Studies on the rearrangement of *ortho*-nitrobenzylidenemalonates and their analogues to 2-aminobenzoate derivatives

Elzbieta Lewandowska, Stefan Kinastowski, and Stanislaw F. Wnuk

Abstract: Reaction of the diethyl 2-nitro-4-(trifluoromethyl)benzylidenemalonate with diethylamine in alcohols resulted in the reduction of the nitro group and the oxidation of the vinylic carbon attached to the phenyl ring. Simultaneous migration of the malonic fragment gave the appropriate 2-amino-4-(trifluoromethyl)benzoate esters. The presence of at least two nitro groups, or one nitro group and trifluoromethyl group on the phenyl ring, attached to the α-carbon and strongly electron withdrawing substituents at the β-carbon (CO_2Et, CN) in *ortho*-nitrobenzylidene systems is necessary for this reductive–oxidative rearrangement to proceed. Reaction of nitrocinnamates with thiols in the presence of triethylamine in tetrahydrofuran gave Michael addition products with different regioselectivity of addition. Ethyl 2-nitrocinnamate undergoes standard β-addition of thiols to a carbon–carbon double bond. However, 2,4-dinitro- and 2,4,6-trinitrocinnamates undergo α-addition of thiols, indicating that the presence of two nitro groups on the phenyl ring can reverse polarity of the carbon–carbon double bond in cinnamate acceptors.

Key words: abnormal Michael reactions, aromatic nitro compounds, benzylidene compounds, rearrangements.

Résumé : La réaction du 2-nitro-4-(trifluorométhyl)benzylidènemalonate d'éthyle avec la diéthylamine dans des alcools conduit à la réduction du groupe nitro et à l'oxydation du carbone vinylique attaché au noyau phényle. La migration simultanée du fragment malonique fournit les esters 2-amino-4-(trifluorométhyl)benzoates appropriés. Pour que ce réarrangement d'oxydoréduction se produise, il est requis d'être en présence d'un système *ortho*-nitrobenzylidène comportant au moins deux groupes nitro ou d'un groupe nitro et d'un groupe trifluorométhyle sur le noyau phényle attaché sur le carbone-α et des substituants fortement électroattracteurs sur le carbone-β (CO_2Et, CN). La réaction des nitrocinnamates avec les thiols en présence de triéthylamine, dans le tétrahydrofurane, conduit à la formation des produits d'addition de Michael avec une régiosélectivité d'addition différente. L'addition de thiols au 2-nitrocinnamate d'éthyle conduit à l'addition β normale sur la double liaison. Toutefois, l'addition de thiols sur les 2,4-dinitro- ou 2,4,6-trinitrocinnamates conduisent à des additions α, ce qui indique que la présence de deux groupes nitro sur le noyau phényle peut inverser la polarité de doubles liaisons carbone–carbone des accepteurs cinnamates.

Mots clés : réactions de Michael anormales, composés nitro aromatiques, composés benzylidènes, réarrangements.

[Traduit par la Rédaction]

Introduction

In previous work, we found that treatment of diethyl 2,4-dinitrobenzylidenemalonate (**1a**) with diethylamine (DEA) in MeOH did not lead to the expected Michael addition of DEA to the carbon–carbon double bond. Instead it gave the 2-amino-4-nitrobenzoic acid derivative **2a** (1) (Scheme 1). Such an unusual reductive–oxidative rearrangement selectively yields a variety of 2-aminobenzoic acid derivatives of type **2** when different primary or secondary alcohols (1, 2), thiols (3), or amines (1, 2) were used in place of MeOH. The new ester, thioester, or amide bond is formed at position 1, and a new ether, thioether, or amine bond is formed at the *C*-malonate carbon.

Such a skeletal rearrangement was also effective for heterocyclic π-deficient analogues in which the electron-withdrawing role of the second nitro group on the phenyl ring was replaced by a sp^2-hybridized nitrogen atom in the ring. Thus, nitropyridylidenemalonate 1-oxides bearing nitro and alkenyl substituents in the *ortho* position to each other (e.g., **3**; Scheme 2) underwent rearrangement to the amino-substituted pyridinecarboxylate derivatives (e.g., **4**) (4).

Synthetic methods involving neighboring group interaction in *ortho*-substituted nitrobenzene derivatives have been reviewed (5, 6), and new examples continue to attract interest (7). Such redox processes, which usually involve an intramolecular aldol condensation of the *ortho* substituent with the nitro group acting as the electrophilic center, have been used to synthesize a variety of heterocyclic compounds. These reactions typically occur under basic conditions with or without external reductive reagents and frequently involve thermal transformations (5).

Photochemically induced transfer of oxygen from a nitro group to an *ortho* substituent of nitrobenzene derivatives is

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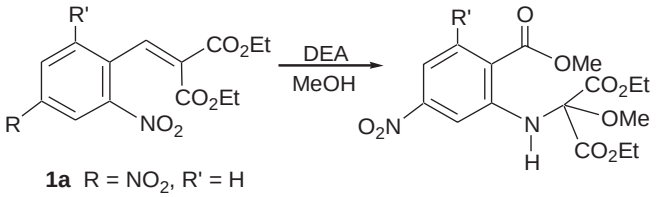
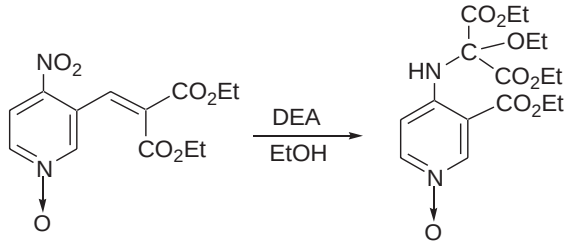
Scheme 1.



1a R = NO_2, R' = H
1b R = R' = NO_2
1c R = R' = H

2a R' = H
2b R' = NO_2

Scheme 2.



3 **4**

also well known and generates uncyclized nitroso products (5). The latter transformations have been elaborated to employ the *ortho*-nitrophenyl group as a photoremovable protective group for aldehydes and ketones (8) as well as phosphate esters of adenine nucleotides (9). The recent theoretical analysis for the isomerization of 2-nitrotoluene to 2-nitrosobenzyl alcohol is in good qualitative agreement with the available experimental results for the thermal and photoinduced rearrangement of *ortho*-nitrobenzyl compounds (9*c*).

To the best of our knowledge, the transformation of α-phenyl-2-nitrocinnamonitrile to *N*-benzoylanthranilic acid in aqueous–ethanolic alkali (10) is the only analogous example to our rearrangement that exists in the literature. Loudon and Tennant (11) suggested that the possible intermediates in this transformation involved addition of hydroxide ions to the carbon–carbon double bond, followed by an intramolecular aldol-type condensation in which the nitro group provides electrophilic center. We now report selected experiments on the one-step rearrangement of *ortho*-nitrobenzylidenemalonates and their analogues to various 2-aminobenzoic acid derivatives. The scope, limitation, and tentative mechanism of the rearrangement are also presented.

Results and discussion

Effect of the substituted aromatic ring

For the series of nitrobenzylidenemalonates **1a**–**c** reactivity toward rearrangement increased with increasing number of nitro groups on the aromatic ring. Thus, diethyl 2,4-dinitrobenzylidenemalonate (**1a**) undergoes the rearrangement in most cases (1), whereas the 2,4,6-trinitro analogue **1b** rearranges in all cases under the mildest conditions (2, 3). In contrast, diethyl 2-nitrobenzylidenemalonate (**1c**) does not rearrange and forms the stable β-carbonyl Michael adducts of type **9** (R, R′ = H) with amines (1), alkoxides (1), or thiolates (3).

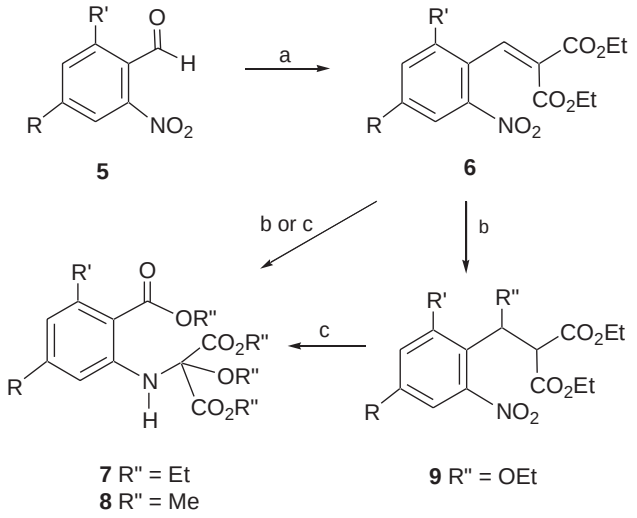
The electron-withdrawing groups influence the rearrangement by (*i*) increasing the acidicity of an α-carbon attached to the aromatic ring, and (*ii*) controlling the oxidative potential of the *ortho*-nitro group. The relative acidities, rates of proton abstraction, and carbanion protonation of 4-nitro-, 2,4-dinitro-, and 2,4,6-trinitrotoluenes in methanolic DMSO have been examined (12). The kinetic ratio for proton abstraction from 2,4-dinitro- and 4-nitrotoluene is 230:1 in DMSO–MeOH (98:2), whereas the ratio for 2,4,6-trinitro- and 2,4-dinitrotoluene is about 100:1 in DMSO–MeOH (60:40). Thus, an increase in kinetic acidity resulting from the introduction of two *ortho*-nitro groups into 4-nitrotoluene is of the order of 2.3×10^4. The corresponding thermodynamic acidities expressed as pK_a values were found to depend strongly on DMSO concentration and are 12.1, 16.6, and 25.7 for 2,4,6-trinitro-, 2,4-dinitro-, and 4-nitrotoluene, respectively (12).

The number of nitro groups also effects the oxidative-reductive properties of these compounds. Bock and Lechner-Knoblauch (13) showed that 1,3,5-trinitrobenzene has the smallest potential for the reduction of the first nitro group (−0.51 V) whereas the reduction potentials of 1,3-dinitrobenzene and nitrobenzene are −0.82 and –1.10 V, respectively. Thus, increasing the number of the nitro groups on the phenyl ring facilitates both formation of the carbanion at the α-carbon (and its subsequent oxidation) and the reduction of first nitro group.

To further study effect of phenyl ring substituents on the rearrangement, 2,6-dinitro- (**6a**), 2-nitro-4-(trifluoromethyl)- (**6b**), and 2-chloro-6-nitrobenzylidenemalonates (**6c**) were prepared in a Knoevenagel condensation ($TiCl_4$–pyridine) (14) between the corresponding aldehydes (**5**) and diethyl malonate (Scheme 3). Reduction of commercially available 2-nitro-4-(trifluoromethyl)benzonitrile with diisobutylaluminum hydride (DIBALH) afforded aldehyde **5b** in 56% yield. This is a substantial improvement on a previously reported synthesis of **5b** when different synthetic approach was used (15). Compound **6a** rearranged under the influence of DEA in ethanol to give **7a** (86%) after 5 days (the rearrangement of **1a** took only a few hours to afford **2a** in 84% yield (1)). It seems that a second nitro group in the *ortho* position in **6a** has some steric influence on the rate of rearrangement.

The 2-nitro-4-trifluoromethyl analog (**6b**) produced under the typical conditions (DEA–EtOH, 24 h at ambient temperature) a stable adduct via ethanol addition to a double bond (**9b**, 51%), plus other by-products including unchanged **6b** and rearranged **7b**. However, prolonged reaction time and elevated temperature (~60°C) led to the expected rearranged product **7b** in 39% yield. Analogous treatment of **6b** with DEA in MeOH gave the rearranged product **8b** (58%) with concomitant transesterification of the malonic moiety. Replacement of the one nitro group by a chloro substituent prevent the rearrangement. Thus, reaction of 2-chloro-6-nitrobenzylidene (**6c**) with DEA–EtOH or amines (DEA, piperidine, or pyrrolidine) under typical conditions resulted in the recovery of **6c**. These results indicate that two strongly electron-withdrawing groups (EWG) must be present in the benzene ring. The data are supported by examination of the Hammett σ values (16) ($\sigma_{NO_2} > \sigma_{CF_3} > \sigma_{Cl}$),

Scheme 3. Reagents and conditions: (*a*) $TiCl_4$/pyridine/THF; (*b*) DEA/EtOH/~25°C; (*c*) DEA/EtOH or MeOH/~55°C.



Series: **a** R = H, R' = NO_2
b R = CF_3, R' = H
c R = H, R' = Cl

which reflect the interaction of the substituents with the reaction site by a combination of resonance and field effects.

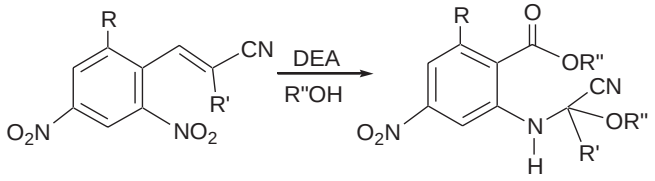
Effect of the substituents on the vinylic carbons

Substituents with strong electron-acceptor properties (CO_2Et, CN) at the β-carbon in *ortho*-nitrobenzylidene substrates also facilitate this rearrangement. Thus, reaction of ethyl α-cyano-2,4,6-trinitrocinnamate (**10**) (17) with DEA–EtOH gave the rearranged product **12** in 66% yield (Scheme 4). 2,4-Dinitrobenzylidenemalononitrile (**11**) rearranges in DEA–EtOH to yield ethyl 2-[*N*-(dicyano)(ethoxy)-methyl]amino-4-nitrobenzoate (**13a**) (56%) in addition to ethyl 2-amino-4-nitrobenzoate (21%). Treatment of **11** with DEA–MeOH gave the methyl ester **13b**.

Ethyl 2,4-dinitrocinnamate (**15a**), which bears only one EWG at the β-carbon, does not undergo this rearrangement (1). The rearrangement also failed with ethyl 2,4,6-trinitrocinnamate (**14**), despite the fact that the aromatic fragment is identical to the most reactive analogue **1b**. This indicated that the number of nitro groups on the phenyl ring, although a significant factor, is not the only force driving this rearrangement.

Interestingly, nitrocinnamates **14** and **15a**,**b** react with ethanethiol in THF in the presence of a catalytic amount of triethylamine (TEA) to give products **16** and **17a**,**b**. Mass spectra of **16** and **17a**,**b**, in addition to the molecular ions, showed peaks for the ions at *m*/*z* (%) 147 (45), 147 (61), and 133 (100) for **16**, **17a**, and **17b**, respectively. Their elemental compositions $C_6H_{11}O_2S$ $[(C_2H_5SCHCO_2C_2H_5)^+]$ for **16** and **17a** and $C_5H_9O_2S$ $[(C_2H_5SCHCO_2CH_3)^+]$ for **17b** were determined by HR-MS. These compounds are formed by the α-addition of the thiol to the α,β-unsaturated carbonyl compounds, a process that is in contrast to the usually observed

Scheme 4.



10 R = NO_2, R' = CO_2Et
11 R = H, R' = CN
12 R = NO_2, R' = CO_2Et, R" = Et
13a R = H, R' = CN, R" = Et
13b R = H, R' = CN, R" = Me

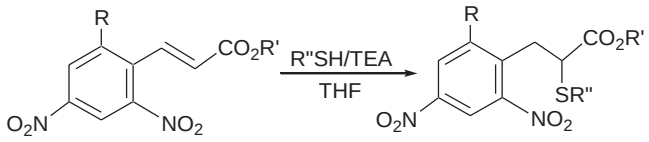
β-addition to the carbonyl activated double bond (Michael addition) (18) including cinnamates (19) (Scheme 5). Reaction of **15a** with propanethiol also gave α-addition product **17c** whose structure was confirmed with 2D-NMR experiments. Thus, the heteronuclear multiple bond coherence (HMBC) spectrum showed that aromatic carbons (C6 (135.4) and C1 (140.5)) had a strong coupling to the diastereotopic CH_2 protons at 3.58 and 3.41, whereas no correlation to CH proton at 3.63 was observed. Conversely, the carbonyl carbon at 171.9 shows correlation to the CH proton at 3.63 and only to the one diastereotopic proton at 3.41.

Ethyl 2-nitrocinnamate does not react with propanethiol under similar conditions (TEA–THF). However, treatment of ethyl 2-nitrocinnamate with sodium propanethiolate in EtOH gave the standard β-addition product **18** (Scheme 6). These results indicate that two nitro groups on the phenyl ring reverse polarity of the carbon–carbon double bond in cinnamate acceptors and redirect the regioselectivity of nucleophile addition from the classical β-addition to an abnormal α-addition. Such regioselectivity is controlled by the resonance effect of the nitro groups on the phenyl ring, as opposed to the carboxylate function. Recently, Trost and Dake (20*a*) reported that phosphine-catalyzed reaction of nitrogen nucleophiles with 2-alkynoates also gave α-addition product. Other examples (18*a*) include α-addition of dimethylamine or methanol to methyl 3,3-di(trifluoromethyl)acrylate (20*b*).

Spectral support for the assumption that Michael addition may occur at either the α or β carbon depending on the carbon–carbon double bond polarization was found by comparing the absorption band of the stretching vibration of the double bond in IR spectra of **1a**–**c** (3) and nitrocinnamates. Thus, 2-nitro derivative **1c** displays a medium absorption band at 1641 cm^{-1} (and shows β-addition), whereas the 2,4-dinitro analogue **1a** has only a very weak band at 1642 cm^{-1}. On the other hand, the latter compound shows an active band at 1637 cm^{-1} in Raman spectrum, which points to a symmetrical distribution of π-electron charge density in the carbon–carbon double bond (21). The introduction of the third nitro group resulted in the appearance of a weak absorption band at 1635 cm^{-1} in IR spectrum of **1b**. Analogously, in the cinnamate series 2,4,6-trinitro **14** [1630 cm^{-1} (weak)] and 2,4-dinitro **15a** [1628 cm^{-1} (very weak)] show α-addition, whereas ethyl 2-nitrocinnamate [1634 cm^{-1} (weak to medium)] and ethyl cinnamate [1634 cm^{-1} (medium to strong)] show the β-addition.

The free rotation of the substituents at β-carbon and steric factors seems also to be a factor in rearrangement. Thus,

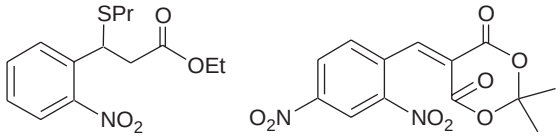
Scheme 5.



14 R = NO_2, R' = Et
15a R = H, R' = Et
15b R' = H, R' = Me

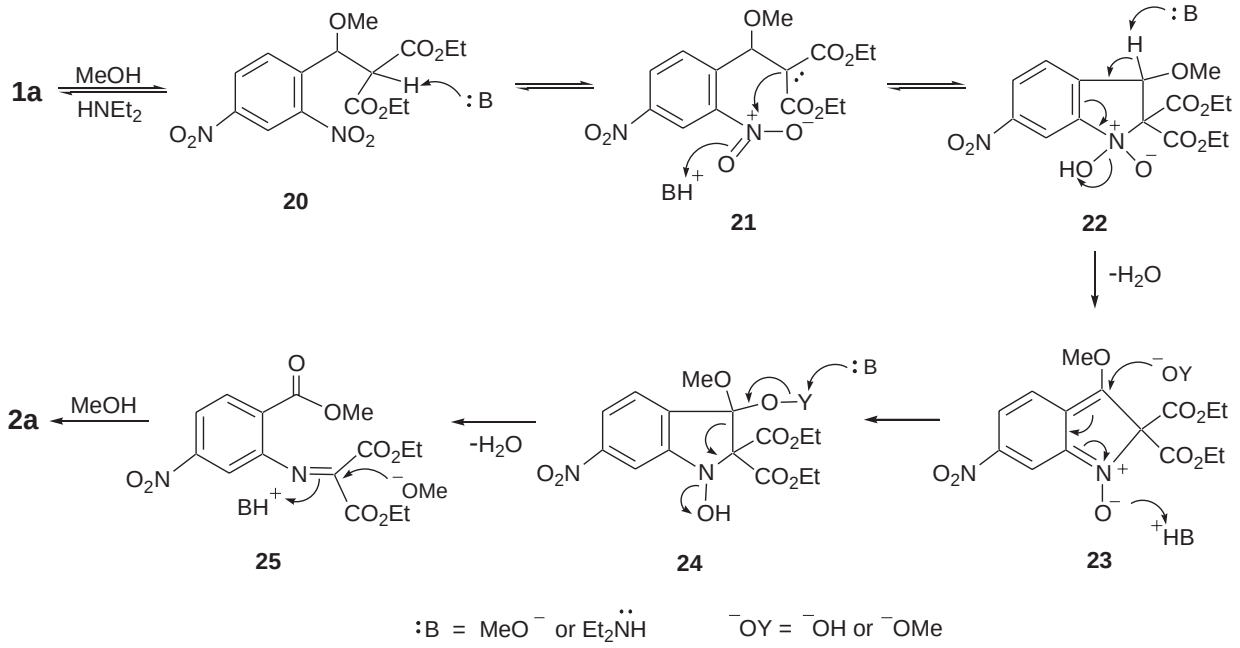
16 R = NO_2, R' = Et, R" = Et
17a R = H, R' = Et, R" = Et
17b R = H, R' = Me, R" = Et
17c R = H, R' = Et, R" = Pr

Scheme 6.



18 **19**

Scheme 7.



$:B = MeO^-$ or $Et_2\ddot{N}H$ $\quad$ $^-OY = {}^-OH$ or ^-OMe

2,4-dinitrobenzylidene derivative of Meldrum's acid **19** did not yield the rearranged product under standard condition (DEA–EtOH).

Tentative mechanism

The intramolecular nature of this rearrangement was previously proven in experiments using isotopically labelled dimethyl-d_6 malonate and dimethyl-d_6 2,4-dinitrobenzylidenemalonate (1). The possible mechanism might involve the following sequence of steps: (*i*) a classical Michael addition of the alcohol molecule to a π-electron deficient carbon–carbon double bond in **1a** to give **20**; (*ii*) an aldol condensation between carbanion **21** and nitro group to yield the cyclic intermediate **22**; (*iii*) redox processes involving the quinonoid intermediate **23** followed by addition of a second alcohol (or water) molecule that results in regeneration of aromaticity; (*iv*) nucleophilic ring opening of **24** and simultaneous migration of the malonic fragment, which leads directly to the formation of the highly conjugated ester at position 1 and Schiff base at position 2; and (*v*) addition of alcohol to the resulting electron-deficient ketimin of mesoxalic ester **25** at position 2 gives the rearranged product **2a** (Scheme 7). Ketimin **25** would be expected to undergo addition quite readily owing the presence of two EWG at the *C*-malonate carbon in addition to the regular polarization of carbon–nitrogen double bond. A similar mechanism for the conversion of α-phenyl-2-nitrocinnamonitrile to *N*-benzoylanthranilic acid has been suggested (11) (vide supra). In our previous mechanism direct transfer of oxygen from a nitro group to an *ortho*-benzylic position was proposed (1). However, such direct transfers are normally induced photochemically rather than thermally (e.g. in the 2-nitrobenzaldehyde into 2-nitrosobenzoic acid and related rearrangements) (**5b**).

In conclusion, an unusual rearrangement of *ortho*-nitrobenzylidenemalonates (e.g., **1a**,**b** or **6**) and their analogues (e.g., **10** or **11**) in the presence of diethylamine in alcohols produces a variety of 2-aminobenzoate ester derivatives (e.g., **2**, **7**, **8**, **12**, or **13**). The presence of at least two nitro groups, or one nitro group and trifluoromethyl group, on the phenyl ring together with strongly electron-withdrawing substituents at the β-carbon (CO_2Et, CN) in *ortho*-nitrobenzylidene systems, appears to be necessary for this reductive–oxidative rearrangement to proceed. Reaction of nitrocinnamates with thiols in the presence of TEA in THF gave Michael addition products with different regioselectivity of addition. Ethyl 2-nitrocinnamate undergoes the standard β-addition of thiols to the carbon–carbon double bond. However 2,4-dinitro- (**15**) and 2,4,6-trinitrocinnamates

(**14**) undergo abnormal Michael-type α-addition of thiols indicating that the presence of two nitro groups on the phenyl ring can reverse polarity of the carbon–carbon double bond in cinnamate acceptors.

Experimental

Uncorrected melting points were determined with a capillary apparatus. UV spectra were measured with solutions in MeOH. ^{1}H (200 or 400 MHz), ^{13}C (50 or 100 MHz), and ^{19}F (376.5 MHz ($CFCl_3$)) NMR spectra were determined with solutions in $CDCl_3$ unless otherwise specified. Mass spectra (MS and HR-MS) were obtained with electron impact (EI, 20 eV) or atmospheric pressure chemical ionization (APCI) techniques. Merck kieselgel 60-F_{254} sheets were used for TLC and products were detected with 254 nm light. Merck kieselgel 60 (230–400 mesh) was used for column chromatography. Elemental analyses were determined at microanalytical laboratories at Adam Mickiewicz University, Poznan, Poland or Galbraith Laboratories, Knoxville, TN. Reagent grade chemicals were used, and solvents were dried by reflux over and distillation from CaH_2 (except THF–potassium) under argon.

2-Nitro-4-(trifluoromethyl)benzaldehyde (5b)

DIBALH (0.9 mL, 0.71 g, 5 mmol) was added dropwise via syringe to a stirred solution of 2-nitro-4-(trifluoromethyl)benzonitrile (1.08 g, 5 mmol) in dried benzene (20 mL) under N_2 at ambient temperature. After 2 h, reaction mixture was cooled down (ice bath) and 1 M H_2SO_4 (~5 mL) was slowly added. The organic layer was washed ($NaHCO_3$–H_2O, brine), dried ($MgSO_4$) and volatiles were evaporated. Column chromatography (5 → 15% EtOAc–hexane) gave **5b** (0.61 g, 56%); mp 42°C (lit. (15) mp 35°C) with data as reported (15).

Diethyl 2,6-dinitrobenzylidenemalonate (6a)

Procedure A

Titanium(IV) chloride (1.1 mL, 10 mmol) in carbon tetrachloride (2.5 mL) was added dropwise to THF (40 mL) and the mixture was cooled to ~5°C. After 15 min 2,6-dinitrobenzaldehyde (0.98 g, 5 mmol) in THF (5 mL) and diethyl malonate (0.76 mL, 0.80 g, 5 mmol) were added dropwise with stirring. Pyridine (1.6 mL, 20 mmol) in THF (5 mL) was then added dropwise over 20 min. After 24 h, water (8 mL) and diethyl ether (8 mL) were added, the organic layer was separated, and the aqueous layer extracted with ether. The combined ether solution was washed with brine, $NaHCO_3$–H_2O and brine, dried ($MgSO_4$), and concentrated. The precipitate formed on cooling was filtered and recrystallized (EtOH) to give **6a** (1.2 g, 71%); mp 56–57°C. IR ($CHCl_3$) (cm^{-1}): 1720 (C=O). ^{1}H NMR δ: 1.02 and 1.37 (2t, J = 7.4 Hz, 6H, $2CH_3$), 3.98 and 4.34 (2q, J = 7.4 Hz, 4H, $2CH_2$), 7.75 (t, J = 8.3 Hz, 1H, H_{Ar}), 8.10–8.37 (m, 3H, H_{Ar}, CH). EI-MS *m/z*: 338 (5, M^+). Anal. calcd. for $C_{14}H_{14}N_2O_8$: C 49.71, H 4.17, N 8.28; found: C 49.74, H 3.83, N 8.29.

Diethyl 2-nitro-4-(trifluoromethyl)benzylidenemalonate (6b)

Treatment of 2-nitro-4-(trifluoromethyl)benzaldehyde (**5b**; 0.9 g, 4.1 mmol) with diethyl malonate by procedure A gave **6b** (1.2 g, 81%); mp 72°C (EtOH). IR ($CHCl_3$) (cm^{-1}): 1733 (C=O), 1628 (C=C). ^{1}H NMR δ: 1.08 (t, J = 7.1 Hz, 3H, CH_3), 1.38 (t, J = 7.1 Hz, 3H, CH_3), 4.12 (q, J = 7.1 Hz, 2H, CH_2), 4.37 (q, J = 7.1 Hz, 2H, CH_2), 7.61 (d, J = 8.0 Hz, 1H, H_{Ar}), 7.92 (d, J = 7.1 Hz, 1H, H_{Ar}), 8.19 (s, 1H, H_{Ar}), 8.50 (s, 1H, CH). ^{13}C NMR δ: 14.1, 14.5, 62.2, 62.7, 122.7 (q, ^3J = 3.7 Hz), 122.9 (q, ^1J = 273.1 Hz), 130.6 (q, ^3J = 3.3 Hz), 130.8, 131.6, 133.0 (q, ^2J = 34.6 Hz), 134.5, 163.4, 164.6. ^{19}F NMR δ: −63.49 (s). APCI-MS *m/z*: 362 (100, $[M + H]^+$). Anal. calcd. for $C_{15}H_{14}F_3NO_6$: C 49.87, H 3.91, N 3.88; found: C 49.84, H 3.95, N 3.78.

Diethyl 2-chloro-6-nitrobenzylidenemalonate (6c)

The 2-chloro-6-nitrobenzaldehyde (0.93 g, 5 mmol) was treated with diethyl malonate by procedure A to give **6c** (1.3 g, 79%); mp 53°C (EtOH). IR ($CHCl_3$) (cm^{-1}): 1720 (C=O). ^{1}H NMR δ: 1.01 and 1.37 (2t, J = 7.2 Hz, 6H, $2CH_3$), 4.02 and 4.35 (2q, J = 7.2 Hz, 4H, $2CH_2$), 7.43–8.15 (m, 4H, H_{Ar}, CH). EI-MS *m/z*: 329 (1, $M^+(^{37}Cl)$), 327 (3, $M^+(^{35}Cl)$), 292 (100, $[M - Cl]^+$). Anal. calcd. for $C_{14}H_{14}ClNO_6$: C 51.31, H 4.31, N 4.27; found: C 51.30, H 4.28, N 4.27.

Ethyl 2-(*N*-(ethoxy)(diethoxycarbonyl)methyl)amino-6-nitrobenzoate (7a)

Procedure B

DEA (0.2mL, 2.0 mmol) was added to a solution of diethyl 2,6-dinitrobenzylidenemalonate (**6a**; 338 mg, 1 mmol) in EtOH (8 mL) and stirring was continued at ambient temperature for 5 days. The resulting mixture was evaporated and the residue was partitioned (EtOAc, diluted with HCl–H_2O). The organic layer was washed ($NaHCO_3$–H_2O, brine), dried ($MgSO_4$), and evaporated to dryness. Column chromatography (CH_3Cl–CCl_4–EtOAc, 10:5:1) gave **7a** (354 mg, 86%); mp 85°C (EtOH). IR ($CHCl_3$) (cm^{-1}): 3300 (NH), 1720 (C=O). ^{1}H NMR δ: 1.18–1.27 (m, 9H, $3CH_3$), 1.34 (t, J = 7.1 Hz, 3H, CH_3), 3.48 (q, J = 7.1 Hz, 2H, CH_2), 4.22–4.44 (m, 6H, $3CH_2$), 7.14 (dd, J = 7.0, 1.8 Hz, 1H, H_{Ar}), 7.30–7.42 (m, 2H, H_{Ar}), 8.27 (br s, 1H, NH). EI-MS *m/z*: 412 (3, M^+), 265 (100). Anal. calcd. for $C_{18}H_{24}N_2O_9$: C 52.42, H 5.87, N 6.86; found: C 52.38, H 5.82, N 6.86.

Ethyl 2-(*N*-(ethoxy)(diethoxycarbonyl)methyl)amino-4-(trifluoromethyl)benzoate (7b)

Treatment of **6b** (180 mg, 0.5 mmol) by procedure B (~60°C, 24 h) and column chromatography (4 → 15% EtOAc–hexane) gave crude **7b** (~115 mg; purity ~75% (^{1}H NMR) contaminated by **6b** and **9b**). This material was column chromatographed again to give **7b** (85mg, 39%) as a solidified oil. IR ($CHCl_3$) (cm^{-1}): 3300 (NH), 1752, 1739, 1697 (C=O). ^{1}H NMR δ: 1.23 (t, J = 7.2 Hz, 3H, CH_3), 1.25 (t, J = 7.1 Hz, 6H, $2CH_3$), 1.44 (t, J = 7.1 Hz, 3H, CH_3), 3.50 (q, J = 7.1 Hz, 2H, CH_2), 4.27–4.35 (m, 4H, $2CH_2$), 4.43 (q, J = 7.1 Hz, 2H, CH_2), 7.01 (d, J = 8.3 Hz, 1H, H_{Ar}), 7.49 (s, 1H, H_{Ar}), 8.09 (d, J = 8.3 Hz, 1H, H_{Ar}), 9.68 (s, 1H, NH). ^{13}C NMR δ: 14.3 (2C), 14.7, 15.3, 59.7, 61.8, 63.5 (2C), 87.9, 111.9, 114.3, 115.8, 123.9 (q, ^1J = 273.0 Hz),

132.8, 135.9 (q, ^2J = 32.3 Hz), 146.8, 167.6 (2C), 167.6. ^{19}F NMR δ: −64.25 (s). APCI-MS *m/z*: 390 (100, [M + H – EtOH]$^+$). Anal. calcd. for $C_{19}H_{24}F_3NO_7$: C 52.41, H 5.56, N 3.22; found: C 52.62, H 5.41, N 3.33.

Methyl 2-(*N*-(methoxy)(dimethoxycarbonyl)methyl)-amino-4-(trifluoromethyl)benzoate (8b)

Treatment of **6b** (180 mg, 0.5 mmol) by procedure B (~50°C, 24 h; MeOH was used instead of EtOH) and column chromatography (4 → 20% EtOAc–hexane) gave **8b** (110 mg, 58%); mp 128–130°C (MeOH). IR ($CHCl_3$) (cm^{-1}): 3300 (NH), 1740, 1698 (C=O). ^{1}H NMR δ: 3.29 (s, 3H, CH_3), 3.86 (s, 6H, $2CH_3$), 3.98 (s, 3H, CH_3), 7.04 (d, J = 8.1 Hz, 1H, H_{Ar}), 7.34 (s, 1H, H_{Ar}), 8.10 (d, J = 8.2 Hz, 1H, H_{Ar}), 9.68 (s, 1H, NH). ^{13}C NMR δ: 51.5, 52.9, 54.3 (2C), 88.5, 111.4, 114.8, 115.7, 123.8 (q, ^1J = 273.2 Hz), 132.8, 136.3 (q, ^2J = 32.5 Hz), 146.6, 167.2 (2C), 168.1. ^{19}F NMR δ: −64.17 (s). APCI-MS *m/z*: 348 (100, [M + H – MeOH]$^+$). Anal. calcd. for $C_{15}H_{16}F_3NO_7$: C 47.50, H 4.25, N 3.69; found: C 47.63, H 4.32, N 3.62.

Diethyl 2-ethoxy-2-(2-nitro-4-(trifluoromethyl)phenyl)-ethane-1,1-dicarboxylate (9b)

DEA (0.06 mL, 0.6 mmol) was added to a solution **6b** (108 mg, 0.3 mmol) in EtOH (3 mL) and stirring was continued for 24 h at ambient temperature and then at ~35°C for 6 h. Evaporation, work-up (as described in procedure B), and column chromatography (5 → 15% EtOAc–hexane) gave **9b** (62 mg, 51%) as a first eluting product followed by recovered **6b** and **7b**. Compound **9b**: IR ($CHCl_3$) (cm^{-1}): 1751, 1733 (C=O). ^{1}H NMR δ: 1.15, 1.16, 1.30 (3t, J = 7.1 Hz, 9H, $3CH_3$), 3.38–3.59 (m, 2H, CH_2), 3.81 (d, J = 8.3 Hz, 1H, CH), 4.08 (q, J = 7.2 Hz, 2H, CH_2), 4.23–4.31 (m, 2H, CH_2), 5.68 (d, J = 8.3 Hz, 1H, CH), 7.90 (d, J = 8.2 Hz, 1H, H_{Ar}), 7.97 (d, J = 8.2 Hz, 1H, H_{Ar}), 8.17 (s, 1H, H_{Ar}). ^{13}C NMR δ: 14.2, 14.5, 15.4, 59.7, 62.1, 62.3, 66.4, 74.3, 122.0 (q, ^3J = 3.6 Hz), 123.0 (q, ^1J = 272.8 Hz), 129.9 (q, ^3J = 3.2 Hz), 131.1, 131.9 (q, ^2J = 34.3 Hz), 139.7, 149.8, 166.7, 166.8. ^{19}F NMR δ: −63.41 (s). APCI-MS *m/z*: 408 (100, [M + H]$^+$). Anal. calcd. for $C_{17}H_{20}F_3NO_7$: C 50.13, H 4.95, N 3.44; found: C 50.19, H 5.18, N 3.46.

Analogous treatment (8 h, ambient temperature) of **6b** (108 mg, 0.3 mmol) with piperidine (0.06 mL, 0.6 mmol) in EtOH (3 mL) also gave **9b** (83 mg, 68%).

Similar treatment (18 h, ambient temperature) of **6b** (0.25 mmol) with DEA (0.5 mmol) or TEA (0.5 mmol) in MeOH (3 mL) gave analogous adduct of MeOH addition to a carbon–carbon double bond (e.g. **9b**, R″ = OMe, 52%; ^{1}H NMR δ: 3.33 (s, 3H, OCH_3), 3.82 (d, J = 7.8 Hz, 1H, CH), 5.59 (d, J = 7.8 Hz, 1H, CH)) in addition to unchanged **6b** and transmethylation by-products.

Treatment (24h, 50°C) of **9b** (41 mg, 0.1 mmol) with DEA (0.02 mL, 0.2 mmol) in EtOH (2 mL) produced **7b** (17 mg, 40%).

Ethyl 2-(*N*-(cyano)(ethoxy)(ethoxycarbonyl)methyl)-amino-4,6-dinitrobenzoate (12)

Procedure C

Ethyl α-cyano-2,4,6-trinitrocinnamate (17) (**10**; 0.168 g, 0.5 mmol) was dissolved in EtOH (4 mL) and DEA (0.1 mL, 1 mmol) was added at ambient temperature. The mixture was allowed to stand for 6 h and then evaporated to dryness under vacum. The residue was chromatographed (CCl_4–$CHCl_3$–Me_2CO, 10:5:1) and crystallized (EtOH) to give **12** (0.135 g, 66%) as a yellow crystals; mp 120–121°C. UV–vis (MeOH) λ (nm) (ε (M^{-1} cm^{-1})): 367 (3500). IR (KBr) (cm^{-1}): 3100 (NH), 2240 (CN), 1730, 1690 (C=O). ^{1}H NMR δ: 1.20–1.65 (m, 9H, $3CH_3$), 4.00–4.60 (m, 6H, $3CH_2$), 8.45 (d, J = 2.1 Hz, 1H, H_{Ar}), 9.61 (d, J = 2.1 Hz, 1H, H_{Ar}), 10.20 (s, 1H, NH). ^{13}C NMR δ: 13.4, 13.9, 62.9, 64.5, 83.2, 113.4, 114.5, 119.5, 124.5, 138.5, 154.7, 159.6, 163.2. EI-MS *m/z*: 410 (1, M$^+$), 383 (5), 236 (100). Anal. calcd. for $C_{16}H_{18}N_4O_9$: C 46.83, H 4.42, N 13.65; found: C 46.76, H 4.40, N 13.71.

Ethyl 2-(*N*-(dicyano)(ethoxy)methyl))amino-4-nitro-benzoate (13a)

Treatment (18 h) of 2,4-dinitrobenzylidenemalononitrile (17) (**11**; 0.122 g, 0.5 mmol) by procedure C (column chromatography: CCl_4–$CHCl_3$–Me_2CO, 60:10:1) gave ethyl 2-amino-4-nitrobenzoate (22 mg, 21%; mp 90–91°C (lit. (22) mp 89–91°C)) and **13a** (89 mg, 56%) as a second eluting compound; mp 63°C (EtOH). UV–vis (MeOH) λ (nm) (ε (M^{-1} cm^{-1})): 327 nm (2750). IR ($CHCl_3$) (cm^{-1}): 3270 (NH), 2270 (CN), 1720 (C=O). ^{1}H NMR δ: 1.31–1.56 (m, 6H, $2CH_3$), 4.25–4.54 (m, 4H, $2CH_2$), 7.75–8.15 (m, 3H, H_{Ar}), 9.33 (s, 1H, NH). EI-MS *m/z*: 291 (16, [M – HCN]$^+$), 263 (21), 218 (100). Anal. calcd. for $C_{14}H_{14}N_4O_5$: C 52.83, H 4.40, N 17.65; found: C 52.78, H 4.43, N 17.60.

Methyl 2-(*N*-(dicyano)(methoxy)methyl)amino-4-nitro-benzoate (13b)

Treatment of **11** (17) (0.122 mg, 0.5 mmol) by procedure C (18 h, MeOH was used instead of EtOH) and purification (as described for **13a**) gave methyl 2-amino-4-nitrobenzoate (22 mg, 23%; mp 158°C (lit. (23) 154–156°C)) and **13b** (86 mg, 59%; mp 82°C (MeOH)). IR ($CHCl_3$) (cm^{-1}): 3270 (NH), 2270 (CN), 1720 (C=O). ^{1}H NMR δ: 3.92 (s, 3H, CH_3), 4.08 (s, 3H, CH_3), 7.76–8.25 (m, 3H, H_{Ar}), 9.35 (s, 1H, NH). EI-MS *m/z*: 263 (12, [M – HCN]$^+$), 232 (100). Anal. calcd. for $C_{12}H_{10}N_4O_5$: C 49.66, H 3.47, N 19.31; found: C 49.58, H 3.42, N 19.35.

Ethyl (*E*)-2,4,6-trinitrocinnamate (14)

Procedure D

To a stirred solution of 2,4,6-trinitrobenzaldehyde (24) (0.24g, 1 mmol) in anhydrous acetonitrile (15 mL) (carbethoxymethylene)triphenylphosphorane (0.37g, 1.1 mmol) was added in one portion. The resulting cherry reaction mixture was stirred overnight at ambient temperature and then evaporated. The oily residue was chromatographed on silica gel (MeOH–$CHCl_3$, 1:99) and crystallized from MeOH to give **14** (0.202 g, 65%, two crops); mp 52–53°C. UV–vis (MeOH) λ (nm) (ε (M^{-1} cm^{-1})): 234 (21 800). IR (KBr) (cm^{-1}): 1710 (C=O), 1630w (C=C). ^{1}H NMR δ: 1.35 (t, J = 7.0 Hz, 3H, CH_3), 4.29 (q, J = 7.0 Hz, 2H, CH_2), 6.01 (d, J = 16.5 Hz, 1H, CH), 7.99 (d, J = 16.5 Hz, 1H, CH), 9.00 (s, 2H, H_{Ar}). EI-MS *m/z*: 266 (100, [M – OEt]$^+$). Anal. calcd. for $C_{11}H_9N_3O_8$: C 42.45, H 2.91, N 13.50; found: C 42.51, H 2.88, N 13.42.

Reaction of **14** with DEA in ethanol by procedure C did not afford rearranged product and only unchanged **14** was recovered (~81%).

Ethyl (*E*)-2,4-dinitrocinnamate (15a)

Treatment of 2,4-dinitrobenzaldehyde (0.196 g, 1 mmol) with $Ph_3P{=}CHCO_2Et$ by procedure D gave **15a** (181 mg, 68%); mp 91–92°C (lit. (25) mp 94°C). IR ($CHCl_3$) (cm^{-1}): 1705 (C=O), 1628w (C=C). ^1H NMR δ: 1.27 (t, *J* = 7.0 Hz, 3H, CH_3), 4.31 (q, *J* = 7.0 Hz, 1H, CH_2), 6.46 (d, *J* = 16.8 Hz, 1H, CH), 7.84 (d, *J* = 8.5 Hz, 1H, H_{Ar}), 8.11 (d, *J* = 16.8 Hz, 1H, CH), 8.48 (dd, *J* = 8.5, 2.3 Hz, 1H, H_{Ar}), 8.89 (d, *J* = 2.3 Hz, 1H, H_{Ar}).

As a less polar product *Z*-isomer of **15a** (40 mg, 15%) was eluted from the column (^1H NMR δ: 6.24 (dd, *J* = 11.9, 1.8 Hz, 1H, CH), 7.43 (d, *J* = 11.9 Hz, 1H, CH)).

Ethyl 2-ethylthio-3-(2,4,6-trinitrophenyl)propionate (16)

Procedure E

Ethanethiol (0.15 mL, 0.124 g, 2 mmol) and then triethylamine (0.03 mL, 0.022 g, 0.22 mmol) were added to a stirred solution of **14** (0.155 g, 0.5 mmol) in anhydrous THF (5 mL) at ambient temperature. TLC (CCl_4–$CHCl_3$–Me_2CO, 15:5:1) taken after 18 h indicated complete consumption of **14** (R_f = 0.52) with formation of less polar product (R_f = 0.58). After evaporation, the yellowish oily residue was chromatographed ($CHCl_3$) to give **16** (0.159 g, 85%) as a slightly yellow spectroscopically pure oil. IR ($CHCl_3$) (cm^{-1}): 1720 (C=O). ^1H NMR δ: 1.17 (t, *J* = 7.5 Hz, 3H, CH_3), 1.26 (t, *J* = 7.0 Hz, 3H, CH_3), 2.56 (q, *J* = 7.5 Hz, 2H, SCH_2), 3.41–3.85 (m, 3H, CH_2-CH), 4.19 (q, *J* = 7.0 Hz, 2H, CH_2), 8.80 (s, 2H, H_{Ar}). EI-HRMS *m*/*z*: 373.0586 (20, M^+ ($C_{13}H_{15}N_3O_8S$) = 373.0579), 147.0474 (45, ($C_6H_{11}O_2S$) = 147.0479, CH(SEt)CO_2Et).

Compound **16** (as well as **17a**,**b**) was stable when kept at ~5°C for a week. However, significant decomposition (~20%, ^1H NMR) was observed after 3 months.

Ethyl 2-ethylthio-3-(2,4-dinitrophenyl)propionate (17a)

Treatment of **15a** (0.133 g, 0.5 mmol) by procedure E gave **17a** (0.15 g, 91%) as a slightly yellow oil. IR ($CHCl_3$) (cm^{-1}): 1720 (C=O). ^1H NMR δ: 1.22 (t, *J* = 7.4 Hz, 3H, CH_3), 1.29 (t, *J* = 7.0 Hz, 3H, CH_3), 2.68 (q, *J* = 7.4 Hz, 2H, SCH_2), 3.39–3.77 (m, 3H, CH_2-CH), 4.26 (q, *J* = 7.0 Hz, 2H, CH_2), 7.69 (d, *J* = 8.6 Hz, 1H, H_{Ar}), 8.37 (dd, *J* = 8.6, 2.3 Hz, 1H, H_{Ar}), 8.83 (d, *J* = 2.3 Hz, 1H, H_{Ar}). EI-HRMS *m*/*z*: 328.0731 (18, M^+ ($C_{13}H_{16}N_2O_6S$) = 328.0728), 147.0476 (61, ($C_6H_{11}O_2S$) = 147.0479, CH(SEt)CO_2Et).

Methyl 2-ethylthio-3-(2,4-dinitrophenyl)propionate (17b)

Treatment of methyl 2,4-dinitrocinnamate (26) (**15b**; 0.129 g, 0.5 mmol) by procedure E gave **17b** (0.15 g, 93%) as a slightly yellow oil. IR ($CHCl_3$) (cm^{-1}): 1705 (C=O). ^1H NMR δ: 1.23 (t, *J* = 7.4 Hz, 3H, CH_3), 2.75 (q, *J* = 7.4 Hz, 2H, SCH_2), 3.41–3.78 (m, 3H, CH_2-CH), 3.72 (s, 3H, CH_3), 7.68 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 8.39 (dd, *J* = 8.4, 2.3 Hz, 1H, H_{Ar}), 8.82 (d, *J* = 2.3 Hz, 1H, H_{Ar}). EI-HRMS *m*/*z*: 314.0566 (14, M^+ ($C_{12}H_{14}N_2O_6S$) = 314.0572), 133.0328 (100, ($C_5H_9O_2S$) = 133.0323, CH(SEt)CO_2Me).

Ethyl 2-propylthio-3-(2,4-dinitrophenyl)propionate (17c)

Treatment of **15a** (133 mg, 0.5 mmol) with propanethiol (2.0 mmol) by procedure E (column chromatography: $CHCl_3$) gave **17c** (150 g, 88%) as a slightly yellow oil. IR (neat) (cm^{-1}): 1734 (C=O). ^1H NMR δ: 0.97 (t, *J* = 7.3 Hz, 3H, CH_3), 1.26 (t, *J* = 7.1 Hz, 3H, CH_3), 1.59 (septet, *J* = 7.3 Hz, 2H, CH_2), 2.58–2.70 (m, 2H, SCH_2), 3.41 (dd, *J* = 13.3, 6.8 Hz, $1H_A$, from 3-CH_2), 3.58 (dd, *J* = 13.3, 8.1 Hz, $1H_{A'}$, from 3-CH_2), 3.63 (t, *J* = 7.3 Hz, 1H, CH), 4.11–4.25 (m, 2H, CH_2), 7.70 (d, *J* = 8.5 Hz, 1H, H_{Ar}), 8.40 (dd, *J* = 8.4, 2.3 Hz, 1H, H_{Ar}), 8.85 (d, *J* = 2.3 Hz, 1H, H_{Ar}). ^{13}C NMR δ: 13.7 (CH_3), 14.5 (CH_3), 22.9 (CH_2), 34.4 (SCH_2), 35.5 ($3CH_2$), 46.6 (CH), 62.1 (CH_2), 121.0 (C6), 127.3 (C5), 135.4 (C6), 140.5 (C1), 147.4 and 149.6 (C2/4), 171.9 (C=O) (assignments based on DEPT and HETCOR experiments). APCI-MS *m*/*z*: 343 (100, $[M + H]^+$). Anal. calcd. for $C_{14}H_{18}N_2O_6S$: C 49.11, H 5.30, N 8.18; found: C 49.25, H 5.39, N 8.18.

Ethyl 3-propylthio-3-(2-nitrophenyl)propionate (18)

Propanethiol (0.21 mL, 179 mg, 2.35 mmol) was added to a stirred solution of EtONa in EtOH (prepared from Na (50 mg, 2.1 mmol) and EtOH (2.0 mL)) at ambient temperature. After 15 min, ethyl (*E*)-2-nitrocinnamate (27) (130 mg, 0.59 mmol; prepared from 2-nitrobenzaldehyde by procedure D (93%)) dissolved in ethanol (4.0 mL) was added dropwise and the stirring was continued for 2 h. The resulting mixture was evaporated and the residue was partitioned ($CHCl_3$–H_2O). The organic layer was dried ($MgSO_4$), evaporated, and column chromatographed ($CHCl_3$) to give **18** (97 mg, 56%) as an oil. IR (neat) (cm^{-1}): 1740 (C=O). ^1H NMR δ: 0.92 (t, *J* = 7.3 Hz, 3H, CH_3), 1.17 (t, *J* = 7.1 Hz, 3H, CH_3), 1.50–1.57 (m, 2H, CH_2), 2.39 (dt, *J* = 12.6, 7.3 Hz, $1H_A$, SCH_2), 2.50 (ddd, *J* = 12.6, 7.8, 6.6 Hz, $1H_{A'}$, SCH_2), 2.88 (dd, *J* = 15.4, 8.2 Hz, $1H_A$, CH_2), 2.94 (dd, *J* = 15.4, 7.2 Hz, $1H_{A'}$, CH_2), 4.07 (q, *J* = 7.1 Hz, 2H, CH_2), 4.99 (t, *J* = 7.8 Hz, 1H, CH), 7.38 (t, *J* = 7.7 Hz, 1H, H_{Ar}), 7.60 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 7.78 (dd, *J* = 8.0, 1.0 Hz, 2H, H_{Ar}). ^{13}C NMR δ: 13.7 (CH_3), 13.8 (CH_3), 23.0 (CH_2), 34.3 (SCH_2), 39.4 (CH), 42.3 ($2CH_2$), 61.4 (CH_2), 124.5 (C3), 128.4 (C4), 130.1 (C6), 133.4 (C5), 137.4 (C1), 150.1 (C2), 170.3 (C=O) (assignments based on DEPT and HETCOR experiments). APCI-MS *m*/*z*: 298 (100, $[M + H]^+$). Anal. calcd. for $C_{14}H_{19}NO_4S$: C 56.55, H 6.44, N 4.71; found: C 56.46, H, 6.66, N 4.79.

Treatment of ethyl 2-nitrocinnamate (27) (0.5 mmol) with propanethiol (2.0 mmol) by procedure E gave unchanged ethyl 2-nitrocinnamte (91%).

2,2-Dimethyl-5-(2,4-dinitrobenzylidene)-1,3-dioxan-4,6-dione (19)

2,4-Dinitrobenzaldehyde (0.98 g, 5 mmol) was treated with 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid) (0.72 g, 5 mmol) by procedure A to give **19** (0.69 g, 43%); mp 138–139°C (EtOH). IR ($CHCl_3$) (cm^{-1}): 1720 (C=O). ^1H NMR δ: 1.82 (s, 6H, $2CH_3$), 7.68 (dd, *J* = 8.4, 0.6 Hz, 1H, H_{Ar}), 8.58 (dd, *J* = 8.4, 2.1 Hz, 1H, H_{Ar}), 8.76 (d, *J* = 0.6 Hz, 1H, CH), 9.12 (d, *J* = 2.1 Hz, 1H, H_{Ar}). EI-MS *m*/*z*: 322 (3, M^+). Anal. calcd. for $C_{13}H_{10}N_2O_8$: C 48.46, H 3.13, N 8.69; found: C 48.38, H 2.86, N 8.56.

Reaction of **19** with DEA in ethanol by procedure C did not afford rearranged product and only unchanged **19** was recovered (~92%).

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References

1. S. Kinastowski and S. Wnuk. Synthesis, 654 (1983).
2. S. Kinastowski, S. Wnuk, and E. Kaczmarek. Synthesis, 111 (1988).
3. S. Kinastowski, E. Kaczmarek, and S. Wnuk. Pol. J. Chem. **64**, 595 (1990).
4. S.F. Wnuk, E. Lewandowska, C.A. Valdez, and S. Kinastowski. Tetrahedron, **56**, 7667 (2000).
5. (*a*) J.D. Loudon and G. Tennant. Quart. Rev. **18**, 389 (1964); (*b*) P.N. Preston and G. Tennant. Chem. Rev. **72**, 627 (1972).
6. R. Behnisch. Aromatische Nitro-Verbindungen. *In* Houben-Weyl. Methoden der Organischen Chemie, 4. Vol. E16d. *Edited by* D. Klamann. Thieme, Stuttgart. 1992. pp. 389–405 (part 1).
7. (*a*) G. Tennant, C.J. Wallis, and G.W. Weaver. J. Chem. Soc. Perkin Trans. 1, 817 (1999); (*b*) J.E.T. Corrie, M.J. Gradwell, and G. Papageorgiou. J. Chem. Soc. Perkin Trans. 1, 2977 (1999).
8. (*a*) V.N.R. Pillai. Synthesis, 1 (1980); (*b*) D. Gravel, J. Hebert, and D. Thoraval. Can. J. Chem. **61**, 400 (1983).
9. (*a*) J.W. Walker, G.P. Reid, J.A. McCray, and D.R. Trentham. J. Am. Chem. Soc. **110**, 7170 (1988); (*b*) J.E.T. Corrie, B.C. Gilbert, V.R.N. Munasinghe, and A.C. Whitwood. J. Chem. Soc. Perkin Trans. 2, 2483 (2000); (*c*) Y.V. Il'ichev and J. Wirz. J. Chem. Phys. A, **104**, 7856 (2000).
10. R. Pschorr and O. Wolfes. Ber. Dtsch. Chem. Ges. **32**, 3399 (1899).
11. J.D. Loudon and G. Tennant. J. Chem. Soc. 3466 (1960).
12. J.P. Lelievre, P.G. Farrell, and F. Terrier. J. Chem. Soc. Perkin Trans. 2, 333 (1986).
13. H. Bock and U.Z. Lechner-Knoblauch. Naturforsch. Teil B, **40B**, 1463 (1985).
14. W. Lehnert. Tetrahedron, **29**, 635 (1973).
15. M.C. Wani, A.W. Nicholas, G. Manikumar, and M.E. Wall. J. Med. Chem. **30**, 1774 (1987).
16. L.P. Hammett. Physical organic chemistry. Reaction rates, equilibria, and mechanism. 2nd ed. McGraw–Hill, New York. 1970. pp. 347–390.
17. S. Kinastowski, S. Wnuk, and E. Kaczmarek. Pol. J. Chem. **63**, 495 (1989).
18. (*a*) E.D. Bergmann, D. Ginsburg, and R. Pappo. Org. React. **10**, 179 (1959); (*b*) R.D. Little, M.R. Masjedizadeh, O. Wallquist, and J.I. McLoughlin. Org. React. **47**, 315 (1995).
19. (*a*) P. Bravo, G. Gaudiano, and T. Salvatori. Gazz. Chim. Ital. **98**, 1046 (1968); (*b*) G. Faust, M. Verny, and R. Vessiere. Bull. Soc. Chim. Fr. 2707 (1975); (*c*) D.W. Lee, J. Choi, and N.M. Yoon. Synth. Commun. **26**, 2189 (1996).
20. (*a*) B.M. Trost and G.R. Dake. J. Am. Chem. Soc. **119**, 7595 (1997); (*b*) I.V. Solodin, A.V. Eremeev, I.I. Chervin, and R.G. Kostyanovskii. Khim. Geterotsikl. Soedin. 1359 (1985).
21. S. Kinastowski and S. Wnuk. Pol. J. Chem. **57**, 625 (1983).
22. H. Seidel and J.C. Bittner. Monatsh. Chem. **23**, 430 (1902).
23. M.P. Hay, B.M. Sykes, W.A. Denny, and C.J. O'Connor. J. Chem. Soc. Perkin Trans. 1, 2759 (1999).
24. F. Sachs and R. Kempf. Ber. Dtsch. Chem. Ges. **35**, 1224 (1902).
25. P. Friedlander and R. Fritsch. Monatsh. Chem. **23**, 534 (1902).
26. P. Pfeiffer. Liebigs Ann. Chem. **411**, 153 (1916).
27. J.V. Sinisterra, Z. Mouloungui, M. Delmas, and A. Gaset. Synthesis, 1097 (1985).