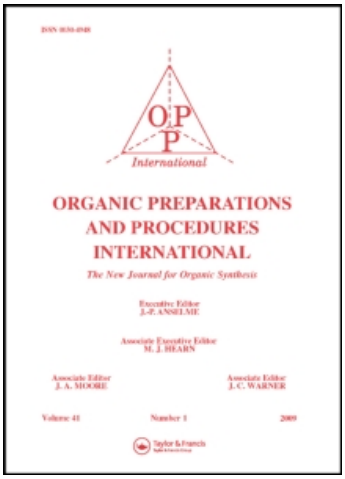

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CONSTRUCTION OF THE PYRAZOLO[1,5-*a*][6,1]BENZODIAZONINE AND PYRAZOLO[1,5-*a*][7,1]BENZODIAZECINE SKELETONS

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CONSTRUCTION OF THE PYRAZOLO[1,5-*a*][6,1]BENZODIAZONINE AND PYRAZOLO[1,5-*a*][7,1]BENZODIAZECINE SKELETONS

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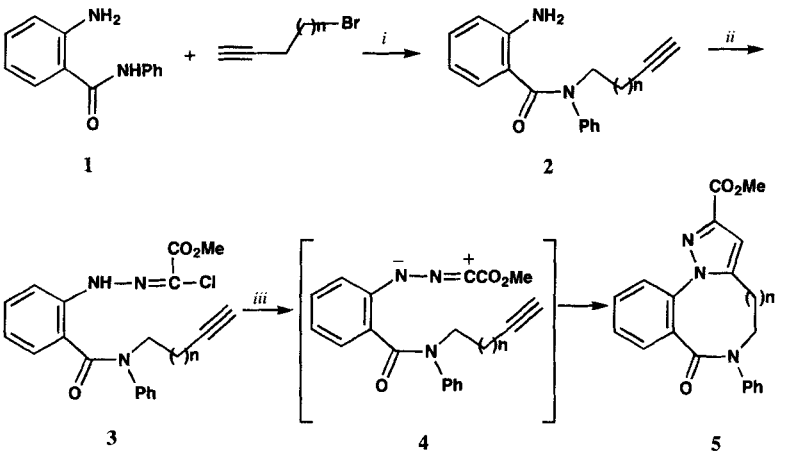
Intramolecular 1,3-dipolar cycloadditions offer a synthetic entry to a large variety of heterocyclic systems containing a five-membered ring fused to another ring of variable size.[1] The latter parameter, however, markedly affects the entropy aspect and thus the effectiveness of the intramolecular process.[2] We now report the successful use of intramolecular nitrilimine cycloaddition to construct the hitherto unreported pyrazolo[1,5-*a*][6,1]benzodiazonine and pyrazolo[1,5-*a*][7,1]benzodiazecine systems.

The synthetic sequence involves the following stages: (*i*) site-selective alkynylation of the *o*-aminobenzanilide (**1**);[4] (*ii*) diazotisation of **2** and subsequent coupling with methyl α-chloroacetoacetate to give the hydrazonyl chlorides **3**; (*iii*) treatment of the latter with silver carbonate in order to generate the transient nitrilimines **4**, whose intramolecular cycloadditionled to the target system **5**. In view of the well-known factors working against the formation of large rings,[3] the cyclization yields of **4** are highly satisfactory thus making the present synthesis worthy of attention.

EXPERIMENTAL SECTION

Melting points were determined on a Büchi apparatus and are not corrected. IR spectra were recorded on a FT IR Perkin Elmer 1725 X spectrophotometer. Mass spectra were taken with a WG-70EQ apparatus. ^{1}H NMR spectra were obtained on a Bruker 300 MHz apparatus, chemical shifts are given as ppm from TMS. Compound **1** was prepared according to the literature.[4]



i) K_2CO_3, NaOH, *n*-Bu_4N^+ HSO_4^-, benzene, 70° *ii*) 1) $NaNO_2$, HCl, AcOH 2) $MeCOCHClCO_2Me$

iii) Ag_2CO_3, dioxane, Δ

Alkynyl Anthranilates 2. Typical Procedure.- A solution of **1** (18 mmol) in dry benzene (80 mL) was treated with K_2CO_3 (20 mmol), NaOH (68 mmol) and *n*-Bu_4N^+ HSO_4^- (2 mmol) and heated to 70°. Then the appropriate alkynyl bromide (25 mmol) in dry benzene (12 mL) was added dropwise (20 min) at 70°. The mixture was refluxed for 8 hrs, then washed with water (250 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column with light petroleum-ethyl acetate 2:1 as eluent to give **2**.

Cmpd **2a:** 2.00 g (40%); thick oil; IR (nujol): 3475, 3360, 3280, 1640 (cm^{-1}); ^1H NMR ($CDCl_3$): δ 1.92 (t, *J* = 2.5, 1H), 2.10-2.45 (m, 4H), 3.95 (t, *J* = 7.0, 2H), 4.60 (br s, 2H), 6.12-7.70 (m, 9H); MS *m/z* 278 (M^+).

Anal. Calcd. for $C_{18}H_{18}N_2O$: C, 77.66; H, 6.52; N, 10.07. Found: C, 77.53; H, 6.47; N, 9.95

Cmpd **2b:** 1.84 g (35%); thick oil; IR (nujol): 3460, 3360, 3300, 1645 (cm^{-1}); ^1H NMR ($CDCl_3$): δ 1.55-1.74 (m, 4H), 1.91 (t, *J* = 2.5, 1H), 2.21 (dt, *J* = 7.0,2.5, 2H), 3.95 (t, *J* = 7.0, 2H), 4.60 (br s, 2H), 6.20-7.60 (m, 9H); MS *m/z* 292 (M^+).

Anal. Calcd. for $C_{19}H_{20}N_2O$: C, 78.04; H, 6.90; N, 9.59. Found: C, 77.91; H, 6.89; N, 9.70

Hydrazonyl Chlorides 3. Typical Procedure.- Sodium nitrite (13 mmol) was added portionwise to a solution of the alkynyl anthranilate **2** (6 mmol) in 1N aqueous HCl (30 mL) and glacial acetic acid (5 mL) with vigorous stirring and cooling at 0°C. After 30 min, the cold mixture was treated with sodium acetate to adjust the pH to 5 and then methyl 2-chloroacetoacetate (6 mmol) was added with cooling and stirring for 4hrs. The mixture was extracted with Et_2O (50 mL) and the organic layer was washed with 5% aqueous $NaHCO_3$ until neutral, dried and evaporated. Crystallization from diisopropyl ether gave the hydrazonyl chlorides **3**.

Cmpd **3a:** 1.43 g (60%); mp. 97°; IR (nujol): 3250, 1740, 1690 (cm^{-1}); ^1H NMR ($CDCl_3$): δ 1.93 (t, *J* = 2.5, 1H), 2.10-2.35 (m, 4H), 3.90 (s, 3H), 4.02 (t, *J* = 8.0, 2H), 6.55-7.65 (m, 9H), 10.45 (br s, 1H);

MS *m/z* 397 (M^+).

Anal. Calcd. for $C_{21}H_{20}ClN_3O_3$: C, 63.46; H, 5.08; Cl, 8.81; N, 10.58
Found: C, 63.30; H, 4.92; Cl, 8.88; N, 10.64

Cmpd **3b:** 1.85 g (75%); mp. 89°; IR (nujol): 3290, 1760, 1640 (cm^{-1}); ^1H NMR ($CDCl_3$): δ 1.55-1.73 (m, 4H), 1.91 (t, *J* = 2.5, 1H), 2.22 (dt, *J* = 7.0,2.5, 2H), 3.94 (s, 3H), 3.97 (t, *J* = 7.0, 2H), 6.55-7.61 (m, 9H), 10.45 (br s, 1H); MS *m/z* 411 (M^+).

Anal. Calcd. for $C_{22}H_{22}ClN_3O_3$: C, 64.21; H, 5.39; Cl, 8.51; N, 10.22
Found: C, 64.32; H, 5.45; Cl, 8.60; N, 10.35.

Reaction of Hydrazonyl Chlorides 3 with Silver Carbonate. Typical Procedure.- A solution of the hydrazonyl chloride **3** (3 mmol) in dry dioxane (300 mL) was treated with silver carbonate (14 mmol) and the mixture was refluxed *in the dark* for 12 hrs. The undissolved material was filtered off and the filtrate was evaporated under reduced pressure. The residue was chromatographed on a silica gel with dichloromethane-diethyl ether 1:1 as eluent to give **5**.

Cmpd **5a:** 0.51 g (47%); mp. 197° (from hexane-benzene); IR (nujol): 1730, 1720 (cm^{-1}); ^1H NMR ($CDCl_3$): δ 1.50-1.82 (m, 4H), 2.35-2.45 (m, 1H), 3.00-3.08 (m, 1H), 3.90 (s, 3H), 6.78 (s, 1H), 6.80-7.63 (m, 9H); MS *m/z* 361 (M^+).

Anal. Calcd. for $C_{21}H_{19}N_3O_3$: C, 69.78; H, 5.30; N, 11.63. Found: C, 69.65; H, 5.25; N, 11.71

Cmpd **5b:** 0.48 g (43%); mp. 203° (from hexane-benzene); IR (nujol): 1730, 1720 (cm^{-1}); ^1H NMR ($CDCl_3$): δ 1.20-2.30 (m, 6H), 2.90 (br t, *J* = 7.5, 2H), 3.92 (s, 3H), 6.78 (s, 1H), 6.80-7.60 (m, 9H); MS *m/z* 375 (M^+).

Anal. Calcd. for $C_{22}H_{21}N_3O_3$: C, 70.37; H, 5.64; N, 11.20. Found: C, 70.41; H, 5.73; N, 11.36

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