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# THE DIELS-ALDER REACTION OF THIOPHENE

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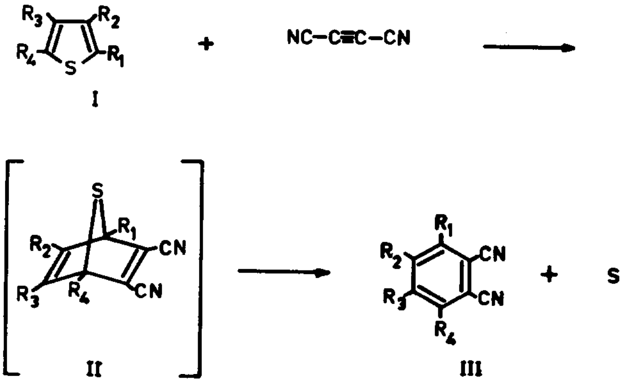
Several unsuccessful attempts to affect Diels-Alder reactions with thiophenes have been reported in the literature.[1] As a consequence the statement "Thiophene does not undergo Diels-Alder reactions" has found its way into virtually all textbooks.[2]

In contradiction to the above reports we have found that a variety of thiophenes react smoothly with dicyanoacetylene[3] in a Diels-Alder manner to produce phthalonitriles in reasonable yields:



| thiophenes (I) | conditions | yield[4] | m.p. phthalonitriles (III)[5] |
|---|---|---|---|
| a. $R_1 = R_4 = CH_3$, $R_2 = tert.C_4H_9$, $R_3 = H$ | 10 hr. 60° | 51% | 144 -144.5° |
| b. $R_1 = R_4 = CH_3$, $R_2 = R_3 = H$ | 12 hr. 100° | 49% | 162.5-163° |
| c. $R_1 = R_4 = H$, $R_2 = R_3 = C_6H_5$ | 72 hr. 100° | 18% | 176.5-177° |
| d. $R_1 = CH_3$, $R_2 = R_3 = R_4 = H$ | 44 hr. 80° | 9% | 144.5-145.5° |
| e. $R_1 = R_2 = R_3 = R_4 = H$ | 48 hr. 120° | 8% | 139 -140.5° |

Thus 2,5-dimethylthiophene (Ib), upon heating for 12 hours in a closed tube at 100° with an excess of freshly prepared dicyanoacetylene[3] furnishes 3,6-dimethylphthalonitrile (IIIb) in 49% yield. In addition to the normal spectral and analytical support for the structure of the product (IIIb), hydrolysis of this dinitrile (IIIb) furnished an anhydride m.p. 143° whose spectral properties agreed in all respects with those reported[6] for 3,6-dimethylphthalic anhydride (lit.[6a] m.p. 143°).

As was already noted by Kloetzel[7], the presence of alkyl substituents activates an aromatic hydrocarbon towards the Diels-Alder reaction with an appropriate dienophile. In our case both the yields as well as the reaction conditions are in agreement with this finding (see table).

Several features make the Diels-Alder reaction of thiophenes with dicyanoacetylene of considerable interest. In sharp contrast to the Diels-Alder addition to furans, it is evident that our thiophene reaction becomes irreversible through the facile loss of a small stable moiety (sulfur).[8] In this respect the reaction resembles the Diels-Alder addition to tetraphenylcyclopentadienone (-CO).[8a]

A wide variety of alkylthiophenes can be prepared in good yields.[9] The same cannot be said for the corresponding furans, cyclopentadienones or even butadienes. Thus the Diels-Alder reaction of alkylthiophenes with dicyanoacetylene will be a valuable new route to alkylated phthalonitriles and derivatives.[10]

The extrusion of sulfur, possibly from a bicyclic intermediate (II) warrants further study and attempts are being made to isolate an appropriately substituted 7-thiabicyclo[2.2.1] hepta-2,5-diene (II). Mechanistically it is intriguing to note that sulfur has been shown to react with acetylenic dienophiles.[11a] Thus it is not unlikely that the dicyanoacetylene fulfils a double role in this reaction. Finally it is worthy to note that the formation of a stable benzenoid system - an important driving force in this reaction - is achieved without dehydrogenation using an acetylenic dienophile.

We will return to a discussion of the mechanistic aspects after more experimental facts are known.[11]

## REFERENCES

1. a. Unsuccessful attempts include inter alia the reaction of tetramethylthiophene with maleic anhydride.

   R. Gaertner and R.G. Tonkyn, J. Amer. Chem. Soc., **73**, 5872 (1951).

   b. The one successful Diels-Alder reaction recorded previously appears to be that of thiophene with tetrafluorobenzyne furnishing the corresponding naphthalene in 40% yield.

   D.D. Callander, P.L. Coe and J.C. Tatlow, Chem. Comm., 143 (1966).

   c. Diels-Alder additions to thiophenes which are part of a condensed system have been known for about thirty years and are not considered here.

   D.B. Clapp, J. Amer. Chem. Soc., **61**, 2733 (1939);

   C.F.H. Allen and J.W. Gates Jr., J. Amer. Chem. Soc., **65**, 1283 (1943).

2. For very recent examples see:

   N.L. Allinger, M.P. Cava, D.C. De Jongh, C.R. Johnson, N.A. Lebel and C.L. Stevens, "Organic Chemistry", Worth Publishers, Inc., New York, 1971, p. 727.

   P.J. Garratt, "Aromaticity", McGraw-Hill Book Company (UK) Limited, 1971, p. 122.

3. a. A.T. Blomquist and E.C. Winslow, J. Org. Chem., **10**, 149 (1945);

   b. E. Ciganek and C.G. Krespan, J. Org. Chem., **33**, 541 (1968).

4. In this preliminary study no attempts were made to optimize the yields.

5. All new compounds gave satisfactory analytical results.

6. a. J. Polonsky, C. Fouquey and M.A. Gaudemer, Bull. Soc. Chim. France, 1255 (1962).

   b. J.S. Scarpa, M. Ribi and C.H. Eugster, Helv. Chim. Acta, **49**, 858 (1966).

   Polonsky[6a] and Scarpa[6b] give different ultraviolet spectra for 3,6-dimethylphthalic anhydride. The ultraviolet spectrum that we found corresponded to that given by Scarpa.[6b]

7. M.C. Kloetzel and H.L. Herzog, J. Amer. Chem. Soc., **72**, 1991 (1950).

8. For reviews on extrusion reactions see:

   a. B.P. Stark and A.J. Duke, "Extrusion Reactions", Pergamon Press Ltd., Oxford, 1967;

   b. J.D. Loudon in "Organic Sulfur Compounds", Vol. I, Edited by N. Kharasch, Pergamon Press, Oxford, 1961, p. 299.

9. a. H.D. Hartough, "Thiophene and Its Derivatives", Interscience, New York, 1952, p. 47.

   b. S. Gronowitz, "Recent Advances in the Chemistry of Thiophenes",

Vol. I of "Advances in Heterocyclic Chemistry", Edited by A.R. Katritzky, Academic Press, New York and London, 1963, p. 1.

10. We have found no steric limitation to the reaction thus far; tetramethylthiophene reacted with dicyanoacetylene to furnish the corresponding tetramethylphthalonitrile, Mr. E.J. Kwak, (unpublished results).

11. a. A. Michael, Chem. Ber., 28, 1633 (1895);

    b. W.A. Pryor, "Mechanisms of Sulfur Reactions", McGraw-Hill Book Company, Inc., New York, 1962, p. 117.

    One of the reaction products is sulfur. Michael[11a] isolated the tetramethylester of thiophenetetracarboxylic acid from the reaction mixture of sulfur with dimethyl acetylenedicarboxylate. Furthermore the dehydrogenating action of sulfur on alkylaromatics is well known.[11b]
    This generates hydrogen sulfide which in turn can also react with dicyanoacetylene.[3b]
    The complexity of the detailed mechanism is a challenge indeed.