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THE DIELS-ALDER REACTIONS OF FURANS 1:
THE REACTIONS OF FURANS WITH α-CHLOROACRYONITRILE

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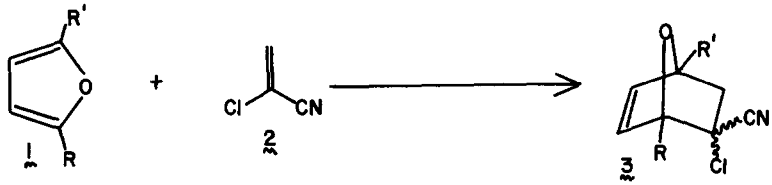
Abstract: The intermolecular Diels-Alder reactions of several furans with α-chloroacrylonitrile occurs at atmospheric pressure. The role of temperature in affecting starting material: product ratio is examined from a preparative viewpoint.

The intermolecular Diels-Alder reactions of furans has been examined in a relatively limited number of cases.[1] Many of these reports deal with the use of very reactive dienophiles.

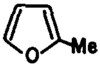
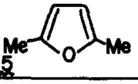
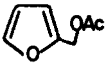
We have been interested for some time in using the intermolecular Diels-Alder reaction of furans (1) with ketene equivalents such as α-chloroacrylonitrile (2) to prepare oxygen containing heterocycles (3). Kotsuki and co-workers[2] have communicated that furans undergo this cycloaddition reaction at very high pressure (30°C; 15 kbar). A more recent report, by Schmidt and co-workers,[3] indicates that the pressure is not necessary for this reaction. This result parallels our own findings. Therefore, herein we report our data on the Diels-Alder reactions of several furans (1) with α-chloroacrylonitrile (2).



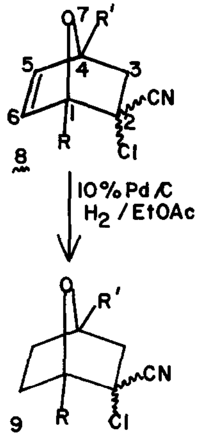
Kienzle[4] has found that acrylonitrile reacts with furan at room temperature to give the Diels-Alder adduct, but that at higher temperatures, lower yields are obtained because the retro Diels-Alder process is predominant. This is reasonable, since entropy considerations would predict that a lower temperature should favor a one particle system over a two particle one in an equilibrium. We felt that this effect might also be felt in Diels-Alder reactions of α-chloroacrylonitrile (2).

We tested this by reacting a series of furans (see Table 1) with an equimolar amount of α-chloroacrylonitrile (2) in NMR tubes (neat). The reactions were run in duplicate and proton NMR spectra taken at intervals. One set of NMR tubes was cooled to the specified temperature at the designated time (see Table 1), and the other maintained at room temperature as a control. The ratios of starting material (furans) to products were determined by relative integral amplitudes of the protons designated in Table 1.

Table 1 Ratio of Furan : Adduct

Furan / Temp. °C(days)	4 	5 	6 	7 
26 (0)	0	0	0	0
26 (9)	1.2:1	1:2.3	>20:1	>20:1
26 (88)	1:1.1	1:2.5	1.5:1	10:1
26 (0-9) 4 (10-37)[1]	1:1.5	1:3	7:1	>20:1
26(0-9) 4 (10-37) -12 (38-88)[2]	1:2.3	1:4	3:1	>20:1
Protons: Furan/Adduct 8	C5H / C4H	C3H / C3H	C2H / C3H	C5H / C3H

1) Ratio at day 37; 2) Ratio at day 88



The ratios shown for the reactions of 2-methylfuran (4) and 2,5-dimethylfuran (5) indicate that the amount of Diels-Alder adduct in the mixture increased at lower reaction temperatures. Furan (6), on the other hand, produced less adduct at lower temperatures. A possible explanation for this is that furan (6) has no electron donating (activating) methyl groups. Therefore, the energy of activation should be higher, and the reaction rate would be correspondingly more sensitive to temperature effects. Acetoxymethylfuran (7) proved to be a relatively poor diene at the temperatures used for these reactions. This may be due to the electron withdrawing (deactivating) influence of the acetoxy group.[5]

The usefulness of these Diels-Alder reactions from a preparative standpoint is illustrated by the following experiments. The furans listed in Table 2 (0.050 moles) were each combined with an equimolar amount of α-chloroacrylonitrile (2) and allowed to stand at the designated temperatures for four weeks. The crude reaction mixtures were hydrogenated,[6] and the products isolated and characterized.[7] The results of these product isolation experiments parallel those of the NMR studies (Table 1).

It is also interesting to note that the ratio of the C-2 epimeric adducts appears to be greatly influenced by the reaction temperature. Much greater stereoselectivity was evidenced in the lower temperature runs for 2-methylfuran (4) and 2,5-dimethylfuran (5) (Table 2).[9]

Table 2

Furan → (Temp. °C)	4 (26)	4 (4)	5 (26)	5 (4)	6 (26)	6 (4)	
Isolated Yield (4 weeks) 1)	52 %	62 %	58%	65%	33 %	7 % 2)	
Isomer Ratio 3)	1.3:1	5.4:1	2.1:1	5.6:1	2.5:1	1.7:1	

1) 0.050 mole scale after hydrogenation (10% Pd on C/EtOAc) and chromatography (50g silica gel; 10% ether in pentane)

2) contains ca. 20% MeCHClC≡N — unable to separate

3) Hewlett-Packard 5750 Gas Chromatograph - 6ft. UC-W98 column ; Flame ionization

In conclusion, our experiments empirically show that temperature can be an important factor in determining the yield of Diels-Alder reactions of furans and α-chloroacrylonitrile. We have also demonstrated that these reactions may be conveniently carried out on a relatively large scale. Although the yields of the adducts are undeniably higher if high pressure is used,[2] the expense of the pressure apparatus and the limited reaction volume of such equipment are serious disadvantages.

Further studies dealing with the use of other furans, as well as other dienophiles, are currently being conducted.

Representative Experimental Procedure: A solution of 26.25g (0.30 moles) of α-chloroacrylonitrile in 60.00g (0.88 moles) of furan was refluxed (32°C) under N_2 for 14d. The mixture was dissolved in 100mL of ethyl acetate and transferred to a Parr Bottle. Catalyst (0.75g of 10% Pd on C) was added and the mixture was hydrogenated at 65 psig of H_2 for 48 hours. The solution was filtered through celite and the filtrate evaporated in vacuo, keeping the evaporator bath temperature <30°C. The residue was distilled in vacuo to give 13.80g (29%) of a light yellow oil 9 (R=R'=H), bp=122-125°C @ 23mm of Hg. The NMR and IR were identical to those of Kotsuki.[2a]

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References

1. a. "Diene Synthesis", by A. Onishchenko, p. 556, English Translation, Daniel Davy and Co., 1964; b. Pelter, A. and Singaram, B. *Tetrahedron Letters* 1982, 245.
2. a. Kotsuki, H. and Nishizawa, H. *Heterocycles* 1981, 16, 1287; b. For a general review of heterocycle synthesis at high pressure see: Matsumoto, K.; Uchida, T. and Acheson, R.M. *Heterocycles* *1981*, *16*, 1367.
3. Schmidt, R.R.; Bietzke, C. and Forrest, A.K. *J. Chem. Soc. Chem. Commun.* *1982*, 909.
4. Kienzle, F. *Helv. Chim. Acta* *1975*, 58, 1180.
5. The Diels-Alder reaction of 2-hydroxymethylfuran with α-chloroacrylonitrile proceeds relatively quickly. However, the adduct appears to undergo an unknown decomposition reaction. Comparable data on this reaction has not yet been obtained.
6. This procedure was followed so that the adducts formed would not re-equilibrate during handling at room temperature. Although some equilibration may place before hydrogenation has occurred, the isolated yields (Table 2) show that this process is not extremely rapid.
7. All compounds exhibited satisfactory NMR, IR, and GC data. NMR and IR data for compound **9**: (R=R'=H) NMR $\delta(CDCl_3)$ (100 MHz) 1.50-2.20 (m, 4H), 2.30-2.95 (m, 2H), 4.60-5.00 (m, 2H); IR (neat) 2255 (C≡N) CM^{-1}; (R=CH_3; R'=H) NMR $\delta(CDCl_3)$ (100 MHz) 1.40-2.20 (m, 4H), 2.35-2.67 (m, 1H), 2.90 (q of d, J=13.5, 6.0 and 2.5 Hz, 1H), 4.65 (t, J=6.0 Hz, 1H); IR (neat) 2245 (C≡N) CM^{-1}; (R=R'=CH_3) NMR $\delta(CDCl_3)$ (100 MHz) 1.40-1.90 (m, 4H), 1.50 (s, 3H), 1.66 (s, 3H), 2.23 (d, J=14.0 Hz, 1H), 2.63 (d, J=14.0Hz, 1H); IR (neat) 2260 (C≡N) CM^{-1}.
8. Yields as high as 38% have been obtained on a 0.50 mole scale.
9. The isomeric chloronitriles have not been separated. We know however, that both are present through gas chromatographic analysis (see Table 2).

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