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Received March 7, 1990

The title compound was synthesized *via* 1,3-dipolar cycloaddition of diazoacetonitrile and diethyl fumarate.

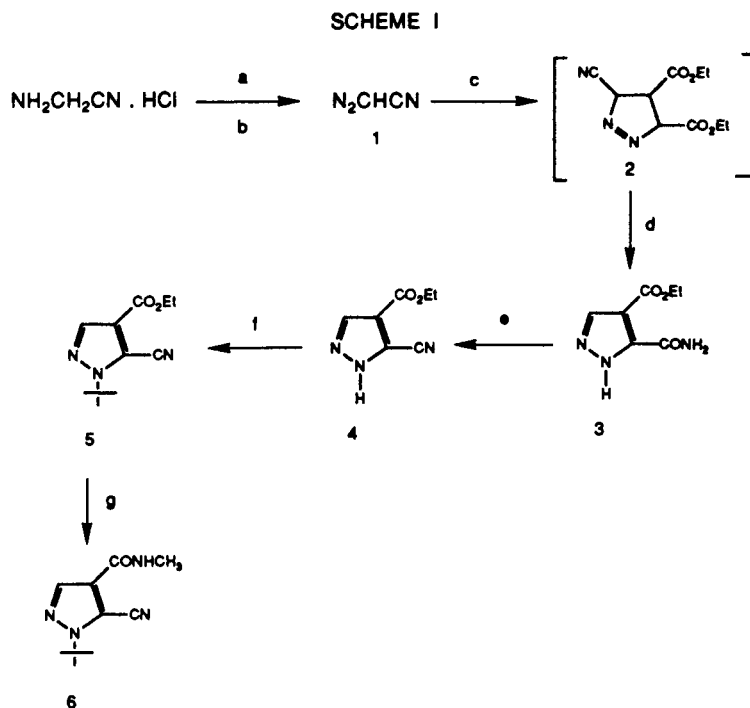
*J. Heterocyclic Chem.*, **27**, 1655 (1990).

Various substituted pyrazole derivatives are outstanding herbicides [1-3], and novel syntheses for these compounds are constantly being sought [4-7]. Following our previous report [6] in which we brought to light the use of isobutylene as a useful reagent to prepare regiospecific *t*-butylpyrazole, we have now exploited the potential of diazoacetonitrile to synthesize 5-cyano-1-(1,1-dimethylethyl)-*N*-methyl-1*H*-pyrazole-4-carboxamide (**6**).

Numerous studies have been reported in the literature that 3-substituted pyrazolines were formed as the major products in the 1,3-dipolar cycloadditions of diazo compounds with alkenes [8]. Pechman and Manck prepared the dipotassium diazomethane disulfonate from the potassium salt of aminomethionate which in turn was prepared from potassium cyanide and potassium bisulfite [9]. The

disulfonate was reacted with acrylonitrile to afford pyrazoline cyanosulfonate [10]. Pitlik *et al.* recently reported that the initially formed pyrazoline from *exo*-2-methylenecephem and diphenyldiazomethane decomposed to form spirocyclopropyl cephalosporin [11]. Kalvoda reported that the reaction of esters of 3-cyano-2-propanoic acids with diazo compounds afforded pyrazoles with simultaneous elimination of hydrogen cyanide [12].

We report herein a convenient two-step synthesis of **6** *via* 1,3-dipolar cycloaddition of diazoacetonitrile and diethyl fumarate. Our synthetic strategy began with diazoacetonitrile **1** which was prepared from aminoacetonitrile hydrochloride and sodium nitrite in water and ethyl acetate. Reaction of **1** with diethyl fumarate provided the pyrazoline intermediate **2** which was not isolated, but instead



a.  $\text{NaNO}_2$ ; b.  $\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5$ ; c. Di-Ethyl Fumarate; d.  $\text{NH}_4\text{OH}$ ; e.  $\text{POCl}_3, \text{K}_2\text{CO}_3$ ; f. Isobutylene; g.  $\text{CH}_3\text{NH}_2$

reacted with ammonium hydroxide (dehydrocyanation and amidation) to afford **3** in 78% yield from aminoacetonitrile. A slightly lower yield of **3** was obtained when diethyl maleate was employed in the same reaction. Completion of the synthesis was accomplished by the established protocol [6]. Thus, treatment of **3** with phosphorus oxychloride gave the corresponding pyrazole cyano ester **4**, which was not isolated, but was reacted with isobutylene to provide the desired *t*-butyl pyrazole cyano ester **5**. Finally, the solution containing **5** was reacted with 40% aqueous methylamine to produce **6** in 65% yield from **4** (Scheme 1). The overall yield was 51% from aminoacetonitrile hydrochloride.

In conclusion, we have developed an economical, efficient synthesis of **6** via 1,3-dipolar cycloaddition of diazoacetonitrile and diethyl fumarate. Our experimental results led us to conclude that the pyrazoline intermediate **2** was produced initially, followed by elimination of hydrogen cyanide, to form the desired pyrazole **3**. However, formation of cyclopropane although not observed, could not be ruled out as a possible side reaction.

The regiochemistry of the 1,3-dipolar cycloaddition reaction is an interesting topic that brings both electronic and steric effects into consideration. The most generally accepted interpretation of the regiochemical results has been based on frontier orbital concepts. A theoretical approach (MNDO, AMI) concerning the results of this methodology will be the subject of future publication.

## EXPERIMENTAL

### 5-Aminocarbonyl-1*H*-pyrazole-4-carboxylic Acid Ethyl Ester (**3**).

To a cold slurry (0°) containing 46.3 g (0.5 mole) of aminoacetonitrile hydrochloride and 33 ml (0.2 mole) of diethyl fumarate in 200 ml of ethyl acetate, was added a solution containing sodium nitrite (34.5 g, 0.5 mole) and 90 ml of water while the temperature of the reaction mixture was maintained between 0-5°. The reaction mixture was allowed to come to room temperature and was stirred for 3 hours. The layers were separated and the organic layer was stirred at ambient temperature for 16 hours. To this solution was added 104 ml of concentrated ammonium hydroxide, and the resulting slurry was stirred at ambient temperature for 16 hours. The solid was collected, washed with methanol (5

ml), and dried at 40° *in vacuo* to afford 25.5 g (78%) of **3**, mp > 300°; <sup>1</sup>H nmr (300 MHz, DMSO-d<sub>6</sub>, tetramethylsilane): δ 1.3 (t, 3H, CH<sub>3</sub>, J = 7 Hz), 4.3 (q, 2H, CH<sub>2</sub>, J = 7 Hz), 8.05 (s, 2H, NH<sub>2</sub>), 9.05 (s, 1H, CH).

*Anal.* Calcd. for C<sub>7</sub>H<sub>9</sub>N<sub>3</sub>O<sub>3</sub>: C, 45.90; H, 4.95; N, 22.94. Found: C, 45.66; H, 5.06; N, 23.21.

### 5-Cyano-1-(1,1-dimethylethyl)-*N*-methyl-1*H*-pyrazole-4-carboxamide (**6**).

To a suspension containing **3** (28.3 g, 0.16 mole) and potassium carbonate (7.1 g, 0.052 mole) in 160 ml of acetonitrile was added phosphorus oxychloride (11 ml). The reaction mixture was refluxed for 3.5 hours, cooled to room temperature, and filtered. To the cold filtrate (dry ice/acetone) placed in a Parr bottle was added 62 ml (0.62 mole) of isobutylene and 9.8 g (0.052 mole) of *p*-toluenesulfonic acid monohydrate. The solution was refluxed for 16 hours, cooled, and excess isobutylene was slowly vented. The reaction mixture was filtered, and the solvent was removed *in vacuo* to afford an oil which was dissolved in 25 ml of methanol and 73 ml of 40% aqueous methylamine. The resulting solution was stirred at room temperature for 16 hours and water (35 ml) was added. The resulting solid was collected to yield 20.9 g (65.2%) of **6**, mp 162-165°, lit mp 163-165° [6].

### Acknowledgement.

We thank the Lilly Molecular Structure Research Laboratory for providing the spectroscopic and analytical data.

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