

## Conjugated Azoalkenes. Part II. Synthesis of Some Heterocyclic Azoalkenes

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The synthesis of a new class of unknown heterocyclic conjugated azoalkene derivatives is reported.

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In our previous studies concerning the reactivity of conjugated azoalkenes, we occasionally reported the synthesis of some unknown derivatives of this type [1-4]. In view of the more general interest in these compounds both as products and intermediates in organic and pharmaceutical chemistry, we focused our attention on a systematic investigation aimed at obtaining new classes of azoalkene derivatives [5].

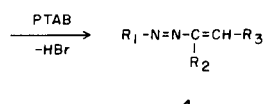
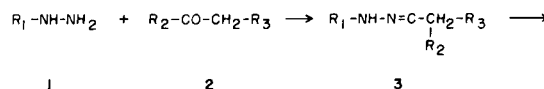
In fact, we previously obtained related *N*-( $\alpha$ -chlorobenzylidene)-*N'*-arylhydrazines by reaction of copper(II) chloride and some arylazoalkenes [2]. Furthermore, the C=C-N=N system in these latter derivatives frequently exhibits a reactivity analogous to that of other conjugated double bonds. Thus, the azo-ene system of aliphatic and aromatic azoalkenes with or without electron-withdrawing groups gave (2 + 2)- and (4 + 2)-cycloadditions with some dienophiles, providing six-membered heterocyclic compounds [6]. Diazaphosphole derivatives (five-membered heterocycles containing *P*- and *N*-atoms) have been produced by cycloaddition (McCormack-type) of some phenylazoalkenes and phenyldichlorophosphine [7]. Furthermore, conjugated azoalkenes may easily undergo the 1,4-conjugate additions (Michael-type) with a wide variety of nucleophiles, leading to the corresponding hydrazone derivatives with simultaneous *C*-functionalization [3,8]. In the case of 1,4-conjugate addition of compounds containing an activated methylene group, the preliminary formation of the 1,4-adduct intermediate may be followed by a ring closure, affording interesting 1-aminopyrrole derivatives [4,9].

Unfortunately, the predictable synthesis and use of new conjugated azoalkenes frequently present considerable practical difficulties, mainly because of their different stabilities and reactivities. These properties may make it problematical in order to find the more suitable strategies for chemical treatment and work-up procedures for the preparation and isolation of the reaction products. This fact represents the limiting factor for the potential usefulness of these compounds in organic chemistry, each additional class of azoalkene derivatives requiring the appropriate reaction conditions for these investigations.

We now report the synthesis of some heterocyclic conjugated azoalkenes prepared by bromination of the parent

heterocyclic hydrazone derivatives with phenyltrimethylammonium tribromide (PTAB), followed by a dehydrohalogenation *in situ* effected with a basic treatment [10].

### Scheme



| 1 | $R_1$             | 2 | $R_2$   | $R_3$  |
|---|-------------------|---|---|--|
| a | 3-Nitro-2-pyridyl | a | CH <sub>3</sub>   | COOCH <sub>3</sub>                               |
| b | 2-Pyrimidyl       | b | CH <sub>3</sub>   | COOC <sub>2</sub> H <sub>5</sub>                 |
| c | 2-Benzimidazolyl  | c | CH <sub>3</sub>   | COOCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> |
|   |                   | d | <i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>3</sub> | COOC <sub>2</sub> H <sub>5</sub>                 |

This reaction takes place under very mild conditions (magnetic stirring at room temperature, with commercial purity grade solvents, without nitrogen atmosphere, do not require expensive and difficultly available reagents, or complicated procedures. In addition, heterocyclic azoalkenes are often obtained in good yields.

Table  
Moles of PTAB with Respect to Hydrazones **3a-i**,  
Yields and Melting points of Azoalkenes **4a-i**

| Hydrazine No. | Ketone No. | Azoalkene No. | PTAB | Yield (%) | Mp (°C) [a] |
|---------------|------------|---------------|------|-----------|-------------|
| <b>1a</b>     | <b>2a</b>  | <b>4a</b>     | 2.5  | 60        | 139-140     |
|               | <b>2b</b>  | <b>4b</b>     | 3.0  | 70        | 64-66       |
|               | <b>2c</b>  | <b>4c</b>     | 1.5  | 72        | 69-70       |
|               | <b>2d</b>  | <b>4d</b>     | 3.0  | 35        | 104-105     |
| <b>1b</b>     | <b>2a</b>  | <b>4e</b>     | 1.5  | 61        | 97-98       |
|               | <b>2b</b>  | <b>4f</b>     | 1.1  | 49        | 67-68       |
|               | <b>2c</b>  | <b>4g</b>     | 1.1  | 34        | 65-66       |
| <b>1c</b>     | <b>2a</b>  | <b>4h</b>     | 1.1  | 93        | 132-134     |
|               | <b>2b</b>  | <b>4i</b>     | 1.1  | 78        | 88-89       |

[a] Melting points are uncorrected.

## EXPERIMENTAL

Hydrazones **3a-i**.

These compounds were synthesized according to well known methodologies.

Azoalkenes **4a-i**. General Procedure.

To a stirred solution of hydrazones **3a-i** dissolved in tetrahydrofuran (15 ml) was slowly added (30 minutes) PTAB in the molar ratio reported in the Table. After a further 30 minutes, the reaction mixture was poured into a separatory funnel containing ether and 10% aqueous sodium hydrogen carbonate. The mixture was vigorously shaken until the reaction was complete (monitored by silica gel tlc). The organic phase was separated, dried with anhydrous sodium sulfate and evaporated under reduced pressure, affording the products **4a-i** in satisfactory purity. The products were purified by crystallization from ethyl acetate/*n*-pentane in the refrigerator (at  $-20^{\circ}$ ) and may be stored at room temperature without appreciable decomposition for several days.

Analytical Data of Azoalkenes **4a-i**.Methyl  $\beta$ -Methyl- $\beta'$ -(2-azo-3-nitropyridyl)acrylate (**4a**).

This compound was obtained in a yield of 60%, mp 139-140° (uncorrected); ir (nujol): 1720 (COO), 1595 (pyridyl), 1530 and 1350  $\text{cm}^{-1}$  ( $\text{NO}_2$ );  $^1\text{H}$  nmr (DMSO- $d_6$ , TMS):  $\delta$  2.37 (3H, s, Me), 3.87 (3H, s, COOMe), 7.0 (1H, s, CH), 7.67-8.0 and 8.57-9.0 ppm (3H, m, pyridyl).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{10}\text{N}_4\text{O}_4$ : C, 48.0; H, 4.0; N, 22.4. Found: C, 47.7; H, 4.2; N, 22.5.

Ethyl  $\beta$ -Methyl- $\beta'$ -(2-azo-3-nitropyridyl)acrylate (**4b**).

This compound was obtained in a yield of 70%, mp 64-66° (uncorrected); ir (nujol): 1715 (COO), 1600 (pyridyl), 1525 and 1345  $\text{cm}^{-1}$  ( $\text{NO}_2$ );  $^1\text{H}$  nmr (deuteriochloroform, TMS):  $\delta$  1.4 (3H, t, COOEt), 2.43 (3H, s, Me), 4.33 (2H, q, COOEt), 7.1 (1H, s, CH), 7.5-7.76, 8.3-8.57 and 8.8-8.97 ppm (3H, m, pyridyl).

*Anal.* Calcd. for  $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O}_4$ : C, 50.0; H, 4.6; N, 21.2. Found: C, 50.4; H, 4.4; N, 20.9.

Benzyl  $\beta$ -Methyl- $\beta'$ -(2-azo-3-nitropyridyl)acrylate (**4c**).

This compound was obtained in a yield of 72%, mp 69-70° (uncorrected); ir (nujol): 1715 (COO), 1600 (pyridyl), 1530 and 1340  $\text{cm}^{-1}$  ( $\text{NO}_2$ );  $^1\text{H}$  nmr (DMSO- $d_6$ , TMS):  $\delta$  2.34 (3H, s, Me), 5.35 (2H, s,  $\text{CH}_2$ ), 7.07 (1H, s, CH), 7.52 (5H, s, aromatic), 7.73-8.0 and 8.6-9.04 ppm (3H, m, pyridyl).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{14}\text{N}_4\text{O}_4$ : C, 58.9; H, 4.3; N, 17.2. Found: C, 60.3; H, 4.0; N, 17.1.

Ethyl  $\beta$ -(4-Nitrophenyl)- $\beta'$ -(2-azo-3-nitropyridyl)acrylate (**4d**).

This compound was obtained in a yield of 35%, mp 104-105° (uncorrected); ir (nujol): 1720 (COO), 1605 (pyridyl), 1515 and 1345  $\text{cm}^{-1}$  ( $\text{NO}_2$ );  $^1\text{H}$  nmr (DMSO- $d_6$ , TMS):  $\delta$  1.2 (3H, t, COOEt), 4.17 (2H, q, COOEt), 7.2-7.77 and 8.1-8.53 and 8.7-8.93 ppm (8H, m, CH, aromatic and pyridyl).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{13}\text{N}_5\text{O}_6$ : C, 51.8; H, 3.5; N, 18.9. Found: C, 51.7; H, 3.4; N, 19.2.

Methyl  $\beta$ -Methyl- $\beta'$ -(2-azopyrimidin)acrylate (**4e**).

This compound was obtained in a yield of 61%, mp 97-98° (uncorrected); ir (nujol): 1715 (COO), 1565  $\text{cm}^{-1}$  (quinoline);  $^1\text{H}$  nmr (deuteriochloroform, TMS):  $\delta$  2.5 (3H, t, Me), 3.87 (3H, s, COOMe), 7.17 (1H, s, CH), 7.23-7.57 (1H, m, quinoline), 8.97 ppm (2H, d, quinoline).

*Anal.* Calcd. for  $\text{C}_9\text{H}_{10}\text{N}_4\text{O}_2$ : C, 52.4; H, 4.9; N, 27.2. Found: C, 52.7; H, 4.7; N, 27.0.

Ethyl  $\beta$ -Methyl- $\beta'$ -(2-azopyrimidin)acrylate (**4f**).

This compound was obtained in a yield of 49%, mp 67-68° (uncorrected); ir (nujol): 1715 (COO), 1565  $\text{cm}^{-1}$  (quinoline);  $^1\text{H}$  nmr (deuteriochloroform, TMS):  $\delta$  1.38 (3H, t, COOEt), 2.55 (2H, q, COOEt), 7.22 (1H, s, CH), 7.33-7.63 (1H, m, quinoline), 9.07 ppm (2H, d, quinoline).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}_2$ : C, 54.5; H, 5.5; N, 25.4. Found: C, 54.1;

H, 5.7; N, 25.7.

Benzyl  $\beta$ -Methyl- $\beta'$ -(2-azopyrimidin)acrylate (**4g**).

This compound was obtained in a yield of 34%, mp 65-66° (uncorrected); ir (nujol): 1715 (COO), 1565  $\text{cm}^{-1}$  (quinoline);  $^1\text{H}$  nmr (DMSO- $d_6$ , TMS):  $\delta$  2.33 (3H, s, Me), 5.33 (2H, s,  $\text{CH}_2$ ), 7.1 (1H, s, CH), 7.53 (5H, s, aromatic), 7.57-7.83 (1H, m, quinoline), 9.1 ppm (2H, d, quinoline).

*Anal.* Calcd. for  $\text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_2$ : C, 63.8; H, 5.0; N, 19.85. Found: C, 63.7; H, 5.1; N, 19.9.

Methyl  $\beta$ -Methyl- $\beta'$ -(2-benzothiazol)acrylate (**4h**).

This compound was obtained in a yield of 93%, mp 132-134° (uncorrected); ir (nujol): 1720 (COO), 1630 (aromatic);  $^1\text{H}$  nmr (deuteriochloroform, TMS):  $\delta$  2.5 (3H, s, Me), 3.88 (3H, s, COOMe), 7.0 (1H, s, CH), 7.33-8.37 ppm (4H, m, aromatic).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}_2\text{S}$ : C, 55.2; H, 4.2; N, 16.1. Found: C, 55.5; H, 4.0; N, 16.0.

Ethyl  $\beta$ -Methyl- $\beta'$ -(2-benzothiazol)acrylate (**4i**).

This compound was obtained in a yield of 81%, mp 88-89° (uncorrected); ir (nujol): 1720 (COO), 1625 (aromatic);  $^1\text{H}$  nmr (deuteriochloroform, TMS):  $\delta$  1.4 (3H, t, COOEt), 2.53 (3H, s, Me), 4.37 (2H, q, COOEt), 7.05 (1H, s, CH), 7.4-8.4 ppm (4H, m, Ar).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$ : C, 56.7; H, 4.8; N, 15.3. Found: C, 56.7; H, 4.7; N, 15.2.

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