}H NMR ($CDCl_3$): δ 8.63 (s, 1H), 7.97 (d, J = 16.0 Hz, 1H), 7.91 (s, 1.6 Hz, 1H), 7.28−7.31 (m, 1H), 6.45 (d, J = 16.0 Hz, 1H), 4.28 (q, J = 7.0, 2H), 1.37 (t, J = 7.0, 3H). ^{13}C NMR ($CDCl_3$): δ 165.8, 151.3, 150.4, 138.8, 135.9, 129.6, 123.0, 122.8, 60.9, 14.2. LRMS (ES-MS) [$(M + H)^+$]: for $C_{10}H_{10}O_2ClN$ 211.04, found 212.1.

(*E*)-Ethyl 3-(6-Chloropyridin-3-yl)acrylate (Entry 2 in Table 2). ^{1}H NMR ($CDCl_3$): δ 8.68 (d, J = 2.4 Hz, 1H), 7.80 (dd, J = 2.4, 5.6 Hz, 1H), 7.63 (d, J = 16.2 Hz, 1H), 7.40 (d, J = 5.6 Hz, 1H), 6.47 (d, J = 16.4 Hz, 1H), 4.34 (q, J = 7.2, 2H), 1.34 (t, J = 7.2, 3H). ^{13}C NMR ($CDCl_3$): δ 166.4, 153.4, 149.8, 139.6, 136.9, 129.6, 124.9, 121.5, 61.2, 14.6. LRMS (ES-MS) [$(M + H)^+$]: for $C_{10}H_{10}O_2ClN$ 211.04, found 212.1.

(*E*)-Ethyl 3-(2-Chloropyridin-4-yl)acrylate (Entry 3 in Table 2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.43(d, J = 5.1 Hz, 1H), 7.53 (d, J = 15.9 Hz, 1H), 7.40 (s, 1H), 7.12−7.30 (m, 1H), 6.58 (d, J = 15.9 Hz, 1H), 4.29(q, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 165.6, 152.5, 150.3, 144.8, 140.0, 124.2, 122.5, 120.3, 61.1, 14.2.

(*E*)-Ethyl 3-(Pyridin-3-yl)acrylate (Entry 4 in Table 2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.90 (s, 1H), 6.11 (t, J = 3.3 Hz, 1H), 7.82−7.86 (m, 1H), 7.64−7.71 (m, 1H), 7.31−7.36 (m, 1H), 6.50−6.57 (m, 1H), 4.24−4.33 (m, 2H), 1.32−1.38 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 166.2, 150.7, 149.7, 140.8, 134.1, 130.2, 123.7, 120.5, 119.9, 60.7, 14.2.

(*E*)-1,2-Di(pyridin-3-yl)ethane (Entry 5 in Table 2). ^{1}H NMR ($CDCl_3$): δ 8.62−8.63 (m, 2H), 7.43−7.70 (m, 4H), 7.42 (d, J = 5.6 Hz, 2H), 7.04−7.19 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 155.5, 150.1, 137.0, 132.1, 124.5, 123.2.

(*E*)-*N*,*N*-Dimethyl-4-(2-(pyridin-4-yl)vinyl)aniline (Entry 6 in Table 2). ^{1}H NMR ($CDCl_3$, 300z): δ 8.56 (d, J = 4.8 Hz, 1H), 7.46−7.64 (m, 4H), 7.35 (d, J = 8.1 Hz, 1H), 7.06−7.08 (m, 1H), 7.00 (d, J = 12.3 Hz, 1H), 6.95 (d, J = 8.7 Hz, 2H), 3.0 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 156.5, 149.5, 136.3, 132.9, 128.3, 124.9, 121.3, 121.1, 122.2, 40.3.

(*Z*)-2-Bromo-3-(3-methylthiophen-2-yl)acrylic Acid Methyl Ester (Entry 2 in Table 3). ^{1}H NMR ($CDCl_3$): δ 8.52 (s, 1H),

(17) (a) Cossy, J.; Pete, J. P. *Bull. Soc. Chim. Fr.* **1979**, 559. (b) Sanchez B. J.; Hernandez, M. D.; McPhee, D. J. *Bol. Soc. Quim. Peru* **1982**, *48*, 195.

(18) Solo, A. J.; Singh, B. J. *J. Org. Chem.* **1965**, *30*, 1658.

(19) Soday, F. J.; Boord, C. E. *J. Am. Chem. Soc.* **1933**, *55*, 3293.

(20) (a) It is worth mentioning here that the following cited preparation of a ^{14}C-labeled dibenzosuberenone was made with a key step of the reductive debromination. Such a reduction was carried out using copper bronze in DMSO. As clearly stated in the paper, copper bronze was the reducing agent, while the DMSO was used as the reaction solvent and was not credited for the reduction. Appreaently, DMSO must have partially contributed to the reduction. Nonetheless, this is a good example to illustrate the synthetic value of the reductive debromination. Kendall, J. T. *J. Labelled Cpd. Radiopharm.* **1999**, *42*, 477. (b) Allred, E. L.; Beck, B. R.; Voorhees, K. J. *J. Org. Chem.* **1974**, *39*, 1426.

(21) (a) Khurana, J. M.; Maikap, G. C.; Sahoo, P. K. *Synthesis* **1991**, 827 (Debromination at high temperature). (b) Vijayashree, N.; Samuelson, A. G. *Tetrahedron Lett.* **1992**, *33*, 559 (Cu/Cu(II) mediated debromination of activated vicinal dibromides). (c) Fukunaga, K.; Yamaguchi, H. *Synthesis* **1981**, 879 (Debromination of *vic*-dibromides with Na_2S/DMF). (d) Nakayama, J.; Machida, H.; Hishino, M. *Tetrahedron Lett.* **1983**, *24*, 3001 (Debromination of vic-dibromides with $Na_2S/R_3NMe^+Cl^-$).

7.52 (d, $J = 4.8$ Hz), 6.98 (d, $J = 5.1$ Hz, 2H), 3.90 (s, 3H), 2.39 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 164.1, 144.4, 1232.6, 131.6, 130.1, 130.0, 108.4, 53.5, 15.0. HRMS (ES-MS) [$(M+H)^+$]: for $C_9H_9O_2$-SBr 260.5975 found 260.9581.

(*Z*)-Ethyl 2-Bromo-3-(4-bromo-5-phenylthiophen-2-yl)acrylate (Entry 3 in Table 3). ^{1}H NMR ($CDCl_3$): δ 8.31 (s, 1H), 7.69−7.72 (m, 2H), 7.42−7.50 (m, 4H), 4.34 (q, $J = 7.2$ Hz, 2H), 1.38 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 162.8, 143.2, 138.3, 136.5, 133.0, 132.2, 129.0, 128.9, 128.6, 111.4, 108.4, 62.8, 14.2. HRMS (ES-MS) [$(M + H)^+$]: for $C_{15}H_{12}O_2SBr_2$ 414.8997, found 414.9004.

(*E*)-Ethyl 3-(4-Bromothiophen-2-yl)acrylate (Entry 4A in Table 3). ^{1}H NMR ($CDCl_3$): δ 7.65 (d, $J = 15.6$ Hz, 1H), 7.26 (d, $J = 5.2$ Hz, 1H), 6.24 (d, $J = 15.6$ Hz, 1H), 4.26 (q, $J = 7.2$ Hz, 2H), 1.34 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR ($CDCl_3$); δ 166.3, 140.3, 135.5, 132.3, 125.1, 118.4, 110.9, 60.7, 14.2. LRMS (ES-MS) [$(M + H)^+$]: for $C_9H_9O_2SBr$ 261.0, found 261.0.

(*Z*)-Ethyl 2-Bromo-3-(4-bromothiophen-2-yl)acrylate (Entry 4B in Table 3). ^{1}H NMR (CDCl): δ 8.33 (s, 1H), 7.47 (s, 2H), 4.35 (q, $J = 7.2$ Hz, 2H), 1.36 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 162.7, 138.5, 136.2, 132.7, 127.8, 111.8, 110.962.9, 14.2. HRMS (ES-MS) [$(M + H)^+$]: for $C_9H_8O_2SBr_2$ 338.8684, found 338.8691. Anal. Calcd for $C_9H_8Br_2O_2S$: C, 31.79; H, 2.37. Found: C, 32.15; H, 2.15.

(*E*)-Ethyl 3-(4-Phenylthiophen-2-yl)acrylate (Entry 5A in Table 3). ^{1}H NMR ($CDCl_3$): δ 7.79 (d, $J = 15.6$ Hz), 7.33−7.51 (m, 7H), 6.29 (d, $J = 15.6$ Hz, 1H), 4.26 (q, $J = 6.0$ Hz, 2H), 1.35 (t, $J = 6.0$ Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 166.7, 143.2, 140.1, 136.9, 134.9, 129.6, 128.9, 127.4, 126.2, 123.0, 117.3, 60.5, 14.3. LRMS (ES-MS) [$(M + H)^+$]: for $C_{15}H_{14}O_2S$ 259.1, found 259.1.

(*Z*)-Ethyl 2-Bromo-3-(4-phenylthiophen-2-yl)acrylate (Entry 5B in Table 3). ^{1}H NMR ($CDCl_3$): δ 8.47 (s, 1H), 7.82 (d, $J = 1.2$, 1H), 7.70 (s, 1H), 7.57−7.59 (m, 2H), 7.32−7.44 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 163.1, 142.1, 138.2, 134.7, 134.2, 128.9, 127.7, 126.3. 125.9, 110.5, 62.7, 14.2. HRMS (ES-MS) [$(M + H)^+$]: for $C_{15}H_{13}O_2SBr$ 336.9892, found 336.9890.

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Supporting Information Available: Analytical data (^{1}H, and ^{13}C NMR spectra) for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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