A New Method for the Synthesis of Novel 1-Aryl-3-quinoxalinyl-1,2,4-triazol-5-ones

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The reactions of 3-methoxycarbonylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxaline **1** with aryl diazonium salts gave 3-(α-aryldiazenylmethoxycarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxalines **2a-c**, whose reactions with hydrazine hydrate afforded 3-(α-aryldiazenylhydrazinocarbonylmethylene)-2-oxo-1,2,3,4-tetrahydroquinoxalines **3a-c**. The reactions of **3a-c** with nitrous acid resulted in the Curtius rearrangement to provide the 1-aryl-3-quinoxalinyl-1,2,4-triazol-5-ones **4a-c**.

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Recently, we have synthesized various oxadiazoles [1-3] and triazoles [4-6] from the interest in their pharmacological activities as the bactericidal, fungicidal and herbicidal agents [1a,4a]. The azoles synthesized by us include the quinoxaline moiety in their molecules, and some of the representative compounds are shown in Chart 1. In

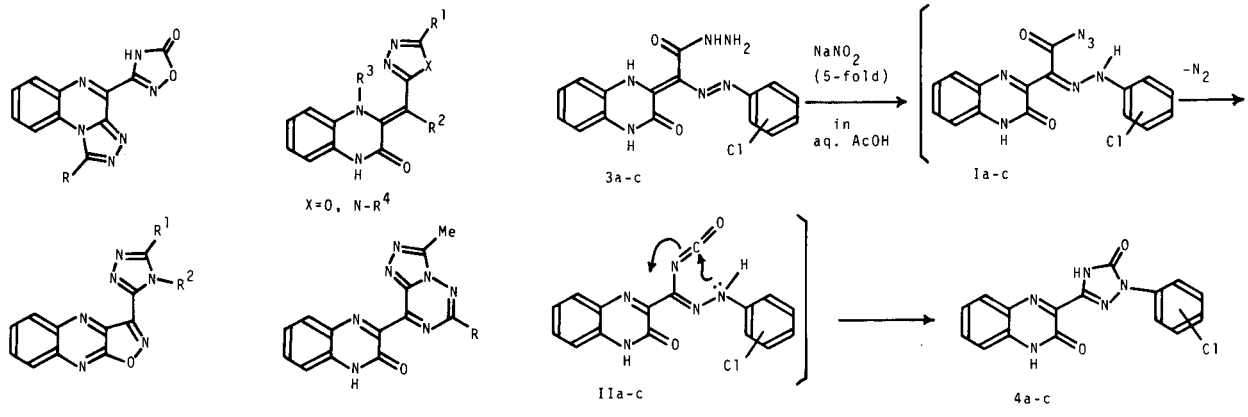
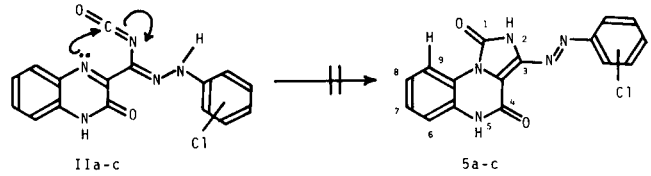


CHART 1

continuation of the above works, we have found a new route to the synthesis of the 1-aryl-3-quinoxalinyl-1,2,4-triazol-5-ones **4a-c**. This paper describes a new method for the synthesis of the novel 1,2,4-triazoles **4a-c**.

The reactions of the ester 1 with aryl diazonium salts resulted in the methylenic C-diazotization [1-9] to give the α-aryldiazenylesters **2a-c**, whose reactions with hydrazine hydrate afforded the α-aryldiazenylhydrazides **3a-c**. The reactions of **3a-c** with nitrous acid effected the Curtius rearrangement [2,10] to provide the 1,2,4-triazoles **4a-c**, presumably via intermediates Ia-c and IIa-c. These results are formulated in Scheme 1.

SCHEME 1



SCHEME 2

The above intermediates IIa-c predominantly cyclized into the 1,2,4-triazoles **4a-c** under the present reaction conditions, which would not favor the cyclizations of IIa-c into the imidazo[1,2-*a*]quinoxalines **5a-c** (Scheme 2). Whereas the pmr spectra of **5a-c** were expected to exhibit the C⁹-H proton signals in much lower magnetic fields than the other aromatic proton signals due to anisotropy by the adjacent C=O groups [10-12], the pmr spectra of **4a-c** did not display the above anisotropy, but showed all the aromatic proton signals as one-grouped multiplets. Therefore, these pmr spectral data reasonably support the structures **4a-c**.

EXPERIMENTAL

General Procedure.

3-[α-(*o*-Chlorophenyldiazenyl)methoxycarbonylmethylene]-2-oxo-1,2,3,4-tetrahydroquinoxaline (**2a**).

A solution of sodium nitrite (6.9 g, 0.10 mole) in water (50 ml) was added to a suspension of *o*-chloroaniline hydrochloride (19.56 g, 0.12 mole) in 10% hydrochloric acid (50 ml)/water (100 ml) with stirring in an ice-water bath to give a clear solution , which was added to a suspension of **1** (20 g, 0.092 mole) in acetic acid (100 ml)/water (200 ml) with stirring in an ice-water bath to precipitate yellow crystals **2a**. Stirring was continued for additional 10 minutes. The suspension was heated on a boiling water bath for 30 minutes. After the reaction mixture was cooled to room temperature, the yellow crystals **2a** were collected by suction filtration (29.3 g, 90%).

Compounds **2b** (19.49 g, 60%) and **2c** (20.46 g, 63%) were obtained by a similar manner to the above.

Recrystallization from *N,N*-dimethylformamide/ethanol gave orange needles **2a-c**, mp 241-242° (**2a**), 240-241° (**2b**), 250-251° (**2c**); ir: ν cm^{-1} 1720, 1665 (**2a**), 1745, 1665 (**2b**), 1720, 1665 (**2c**); ms: m/z 356 (M^+), 358 ($M^+ + 2$) (**2a-c**); pmr (deuteriodimethylsulfoxide): δ 13.72 (s, 1H, NH), 12.83 (s, 1H, NH), 8.00-6.93 (m, 8H, aromatic), 3.83 (s, 3H, Me) (**2a**): δ 12.67 (s, 1H, NH), 11.15 (s, 1H, NH), 8.00-6.90 (m, 8H, aromatic), 3.75 (s, 3H, Me) (**2b**): δ 12.64 (s, 1H, NH), 11.17 (s, 1H, NH), 8.00-7.17 (m, 8H, aromatic), 3.73 (s, 3H, Me) (**2c**).

Anal. Calcd for $C_{17}H_{13}ClN_4O_3$: C, 57.23; H, 3.67; N, 15.70. Found: C, 57.11; H, 3.51; N, 15.89 (**2a**): C, 57.21; H, 3.55; N, 15.81 (**2b**): C, 57.10; H, 3.61; N, 15.80 (**2c**).

3-[α-(*o*-Chlorophenyldiazenyl)hydrazinocarbonylmethylene]-2-oxo-1,2,3,4-tetrahydroquinoxaline (**3a**).

A suspension of **2a** (10 g, 0.028 mole) and hydrazine hydrate (14 g, 0.28 mole) in ethanol (500 ml) was refluxed on a boiling water bath for 3 hours to precipitate yellow needles **3a** as hydrazinium salt, which was collected by suction filtration (9.38 g). The filtrate was evaporated *in vacuo* to provide an additional product **3a** (1.25 g). Total yield, 10.63 g (98%).

Compounds **3b** (hydrazinium salt) (8.41 g, 77%) and **3c** (free base) (7.97 g, 80%) were obtained by a similar manner to the above.

Trituration with hot ethanol gave analytically pure yellow needles **3a-c**, mp 325-326° (**3a**), 289-290° (**3b**), 308-309° (**3c**); ir: ν cm^{-1} 3250, 1580 (**3a**), 3250, 1585 (**3b**), 3250, 1665 (**3c**); ms: m/z 356 (M^+), 358 ($M^+ + 2$) (**3a-c**); pmr (deuteriodimethylsulfoxide): δ 8.00-6.70 (m, 8H, aromatic), 5.27 (br, NH and H_2O) (**3a**): δ 9.33 (br, 1H, NH), 8.00-6.67 (m, 8H, aromatic), 5.37 (br, NH and H_2O) (**3b**): δ 10.53 (s, 1H, NH), 9.43 (s, 1H, NH), 8.00-7.17 (m, 8H, aromatic), other NH proton signals were overlapped with aromatic proton signals (**3c**).

Anal. Calcd for $C_{16}H_{17}ClN_8O_2$ (**3a,b**): C, 49.43; H, 4.41; N, 28.82. Found: C, 49.72; H, 4.36; N, 28.83 (**3a**): C, 49.48; H, 4.31; N, 28.56 (**3b**).

Anal. Calcd for $C_{16}H_{13}ClN_6O_2$ (**3c**): C, 53.87; H, 3.67; N, 23.56. Found: C, 53.96; H, 3.64; N, 23.28 (**3c**).

1-(*o*-Chlorophenyl)-3-(3-oxo-3,4-dihydroquinoxalin-2-yl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one (**4a**)

A solution of sodium nitrite (2.66 g, 0.039 mole) in water (30 ml) was added to a suspension of **3a** (3 g, 0.0077 mole) in acetic acid (100 ml)/water (20 ml) with stirring in an ice-water bath. The suspension was heated on a boiling water bath for 2 hours to precipitate yellow crystals **4a**, which were collected by suction filtration (1.06 g). Evaporation of the filtrate *in vacuo* to provide an additional product **4a** (1.45 g). Total yield, 2.51 g (88%).

Compounds **4b** (1.82 g, 64%) and **4c** (1.52 g, 53%) were obtained by a similar manner to the above.

Trituration with hot *N,N*-dimethylformamide/ethanol gave analytically pure samples **4a-c**, mp 334° dec (**4a**), above 350° (**4b**), above 350° (**4c**), ir: ν cm^{-1} 1680 (**4a**), 1695, 1660 (**4b**), 1695, 1660 (**4c**); ms: m/z 339 (M^+), 341 ($M^+ + 2$) (**4a-c**); pmr (deuteriodimethylsulfoxide): δ 12.83 (s, 1H, NH), 12.30 (s, 1H, NH), 8.10-6.83 (m, 8H, aromatic) (**4a**); (trifluoroacetic acid): δ 8.33-7.33 (m, 8H, aromatic) (**4b**); (trifluoroacetic acid): δ 8.33-7.33 (m, 8H, aromatic) (**4c**). NH proton signals were not observed in **4b** and **4c**.

Anal. Calcd for $C_{16}H_{10}ClN_5O_2$: C, 56.57; H, 2.97; N, 20.73. Found: C, 56.67; H, 3.05; N, 20.62 (**4a**): C, 56.40; H, 2.85; N, 20.73 (**4b**): C, 56.72; H, 2.88; N, 20.88 (**4c**).

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