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Nitroketene Acetal Chemistry. 3. Facile Synthesis of Nitroacetic Acid Triarylmethyl Ortho Esters from 1,1-Di(methylsulfanyl)-2-nitroethylene

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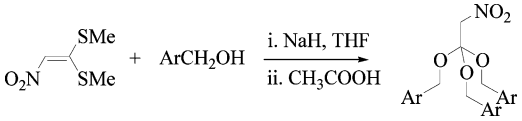
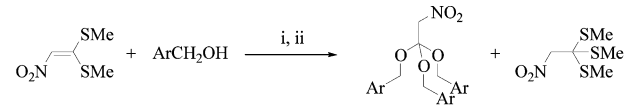


The reaction of 1,1-di(methylsulfanyl)-2-nitroethylene, benzyl alcohols, and sodium hydride furnishes crystalline triarylmethyl ortho esters of nitroacetic acid.

The nitroketene dithioacetals of the type **1** are well-known as two-carbon synthons and for their push−pull electronic nature.[1] The Michael acceptor characteristics of the nitroethylene portion of **1** and the possibility of substitution of the two methylsulfanyl groups with nucleophiles have been well exploited for the synthesis of a variety of heterocycles.[2] Furthermore, the 1,1-di(methylsulfanyl)ethylene moiety in **1** is a latent carboxylic acid and the nitro group is a latent amino group. Thus, the nitroketene dithioacetal **1** can be viewed as glycine equivalent. In continuation of our interest in exploiting multifunctional systems of the type **1** for the synthesis of molecules of diverse structures,[3] we reasoned that sequential attack of oxygen nucleophiles on C-1 of 1,1-di(methylsulfanyl)-2-nitroethylene **1** followed by elimination of the methylsulfanyl groups could lead to ortho esters of nitroacetic acid **3**.

There are several grounds to develop convenient synthesis of ortho esters. The ortho esters are well-known to serve as convenient protecting groups for carboxylic acids since they are stable under basic conditions and are readily hydrolyzed under mild acidic conditions.[4] Not surprisingly, ortho esters found widespread use in synthetic, biological, and commercial applications. Specifically, the ortho esters of nitroacetic acid **3** have been shown to be useful in the fields of adhesive, artificial sweetener, polymer, and liquid crystal chemistry and as vehicles for drug delivery.[5] Furthermore, the nitro group in **3** could serve as a precursor for the nitrile oxide, enroute to 1,3-dipolar cycloaddition reactions.[6]

SCHEME 1[a]



1 **2a-i** **3a-i** **4**

2a, **3a**: Ar = C_6H_5; **2b**, **3b**: Ar = 2-ClC_6H_4; **2c**, **3c**: Ar = 4-ClC_6H_4; **2d**, **3d**: Ar = 4-$CH_3C_6H_4$; **2e**, **3e**: Ar = 4-$CH_3OC_6H_4$; **2f**, **3f**: Ar = 3,4,5-$(CH_3O)_3C_6H_2$; **2g**, **3g**: Ar = 1-$C_{10}H_7$; **2h**, **3h**: Ar = 2-C_4H_3O; **2i**, **3i**: Ar = 2-C_4H_3S.

[a] Reagents and conditions: (i) NaH, dry THF, rt, 6−12 h; (ii) CH_3COOH.

Previously Beuvich and co-workers reported the synthesis of several phenolic ortho esters of nitroacetic acid by the reaction of 1,1-dichloro-2-nitroethylene and phenols in the presence of sodium methoxide in methanol.[7] Similarly, Francotte and co-workers reported the synthesis of the trimethyl ortho ester of nitroacetic acid, 1,1,1-trimethoxy-2-nitroethane from 1,1-dichloro-2-nitroethylene or 1,1,2-trichloro-2-nitroethylene.[8] They have also reported a facile acid-catalyzed synthesis of 3-(nitromethyl)-2,4,10-trioxatricyclo[3.3.1.1^{3,7}]decane from 1,1,1-trimethoxy-2-nitroethane. Essentially following the protocol developed by pioneering studies of ortho ester synthesis by Corey and Raju,[9] recently Fenk[6] developed a four-step route to 4-methyl-1-(nitromethyl)-2,6,7-trioxabicyclo[2.2.2]octane, a nitroacetic acid ortho ester useful in the synthesis of 4,5-dihydroisoxazole derivatives. Thus, there is a continuing interest in the development of new synthetic routes for the stable nitroacetic acid ortho esters. We now report a facile synthesis of hitherto unknown arylmethyl ortho esters of nitroacetic acid **3** starting from 1,1-di(methylsulfanyl)-2-nitroethylene **1** and the arylmethyl alcohols **2** as depicted in Scheme 1.

Reaction of 1,1-di(methylsulfanyl)-2-nitroethylene **1** with 3 equiv of sodium phenylmethanoate in benzyl alcohol at room temperature for 12 h provided crystalline tribenzyl ortho ester **3a** in 30% yield after due workup and purification. The yield increased to 95% when the reaction of **1** was conducted in dry THF using sodium

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TABLE 1. Conversion of Nitroketene Dithioacetal 1 to the Corresponding Ortho Esters 3a−i

entry	benzyl alcohols **2**	ortho esters **3**	yield of **3**, %	yield of **4**, %
1	$C_6H_5CH_2OH$, **2a**	$(C_6H_5CH_2O)_3CCH_2NO_2$, **3a**	95	
2	$2\text{-}ClC_6H_4CH_2OH$, **2b**	$(2\text{-}ClC_6H_4CH_2O)_3CCH_2NO_2$, **3b**	80	15
3	$4\text{-}ClC_6H_4CH_2OH$, **2c**	$(4\text{-}ClC_6H_4CH_2O)_3CCH_2NO_2$, **3c**	90	
4	$4\text{-}CH_3C_6H_4CH_2OH$, **2d**	$(4\text{-}CH_3C_6H_4CH_2O)_3CCH_2NO_2$, **3d**	87	
5	$4\text{-}CH_3OC_6H_4CH_2OH$, **2e**	$(4\text{-}CH_3OC_6H_4CH_2O)_3CCH_2NO_2$, **3e**	90	
6	$3,4,5\text{-}(CH_3O)_3C_6H_2CH_2OH$, **2f**	$\{(3,4,5\text{-}(CH_3O)_3C_6H_2CH_2O\}_3CCH_2NO_2$, **3f**	85	12
7	1-Naphthylmethanol, **2g**	$(1\text{-}C_{10}H_7CH_2O)_3CCH_2NO_2$, **3g**	77	20
8	2-Furylmethanol, **2h**	$(2\text{-}C_4H_3CH_2O_2)_3CCH_2NO_2$, **3h**	80	18
9	2-Thienylmethanol, **2i**	$(2\text{-}C_4H_3SCH_2O)_3CCH_2NO_2$, **3i**	90	

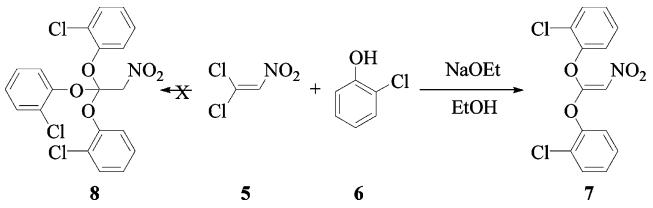
hydride as base. The nitroketene dithioacetal **1** required for the present work was prepared from carbon disulfide, nitromethane, and dimethyl sulfate according to a new and improved procedure (see Experimental Section). The structure of **3a** was confirmed on the basis of spectroscopic (IR, ^{1}H NMR, ^{13}C NMR, DEPT, MS) and analytical data. The tribenzyl ortho ester **3a** displayed characteristic bands at 1551 and 1383 cm^{-1} for the nitro group. The ^{1}H NMR spectrum of **3a** displayed two singlets at 4.78 (6H) and 4.85 (2H) ppm for benzylic and nitromethylenes, respectively. As anticipated, the proton-decoupled ^{13}C NMR spectrum of **3a** displayed six signals, two of which were in the aliphatic region.

To test the generality of the conversion, the nitroketene dithioacetal **1** was subjected to reaction with a variety of benzyl alcohols and sodium hydride in dry THF. Corresponding benzylic ortho esters **3b**−**i** were obtained in good yield (Table 1). The ortho esters **3b**−**i** exhibited analytical and spectral data similar to those of the parent molecule **3a**. In some cases the reactions furnished known trithio ortho ester **4**[10] in minor quantities (Table 1). It is possible that in some cases where the arylmethanoate anion is sluggish to attack **1** in Michael fashion, as in the cases of **2b** and **2f**−**h**, the newly released methylsulfanyl anion competes to furnish **4** in minor amounts.

Further confirmation of the structure of ortho esters **3** came from the analysis of single-crystal X-ray data for nitroacetic acid trifurylmethyl ortho ester **3h**.[11] The X-ray crystal structure shows that, in its solid state, the molecule **3h** stabilizes in a conformation where intramolecular CH−O-type hydrogen bonding interaction between the methylene hydrogen and ether oxygen (259.2 pm) and intermolecular hydrogen bonding interaction between furan hydrogen with the oxygen of the nitro group (258.4 pm) dominate.

The small chain alkyl ortho esters of nitroacetic acid are generally liquids at room temperature and are not very stable. For example, 4-methyl-1-(nitromethyl)-2,6,7-trioxabicyclo[2.2.2]octane was reported to be stable only

SCHEME 2



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

at −20 °C.[6] On the other hand, the benzyl ortho esters **3** are crystalline solids and are stable at room temperature, which makes them amenable to study their physicochemical properties and for use in further transformations.

Beuvich and co-workers reported the formation of corresponding *O*,*O*-acetal **7** instead of the ortho ester **8** on the reaction of 2,2-dichloronitroethylene **5** with 2-chlorophenol **6**, possibly due to steric hindrance to attack by the third 2-chlorophenolate anion (Scheme 2).[7] Interestingly, however, as revealed in Table 1 (entry 2), the reaction of **1** with 2-chlorobenzyl alcohol **2b** furnished corresponding ortho ester **3b** in good yield. Thus, present work shows that the nitroketene-*O*,*O*-acetals are prone to being transformed to more stable ortho esters in the presence of alkoxide anions provided there is no steric resistance to the attack of the third alkoxide anion.

Hydrolysis of ortho esters is one of the well-studied reactions in organic chemistry.[12] We reasoned that because of the presence of the electron-withdrawing nitro group the nitroacetic acid ortho esters **3** are expected to be more stable in acidic conditions compared to corresponding nonactivated ortho esters. In fact, the tribenzylic ortho ester **3a** was stable up to pH 3 for over 3 days and decomposed at pH 2.8 in 30 min, whereas some nonactivated ortho esters were known to hydrolyze at pH 4.75 within a few minutes.[13] Based on this result, we anticipate that the nitroacetic acid ortho esters of type **3** could be used as pro-drugs for anticancerous molecules having a benzyl alcohol moiety, because under hypoxic conditions prevalent in cancerous tissues there is a possibility of reduction of a nitro group to an amino group and on reduction the drug gets released as a result of hydrolysis.

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(11) **X-ray Data for 3h.** X-ray data were collected at 293 K on a CCD diffractometer with graphite monochromated Mo Kα (radiation (λ = 0.7107 **Å**). Structure was solved by direct methods (SIR 92). Refinement was done by full-matrix least-squares procedure on F^2 using SHELXL-97. The non-hydrogen atoms were refined anisotropically whereas hydrogen atoms were refined isotropically. $C_{17}H_{17}NO_8$, MW = 363.32, colorless crystal, triclinic, space group *P*-1. Cell parameters: a = 9.169 (3) **Å**, (α = 92.443 (5) **Å**, b = 9.702 (3) **Å**, (β = 93.616 (5) **Å**, c = 10.523 (4) **Å**, (γ = 112.089 (5) **Å**; V = 863.4 (5) **Å**^{3}; Z = 2, D_c = 1.397 mg m^{-3}, F (000) = 380, (μ = 0.113 mm^{-1}. Total number of I.s. parameters = 235, R_1 = 0.0495 for 1815 $F_o > 2\sigma(F_o)$ and 0.0524 for all 4278 data. wR_2 = 0.2124, GOF = 1.001, restrained GOF = 1.0, for all data (CCDC 250775).

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In conclusion, in this study we have shown that the crystalline tribenzylic nitroacetic acid ortho esters **3** could be prepared conveniently from the readily available nitroketene dithioacetal **1**.

Experimental Section

Preparation of 1,1-Di(methylsulfanyl)-2-nitroethylene (1). To a stirred mixture of nitro methane (10 mL, 1.84 mmol) and carbon disulfide (11.13 mL, 1.84 mmol) in dry methanol (10 mL) under a blanket of dry N_2 at 0 °C was slowly added a solution of potassium hydroxide (23 g, 4.14 mol) in methanol (20 mL) by using a pressure equalizer funnel, and the mixture was vigorously stirred at 0 °C for 3 h. The reddish salt formed in the reaction was filtered and washed with dry methanol (15 mL) followed by dry diethyl ether (15 mL) to furnish 17.6 g of dipotassium 2-nitro-1,1-ethylenedithiolate (45%) as a dry reddish powder. The salt was used for the next step immediately.

To the stirred suspension of the salt (17.6 g, 82.6 mmol) in dry hexanes (50 mL) and dry toluene (5 mL) was added dropwise freshly distilled dimethyl sulfate (10.4 g, 82.6 mmol) in 10 mL of dry toluene through a pressure equalizer funnel at 0 °C during 30 min, and the reaction mixture was vigorously stirred for 2 h at the same temperature to furnish 1,1-di(methylsulfanyl)-2-nitroethylene **1**. The crude product was filtered and recrystallized (ethanol) to get the light yellow crystals (11.58 g, 85%, mp 127 °C, lit.[14] 127 °C). Analytical and spectral data matched well with the authentic commercially available sample.

General Procedure for Preparation of Nitroacetic Acid Ortho Esters. To a stirred and cleaned suspension of NaH (60% suspension in oil; 0.25 gm, 7.2 mmol) in dry THF (5 mL) at 0 °C was added a solution of benzyl alcohols (7.2 mmol) in dry THF (4 mL), and the mixture was vigorously stirred at 0 °C for 30 min. Then a solution of 1,1-di(methylsulfanyl)-2-nitroethylene (400 mg, 2.42 mmol) in dry THF (10 mL) was added dropwise during 30 min. The reaction mixture was then allowed to stir at 0 °C for 90 min to 3 h. After completion of the reaction (TLC), the mixture was carefully acidified with acetic acid up to pH 6.5 followed by dilution with dichloromethane (40 mL). The organic solution was washed with water (3 × 25 mL) and brine (2 × 10 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure resulted in crude ortho esters as solids. In cases where further purification was required to separate ortho esters and thio ortho ester **4**, the crude product were subjected to column chromatography on SiO_2 using increasing amounts of ethyl acetate in hexanes as eluent. Evaporation of the pooled fractions having the required ortho ester resulted in a crystalline product. Analytical samples were obtained by crystallization from DCM/hexanes. Interestingly, all of the orothesters in their pure form exhibited yet to be identified characteristic smells.

1-[1,1-Di(benzyloxy)-2-nitroethoxy]methylbenzene (3a). Following the general procedure described above, reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), benzyl alcohol (786 mg, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 900 mg of 1-[1,1-di(benzyloxy)-2-nitroethoxy]methylbenzene **3a** in 95% yield as colorless crystals: mp 45 °C; R_f 0.68 (80:20 hexanes−EtOAc); IR (KBr), 3035, 2895, 1551, 1237, 1005, 745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.30 (m, 5H), 4.85 (s, 2H), 4.78 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 136.63, 128.47, 127.92, 127.65, 111.36, 75.76, 65.59 ppm. Anal. Calcd for $C_{23}H_{23}NO_5$: C, 70.21; H, 5.89; N, 3.56. Found: C, 70.39; H, 5.87; N, 3.63.

1-Chloro-2-(1,1-di[(2-chlorobenzyl)oxy]-2-nitroethoxymethyl)benzene (3b). Following the general procedure described above the reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), 2-chlorobenzyl alcohol (1.04 g, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 959 mg of 1-chloro-2-(1,1-di[(2-chlorobenzyl)oxy]-2-nitroethoxymethyl)benzene **3b** in 80% yield as colorless crystals: mp 61−63 °C; R_f 0.68 (80:20 hexanes−EtOAc); IR (KBr), 3065, 2987, 2929, 1554, 1222, 1098, 755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.27 (dd, 3H, J = 7.2, 6.6 Hz), 7.31−7.38 (m, 3H) 7.20−7.28 (m, 6H), 4.97 (s, 2H), 4.93 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz),) 134.29, 132.67, 129.23, 129.01(2C), 126.97, 111.71, 75.88, 62.94 ppm. Anal. Calcd for $C_{23}H_{20}NO_5Cl_3$: C, 55.61; H, 4.06; N, 2.82. Found: C, 55.62; H, 4.19; N, 2.74.

1-Chloro-4-(1,1-di[(4-chlorobenzyl)oxy]-2-nitroethoxymethyl)benzene (3c). Following the general procedure described above the reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), 4-chlorobenzyl alcohol (1.04 g, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 1.08 g of 1-chloro-4-(1,1-di[(4-chlorobenzyl)oxy]-2-nitroethoxymethyl)benzene **3c** in 90% yield as colorless crystals after column purification: mp 78−80 °C; R_f 0.73 (80:20 hexanes−EtOAc); IR (KBr), 3097, 2977, 2840, 1590, 1315, 1088, 760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.31 (br d, 3H, J = 8.4 Hz), 7.22 (br d, 3H J = 8.1 Hz), 4.84 (s, 2H), 4.71 (s, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 134.90, 133.90, 128.9, 128.7, 111.39, 76.05, 65.00 ppm. Anal. Calcd for $C_{23}H_{20}NO_5Cl_3$: C, 55.76; H, 4.07; N, 2.82. Found: C, 56.22; H, 4.21; N, 3.45.

1-(1,1-Di[(4-methylbenzyl)oxy]-2-nitroethoxymethyl)-4-methylbenzene (3d). Following the general procedure described above, reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), 4-methylbenzyl alcohol (886 mg, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 915 mg of 1-(1,1-di[(4-methylbenzyl)oxy]-2-nitroethoxymethyl)-4-methylbenzene **3d** in 87% yield after column purification as colorless crystals: mp 88 °C; R_f 0.68 (80:20 hexanes−EtOAc); IR (KBr), 3008, 2957, 2920, 1551, 1315, 1088, 808 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.23 (d, 6H, J = 8.1 Hz), 7.15 (d, 3H, J = 9.0 Hz), 4.83 (s, 2H), 4.73 (s, 6H); 2.34 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 137.70, 133.71, 129.17, 127.86, 111.29, 76.20, 65.51, 21.17 ppm. Anal. Calcd for $C_{26}H_{29}NO_5$: C, 71.70; H, 6.71; N, 3.21. Found: C, 71.02; H, 6.59; N, 3.24.

1-(1,1-Di[(4-methoxybenzyl)oxy]-2-nitroethoxymethyl)-4-methoxybenzene (3e). Following the general procedure described above reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), 4-methoxybenzyl alcohol (1.01 g, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 1.08 g of 1-(1,1-di-[(4-methoxybenzyl)oxy]-2-nitroethoxymethyl)-4-methoxybenzene **3e** in 90% yield as colorless crystals after column purification: mp 44−46 °C; R_f 0.46 (80:20 hexanes−EtOAc); IR (KBr) 3124, 2998, 2959, 1555, 1249, 1046, 822 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.27 (d, 6H, J = 8.7 Hz), 6.87 (d, 6H, J = 8.1 Hz) 4.81(s, 2H), 4.69 (s, 6H), 3.80 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 159.36, 129.40, 128.78, 113.84, 76.12, 65.29, 55.25 ppm. Anal. Calcd for $C_{26}H_{29}NO_8$: C, 64.58; H, 6.04; N, 2.89. Found: C, 64.14; H 5.89; N, 2.80.

1,2,3-Trimethoxy-5-(2-nitro-1,1-di[(3,4,5-trimethoxybenzyl)oxy]ethoxymethyl)benzene (3f). Following the general procedure described above reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), 3,4,5-methoxybenzyl alcohol (1.439 g, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 1.367 g of 1,2,3-trimethoxy-5-(2-nitro-1,1-di[(3,4,5-trimethoxybenzyl)oxy]ethoxymethyl)benzene **3f** in 85% yield as colorless crystal after column purification: mp 103−105 °C; R_f 0.42 (50:50 hexanes−EtOAc); IR (KBr) 2999, 2968, 2942, 2836, 1595, 1550, 1329, 1235, 1096 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 6.56 (s, 6H), 4.88 (s, 2H), 4.74 (s, 6H), 3.83 (s, 27H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 153.69, 138.03, 132.62, 111.80, 105.00, 76.59, 66.19, 61.19, 56.45 ppm. Anal. Calcd for $C_{32}H_{41}NO_{14}$: C, 57.91; H, 6.23; N, 2.11. Found: C, 57.78; H, 6.02; N, 1.81.

5-[1,1-Di(1-naphthylmethoxy)-2-nitroethoxy]methyl-1,4-dihydronaphthalene (3g). Following the general procedure described above the reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), 1-naphthylmethanol (1.119 g, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 1.011 g of 5-[1,1-di(1-naphthylmethoxy)-2-nitroethoxy]methyl-1,4-dihydronaphthalene **3g** in 77% yield after column purification as colorless crystals: mp 127−130 °C; R_f 0.45 (70:30 hexanes−EtOAc); IR (KBr) 3045, 2903, 1553, 1230, 1080, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.00 (d, 3H, J = 9.0 Hz), 7.8−7.9 (m, 6H), 7.3−7.5 (m, 12H), 5.23 (s, 6H), 4.98 (s, 2H) ppm; ^{13}C NMR (75 MHz,

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$CDCl_3$) 133.63, 132.38, 131.51, 128.86, 128.55, 126.37 (2C), 125.87, 125.25, 123.78, 112.13, 76.58, 64.27 ppm. Anal. Calcd for $C_{35}H_{29}NO_5$: C, 77.33; H, 5.38; N, 2.58. Found: C, 77.36; H, 5.19; N, 3.56.

2-[1,1-Di(2-furylmethoxy)-2-nitroethoxy]methylfuran (3h). Following the general procedure described above the reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), furan-2-yl-methanol (713 mg, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 604 mg of 2-[1,1-di(2-furylmethoxy)-2-nitroethoxy]methylfuran **3h** in 80% yield after column purification as colorless crystals: mp 83−85 °C; R_f 0.56 (70:30 hexanes−EtOAc); IR (KBr) 3148, 2962, 2982, 1552, 1383, 1062, 749 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.42 (dd, 3H, J = 1.2 Hz), 6.38 (dd, 3H, J = 3.3 Hz), 6.35 (br d, 3H, J = 3.0 Hz), 4.76 (s, 2H), 4.74 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 150.00, 143.11, 111.10, 110.48, 110.13, 75.88, 57.79 ppm. Anal. Calcd for $C_{17}H_{17}NO_8$: C, 56.20; H, 4.72; N, 3.86. Found: C, 56.51; H, 4.59; N, 4.23.

2-[2-Nitro-1,1-di(2-thienylmethoxy)ethoxy]methylthiophene (3i). Following the general procedure described above the reaction of nitroketene dithioacetal **1** (400 mg, 2.42 mmol), thiophen-2-yl-methanol (828 mg, 7.2 mmol), and sodium hydride (0.25 g, 7.2 mmol) furnished 895 mg of 2-[2-nitro-1,1-di(2-thienylmethoxy)ethoxy]methylthiophene **3i** in 90% yield after column purification as colorless crystals: mp 76 °C; R_f 0.68 (80:20, hexanes−EtOAc); IR (KBr) 3102, 2934, 2880, 1556, 1068, 718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.30 (dd, 3H, J = 5.1, 5.1 Hz), 7.03 (br d, 3H, J = 3.9 Hz), 6.97 (br d, 3H, J = 4.8 Hz), 4.94 (s, 6H), 4.77 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 138.82, 127.12, 126.76, 126.37, 111.20, 76.47, 60.68 ppm. Anal. Calcd for $C_{17}H_{17}NO_5S_3$: C, 49.62; H, 4.16; N, 3.46; S, 23.38. Found: C, 49.45; H, 4.09; N, 3.86; S, 23.63.

1,1,1-Tri(methylsulfanyl)-2-nitroethane (4). R_f 0.75 (80:20, hexanes−EtOAc); IR (Neat) 2988, 2919, 1554, 1370, 960, 652 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 4.72 (s, 2H), 2.29 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 96.18, 80.55, 13.43 ppm.

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Supporting Information Available: ^1H and ^{13}C NMR spectral data for compounds **3a**−**i** and **4** and crystal structure of **3h** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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