THE REACTIVITY OF 2-FORMYLThIOPHENE, 1-METHYL-2-FORMYPYRROLE,  
BENZALDEHYDE AND 2-FORMYLFURANE N,N-DIMETHYLDHYRAZONES WITH  
DIMETHYL ACETYLENEDICARBOXYLATE

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Abstract—N,N-Dimethylhydrazones derived from 2-formylthiophene,  
benzaldehyde, and 1-methyl-2-formylpyrrole react with dimethyl  
acetylenedicarboxylate (DMAD), giving the corresponding nitriles.  
The reaction with furfural N,N-dimethylhydrazone takes place via  
the intermediacy of a Diels-Alder adduct with the furan ring.

It has been shown recently\(^1\) that although 1-aza-1,3-dienes are reluctant to  
participate in Diels-Alder reactions, these systems with an appropriate sub-
stitution can react with electron-poor dienophiles affording the corresponding  
cycloadducts. Looking at this new possibility of synthesis of heterocycles and  
as an extension of our studies on the reactivity, as 1,3-dienes of five mem-
ered heterocyclic compounds bearing olefinic substituents,\(^2\) we have prepared the  
N,N-dimethylhydrazones 1, 2, 3, and 4 and we have studied their reactivity with  
DMAD.

The reaction of the N,N-dimethylhydrazone 1 with DMAD was carried out in  
chloroform or toluene at reflux temperature affording 2-thienylnitrile 5 and  
another compound identified as the aminodiester 6 by spectroscopic analysis.\(^3\)  
No Diels-Alder cycloaddition compounds were found in the crude mixture.  
The same reaction with benzaldehyde N,N-dimethylhydrazone 2 gave the cor-
responding nitrile.
When the hydrazone 3 in chloroform was mixed with DMAD at room temperature, the Michael addition reaction took place and the adducts 7a and 7b, from attack at Cα, could be isolated with good yields. The same reaction with two moles of DMAD at reflux temperature afforded a mixture of the E/Z isomers 8a and 8b, that could be separated chromatographically. Here again the aminoester 6 was isolated from the reaction mixture.

Hydrazones have the well-known capacity to react with electrophilic reagents at either of the three nucleophilic centers, the amino nitrogen, the imino nitrogen and the imino carbon. However when α,β-unsaturated N,N-dimethylhydrazones react with electron-poor dienophiles giving cycloaddition compounds, the mechanism of the reaction involve the initial attack of the Cα to the electrophile, because of the reversed polarity of these 1-amino-1-aza-1,3-diene systems.

Our experiments with the N,N-dimethylhydrazones 1, 2, and 3 have shown that these compounds react with DMAD by the amino nitrogen and afford nitriles as a
result of the elimination of the aminodiester 6 through a six-membered intermediate 9.

Although many methods are described for the synthesis of nitriles from aldehyde hydrazones as starting materials, the acetylenic esters were never used as reagents for this conversion, so the present work provides a new route for the synthesis of these compounds.

In complete contrast with the hydrazones 1, 2, and 3, the 2-formylfuran N,N-dimethylhydrazone 4 reacts with DMAD in chloroform at reflux temperature to give a major compound 10 through a Diels-Alder cycloaddition to the furan ring in a similar way as it has been reported by Potts* in the reaction with maleic anhydride. Small amounts of 2-furylcarbonitrile 11 and the aminodiester 6 were isolated as a result of a competing reaction of the dimethylhydrazone group. Nevertheless, it was not possible to detect any amount of the corresponding nitrile 12.

Reactions with another dienophiles are in progress.

EXPERIMENTAL

'H and 'C nmr spectra were measured for ca. 40% solutions in CDCl₃ using a Bruker WP-80. Ir were determined in CCl₄ with a Perkin-Elmer 843 spectrometer. Melting points are uncorrected and were determined with a Kofler hot-stage apparatus. Combustion analyses were performed at the Instituto de Química Orgánica of the CSIC (Barcelona).

Reaction of N,N-Dimethylhydrazones with DMAD. General Procedure.

DMAD (0.005 mol) in chloroform or toluene (10 ml) was added at room temperature to a solution of the corresponding N,N-dimethylhydrazone (0.005 mol) in chloroform or toluene (10 ml). Then the mixture was heated at reflux temperature for
30-40 h until disappearance of the starting material. Evaporation of the solvent gave a crude product which was purified by column chromatography.

2-Formylthiophene N,N-dimethylhydrazone: Elution of the crude product (1.4 g) with hexane-ethyl acetate (5:1) gave 2-thienylcarbonitrile 5 (0.45 g, 62%) and diethyl 2-dimethylaminomaleate 6 (0.7 g).

Benzaldehyde N,N-dimethylhydrazone: Column chromatography of the crude product (1.3 g) with hexane-ethyl acetate (5:1) gave benzonitrile (0.33 g, 66%) and the adduct 6 (0.6 g).

1-Methyl-2-formylpyrrole N,N-dimethylhydrazone:

a) At room temperature. The reaction of DMAD (0.72 g, 0.005 mol) with the hydrazone 3 (0.75 g, 0.005 mol) in chloroform (20 ml) took place at room temperature when the mixture was stirred for 3 h. Evaporation of the solvent in vacuo and column chromatography with hexane-ethyl acetate (5:1) gave the adduct 7b (0.45 g, 30%) as an oil. Anal. Calc. for C₁₁H₁₁N₂O₄: C, 57.33; H, 6.48; N, 14.33. Found: C, 57.29; H, 6.57; N, 14.27. 1H-nmr 7.1 (s, 1H), 6.75 (s, 1H), 6.0 (d, J=3Hz, 1H), 5.9 (d, J=3Hz, 1H), 3.75 (s, 3H), 3.6 (s, 6H), 2.85 (s, 6H). Further elution gave the isomer 7a (0.42 g, 27.5%), mp 112-113 °C (yellow needles, recrystallized from hexane): Found: C, 57.52; H, 6.78; N, 14.38. 1H-nmr 6.95 (s, 1H), 6.2 (d, J=4Hz, 1H), 6.0 (d, J=4Hz, 1H), 3.85 (s, 3H), 3.7 (s, 3H), 3.6 (s, 3H), 2.85 (s, 6H, NMe₂).

b) At reflux temperature. The reaction of DMAD (1.5 g, 0.1 mol) with the hydrazone 3 in chloroform (20 ml) at reflux temperature and working up as above gave a syrup which was chromatographed using hexane-ethyl acetate (9:1). The first compound eluted was the nitrile 8b (0.28 g, 21.5%) as an oil. Anal. Calc. for C₁₁H₁₁N₂O₄: C, 58.06; H, 4.83; N, 11.29. Found: C, 58.19; H, 4.81; N, 11.05. 1H-nmr 7.2 (s, 1H), 6.75 (s, 1H), 6.0 (d, J=3Hz, 1H), 5.9 (d, J=3Hz, 1H), 3.85 (s, 3H), 3.7 (s, 3H), 3.6 (s, 3H). Further elution gave the isomer 8a (0.2 g, 15.4%), mp 102-103 °C (colorless needles, recrystallized from hexane-dichloromethane): Found: C, 57.9; H, 4.7; N, 11.08. 1H-nmr 6.7 (d, J=4Hz, 1H), 6.3 (d, J=4Hz, 1H), 6.1 (s, 1H), 3.8 (s, 3H), 3.75 (s, 6H).

Furfural N,N-dimethylhydrazone: Chromatography of the crude product obtained after evaporation of the solvent (1.4 g), using hexane-ethyl acetate (5:1) as an eluant gave 2-furylcarbonitrile 11 (0.034 g). The second compound eluted was the adduct 10 (0.467 g, 35%), mp 60-61 °C (yellow needles recrystallized from hexane-dichloromethane): Found: C, 57.29; H, 4.78; N, 14.38. 1H-nmr 7.1 (s, 1H), 6.0 (d, J=4Hz, 1H), 5.9 (d, J=4Hz, 1H), 3.85 (s, 3H), 3.7 (s, 3H), 3.6 (s, 3H).
from hexane). Anal. Calc for C_{12}H_{12}N_{2}O_{4}: C, 55.86; H, 5.66; N, 9.81. Found: C, 55.71; H, 5.71; N, 10.0. IR 1733 cm\(^{-1}\). \(^{1}H\)-nmr 11.10-10.5 (bs, 1H), 7.75 (d, J=9Hz, 1H), 6.75 (d, J=9Hz, 1H), 6.7 (s, 1H), 3.7 (s, 6H), 2.8 (s, 6H). \(^{13}C\)-nmr 169.2 (s), 168.7 (s), 160.7 (s), 152.6 (q), 127.2 (d), 126.2 (s), 119.2 (d), 108.8 (s), 52.6 (q), 52.0 (q), 42.3 (q). Further elution gave the starting material 4 (0.26 g) and then the amino compound 6 (0.53 g).

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REFERENCES


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