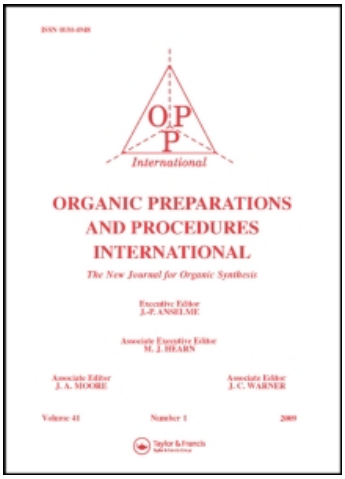

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CONSTRUCTION OF THE PYRAZOLO[1,5-*a*] [4,1]BENZOTHIAZEPINE SYSTEM BY INTRAMOLECULAR NITRILIMINE CYCLOADDITION

Submitted by (1/21/92)

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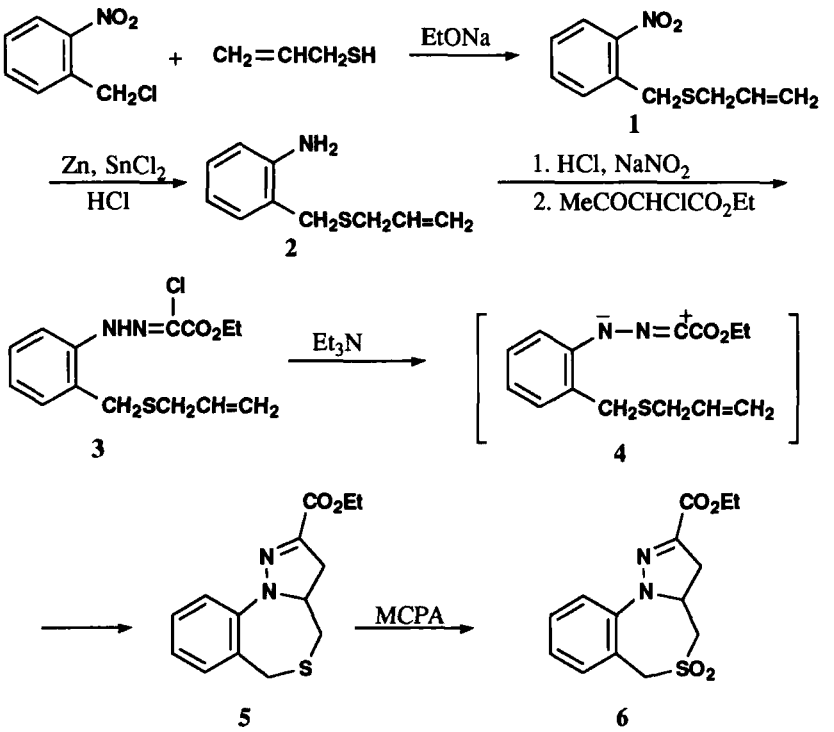
Within our research framework aimed at the synthesis of fused-ring heterocycles *via* intramolecular cycloaddition of functionalized nitrile imines,[1-4] we explored the possibility of applying this strategy to the construction of the unreported pyrazolo[1,5-*a*][4,1]benzothiazepine system.

Starting from the commercially available 2-nitrobenzyl chloride and allyl mercaptan, we prepared nitro derivative **1**, which was then reduced to the corresponding aniline **2** with stannous chloride. Diazotization of **2** and subsequent coupling with ethyl 2-chloroacetoacetate afforded the hydrazonyl chloride **3**. The reaction of **3** with an excess of triethylamine in boiling benzene gave the tricyclic compound **5** resulting from the intramolecular cycloaddition of the transient nitrilimine **4**. Treatment of **5** with 3-chloroperbenzoic acid led to the corresponding *S,S*-dioxide **6**. It is worthwhile to notice that, while intramolecular nitrilimine cycloadditions have been exploited to prepare five/five- and five/six-membered annulated heterocycles,[1-3,5] only a few examples deal with the formation of five/seven-membered systems.[4]



EXPERIMENTAL SECTION

Melting points were determined on a Büchi appanatus and are uncorrected. IR spectra were taken on a Perkin-Elmer 1725X FT spectrophotometer. NMR spectra were recorded on Varian EM-390 and Varian XL-200 instruments; chemical shifts are given in δ ppm from $SiMe_4$. Mass spectra were measured on a WG-70EQ apparatus.

3-(2-Nitrobenzylthio)propene (1).- A solution of 2-nitrobenzyl chloride (5.1 g, 30 mmol) and allyl mercaptan (2.4 g, 30 mmol) in ethanol (100 mL) was added dropwise to 0.5 M sodium ethoxide in ethanol (55 mL). The mixture was stirred overnight at room temperature, the undissolved material was filtered off, and the solvent was evaporated under reduced pressure. The residue was taken up with dichloromethane, washed with 5% aqueous NaOH, dried over Na_2SO_4, and evaporated. The oily residue was practically pure 1 (5.7 g, 90%). ^1H NMR (90 MHz, $CDCl_3$): δ 3.10 (2H, d, J = 7), 4.05 (2H, s), 4.90-5.10 (2H, m), 5.50-6.00 (1H, m), 7.20-8.00 (4H, m); MS (EI, 70 eV): m/z 209 (M^+).

Anal. Calcd. for $C_{10}H_{11}NO_2S$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.56; H, 5.49; N, 6.54

3-(2-Aminobenzylthio)propene (2).- A solution of $SnCl_2 \cdot 2H_2O$ (5.7 g, 25 mmol) in 35% aqueous HCl (100 mL) was added dropwise to a stirred solution of **1** (5.2 g, 25 mmol) in acetic acid (100 mL) at 15°. Zinc powder (16 g, 0.25 mol) was then added portionwise under vigorous stirring and cooling. After 2 hrs, the undissolved material was filtered off and the solution was adjusted to pH 5 with concentrated ammonia. The solvent was partly removed under reduced pressure and the residue was alkalized and extracted with dichloromethane. The organic solution was dried over Na_2SO_4 and evaporated. Distillation of the residue gave amine **2**, bp. 155-160°/0.2 torr (3.0 g, 67%). ^1H NMR (90 MHz, $CDCl_3$): δ 3.08 (2H, d, J 7), 3.69 (2H, s), 4.00 (2H, br s), 5.00-5.20 (2H, m), 5.50-6.00 (1H, m), 6.50-7.20 (4H, m). MS (EI, 70 eV): m/z 179 (M^+).

Anal. Calcd. for $C_{10}H_{13}NS$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.14; H, 7.52; N, 7.71

Ethyl 2-[2-(Allylthiomethyl)phenylhydrazono]-2-chloroacetate (3).- A solution of **2** (3.6 g, 20 mmol) in 2 N aqueous HCl (30 mL) was cooled at 0° and treated with a solution of ethyl 2-chloroacetoacetate (10.8 g, 50 mmol) in methanol (30 mL). A solution of $NaNO_2$ (1.6 g, 22 mmol) in water (20 mL) was then added dropwise under vigorous stirring and ice-cooling. The mixture was adjusted to pH 5 with AcONa, stirred at room temperature for 3 hrs, and extracted with dichloromethane. The organic solution was dried over Na_2SO_4 and evaporated. The residue was chromatographed on silica gel column with light petroleum-ethyl acetate (4:1) as eluent to give compound **3**, mp. 39-41° (from pentane) (2.9 g, 46%). IR (Nujol): 3240, 1725 cm^{-1}; ^1H NMR (90 MHz, CDCl3): δ 1.43 (3H, t, J 7), 3.10 (2H, d, J 7), 3.71 (2H, s), 4.42 (2H, q, J 7), 4.90-5.20(2H, m), 5.50-6.00 (1H, m), 6.80-7.70 (4H, m), 9.50 (1H, br s); MS (EI, 70 eV): m/z 312 (M^+).

Anal. Calcd. for $C_{14}H_{17}ClN_2O_2S$: C, 53.75; H, 5.48; N, 8.96. Found: C, 53.90; H, 5.72; N, 8.72

2-Ethoxycarbonyl-3,3a-dihydro-4H,6H-pyrazolo[1,5-a][4,1]benzothiazepine (5).- A solution of **3** (1.43 g, 4.6 mmol) and triethylamine (2.3 g, 23 mmol) in benzene (230 mL) was refluxed for 12 hrs. The resulting mixture was washed with aqueous HCl, dried over Na_2SO_4, and evaporated. The residue

was taken up with diisopropyl ether and filtered to afford pratically pure **5**, mp. 106-107° (from hexane-benzene) (0.49 g, 39%). IR (Nujol): 1715 cm^{-1} ; ^1H NMR (200 MHz, C_6D_6): δ 1.42 (3H, t, *J* 7), 2.70-4.10 (7H, overlapping), 4.35 (2H, q, *J* 7), 7.00-7.40 (4H, m); MS (EI, 70 eV): m/z 276 (M^+).

Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 60.84; H, 5.84; N, 10.14. Found: C, 60.68; H, 6.01; N, 10.03

2-Ethoxycarbonyl-3,3a-dihydro-4H,6H-pyrazolo[1,5-a][4,1]benzothiazepine 5,5-Dioxide (6).- A solution of **5** (415 g, 154 mmol) and 3-chloroperbenzoic acid (0.28 g, 1.6 mmol) in dichloromethane (20 mL) was stirred at room temperature for 3 hrs. After filtration, the solution was washed with aqueous $NaHCO_3$ and $Na_2S_2O_5$, dried over Na_2SO_4, and evaporated. Recrystallization of the residue from ethanol gave compound **6**, mp. 142-143° (87 mg, 51%). IR (Nujol): 1690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.41 (3H, t, *J* 7), 2.85 (1H, dd, *J* 18 and 11), 3.30-4.20 (5H, overlapping), 4.35 (2H, q, *J* 7), 4.52 (1H, d, *J* 15), 7.00-7.40 (4H, m); MS (EI, 70 eV): m/z 308 (M^+).

Anal. Calcd. for $C_{14}H_{16}N_2O_4S$: C, 54.53 H, 5.23; N, 9.09. Found: C, 54.71; H, 5.47; N, 8.98

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