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# A NOVEL PREPARATION OF POLARIZED ETHYLENES BY THE REACTION OF THIOAMIDES OR DITHIOCARBOXYLATES WITH TETRACYANOETHYLENE OXIDE. SYNTHESIS OF PYRAZOLES AND PYRIMIDINES

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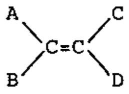
*Abstract* - Polarized ethylenes having both electron-donating (an amino or a methylthio group) and electron-accepting (two cyano groups) groups on the adjacent two olefinic carbon atoms were prepared by the reaction of thioamides or methyl dithiocarboxylates with tetracyanoethylene oxide in good yields. Reactions of these polarized ethylenes with hydrazine or guanidine carbonate gave the corresponding pyrazole and pyrimidine derivatives in good yields.

Ethylenes having electron-donating groups on an olefinic carbon atom and electron-accepting groups on another carbon atom of the olefin are one of the most important and interesting compounds from both synthetic and theoretical points of view.[1] Among these compounds, for example, ketene dithioacetals,[2,3] ethoxymethylene compounds,[4] and aminomethylene compounds[5] are widely used for the preparation of heterocyclic compounds.



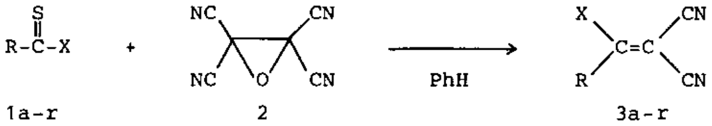
A and/or B; MeS, EtO, $R_2N$, etc.

C and/or D; CN, COOMe, $NO_2$, $SO_2R$, etc.

Although it has been reported that the reaction of thiocarbonyl derivatives with tetracyanoethylene oxide give stable thiocarbonyl ylides, thiazoles, and dicyanomethylene compounds,[6-9] the preparation of the polarized ethylenes using dicyanomethylenation with tetracyanoethylene oxide has been unknown hitherto. We now wish to report a novel and simple preparation of polarized ethylenes bearing push-pull substituents (an amino and a methylthio, and two cyano groups on each of olefinic carbon atoms, respectively) by the reaction of thioamides or methyl dithiocarboxylates with tetracyanoethylene oxide.
Thioamides (1a-j), readily available by the Willgerodt-Kindler reaction[10-12],

were allowed to react with tetracyanoethylene oxide at room temperature in benzene with stirring to give the corresponding dicyanoethylene compounds (3a-j) very smoothly. Moreover the reaction of methyl dithiocarboxylates (1k-r) with tetracyanoethylene oxide also occurred under the similar conditions to yield the corresponding 2-methylthio-1,1-dicyanoethylene derivatives (3k-r) in good yields. The results are listed in Table 1.

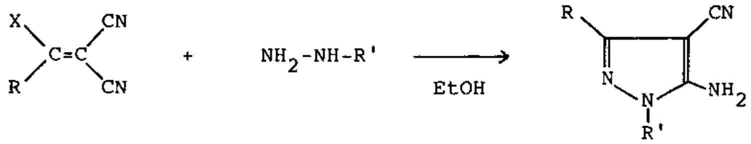
Table 1. Reactions of thioamides and dithiocarboxylates with tetracyanoethylene oxide



| Product (3) | R | X | mp(°C) | % Yield |
|---|---|---|---|---|
| 3a: | $C_6H_5$ | morpholino | 178 | 69 |
| b: | o-MeO-$C_6H_4$ | morpholino | 95 | 91 |
| c: | p-MeO-$C_6H_4$ | morpholino | 114 | 84 |
| d: | p-Cl-$C_6H_4$ | morpholino | 153 | 85 |
| e: | 3,4-$(MeO)_2$-$C_6H_3$ | morpholino | 151 | 90 |
| f: | 3,4-O-$CH_2$-O-$C_6H_3$ | morpholino | 187 | 82 |
| g: | 2-thienyl | morpholino | 145 | 88 |
| h: | $C_6H_5$-$CH_2$ | morpholino | 113 | 77 |
| i: | p-Me-$C_6H_4$-$CH_2$ | morpholino | 120 | 75 |
| j: | $C_6H_5$-$CH_2CH_2$ | morpholino | 111 | 79 |
| k: | methylthio | morpholino | 121 | 62 |
| l: | $C_6H_5$ | methylthio | 95 | 78 |
| m: | o-MeO-$C_6H_4$ | methylthio | 75 | 67 |
| n: | p-MeO-$C_6H_4$ | methylthio | 95 | 72 |
| o: | p-Cl-$C_6H_4$ | methylthio | 155 | 82 |
| p: | p-$Me_2N$-$C_6H_4$ | methylthio | 116 | 91 |
| q: | 2-thienyl | methylthio | 102 | 78 |
| r: | $C_6H_5$-$CH_2$ | methylthio | oil | 68 |

It is well known that the reaction of polarized ethylenes like ketene dithioacetals with bifunctionalized amines such as hydrazine or amidine derivatives gives the corresponding pyrazole or pyrimidine derivatives.[13] The heterocyclic compounds, thus obtained, are not only interesting from a viewpoint of biological activities but also important and useful as the starting materials for the conversion to other heterocyclic compounds.[13,16] Therefore, we attempted to prepare pyrazole and pyrimidine derivatives using 3a-r. Reactions of 3a-f, 3h, 3i with hydrazine hydrate gave the corresponding 3-substituted 5-amino-4-cyanopyrazole derivatives (4a-h) on heating at 100°C for 5 h in good yields. In contrast, reactions of morpholino compounds (3a-k) with phenylhydrazine did not occur under the similar conditions. However this problem can be readily solved by the use of methylthioethylenic compounds (3l-r) instead of 3a-k since dicyanoethylenes bearing the methylthio group is generally more active toward nucleophiles than those of the morpholino group. Namely, reactions of 3e, 3j, 3o with phenylhydrazine gave the corresponding 5-amino-1-aryl-4-cyanopyrazoles (4i-k) at reflux for 1 h in ethanol, as illustrated in Table 2.

Table 2. Synthesis of 5-amino-1-aryl-4-cyanopyrazole derivatives (4)



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4a-k

| Product (4) | R | R' | mp(°C) | % Yield |
|---|---|---|---|---|
| 4a: | $C_6H_5$ | H | 203 | 74 |
| b: | o-MeO-$C_6H_4$ | H | 192 | 88 |
| c: | p-MeO-$C_6H_4$ | H | 158 | 69 |
| d: | p-Cl-$C_6H_4$ | H | 221 | 82 |
| e: | 3,4-O-$CH_2$-O-$C_6H_3$ | H | 215 | 65 |
| f: | 3,4-$(MeO)_2$-$C_6H_3$ | H | 175 | 51 |
| g: | $C_6H_5$-$CH_2$ | H | 141 | 98 |
| h: | p-Me-$C_6H_4$-$CH_2$ | H | 162 | 98 |
| i: | $C_6H_5$ | $C_6H_5$ | 160 | 46 |
| j: | p-MeO-$C_6H_4$ | $C_6H_5$ | 190 | 43 |
| k: | p-Cl-$C_6H_4$ | $C_6H_5$ | 189 | 64 |

Reactions of 3a-d, 3g, 3h with guanidine carbonate on heating at 200°C for 2 h gave the corresponding 2,4-diamino-5-cyanopyrimidine derivatives (5a-e) in 52-96% yield. The results are summarized in Table 3.

In conclusion, the utility of the present method for preparing polarized ethylenes (3) which were otherwise inaccessible was mostly displayed by readily availability of starting materials and simple manipulation of the conversion. The activated ethylenes (3) are also very useful reagents for the preparation of a variety of heterocyclic compounds such as pyrazoles and pyrimidines.

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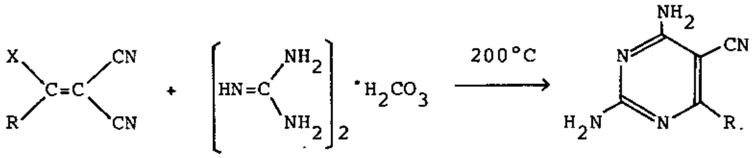
Table 3. Synthesis of 2,4-diamino-6-aryl-5-cyanopyrimidines (5)



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5a-f

| Product (5) | R | mp(°C) | % Yield |
|---|---|---|---|
| 5a: | $C_6H_5$ | 300 | 85 |
| b: | p-MeO-$C_6H_4$ | 245 | 83 |
| c: | p-Cl-$C_6H_4$ | 281 | 90 |
| d: | o-MeO-$C_6H_4$ | 218 | 70 |
| e: | 2-thienyl | 236 | 71 |
| f: | $C_6H_5$-$CH_2$ | 228 | 52 |

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