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DIELS-ALDER REACTIONS OF FURANS.
SYNTHESIS OF 7-OXABICYCLO[2.2.1]HEPTANE DERIVATIVES

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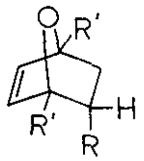
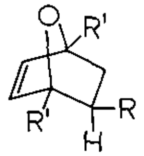
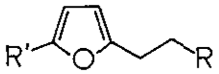
New Diels-Alder reactions of furan and methylfurans with some dienophiles were performed. The adduct from furan and nitroethylene could be used for synthesizing other 7-oxabicyclo[2.2.1]heptane derivatives.

Recent publications (1,2) concerning Diels-Alder reactions of furan prompted us to report some of our results in this field. Several investigators (3-5) examined the reaction of furan with methyl acrylate, which required long reaction times (1-2 months) in order to obtain reasonable yields of the adducts 1a and 2a. We reasoned that these long reaction times might be avoided by using a more reactive dienophile like acryloyl chloride. Reaction of this dienophile with furan for a few days at r.t. produced in high yield a mixture of *endo*-adduct 1b and *exo*-adduct 2b; their ratio depending on the reaction time.

Reaction of 1b and 2b with methanol afforded the methyl esters 1a and 2a, while reaction with water gave the carboxylic acids 1c and 2c, formerly obtained by saponification of 1a and 2a. The carboxylic acids 1c and 2c can also be obtained by Diels-Alder reaction of furan with acrylic acid. This reaction proceeded considerably







	R	R'
1 a	CO_2Me	H
b	COCl	H
c	CO_2H	H
d	NO_2	H
e	NO_2	Me

	R	R'
2 a	CO_2Me	H
b	COCl	H
c	CO_2H	H
d	NO_2	H
e	NO_2	Me

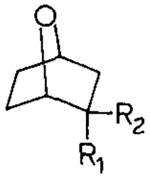
	R	R'
3a	COCl	Me
b	NO_2	Me
c	NO_2	H

faster than the corresponding reaction of methyl acrylate [41% (65%) conversion vs. 8%(15%) after 2(4) weeks]. It is interesting to notice that the heterogeneous reaction of furan and acrylic acid in water is much faster than the homogeneous reaction in DMSO [44%(63%) vs. 0-5% (7%) after 2(4) weeks]; a phenomena we already observed in the reaction of furan with maleic acid (6,7).

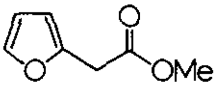
Reaction of acryloyl chloride with 2-methylfuran gave no Diels-Alder adduct, but produced the substitutive addition product 3a.

It has been reported (8) that nitroethylene did not react with furan, whereas 2-methylfuran underwent a substitutive addition reaction affording 3b. We performed the reaction of furan with nitroethylene in a NMR tube and observed ready formation of endo-adduct 1d (55%; isolated by column chromatography), which was complete within 24 hr. Only a minor amount of exo-adduct 2d was formed, while in reactions on extended scale a small amount of 3c could be isolated. Reaction of nitroethylene with 2-methylfuran indeed gave 3b (70%), whereas reaction with 2,5-dimethylfuran afforded - according to NMR - a 2.5:1 mixture of 1e and 2e.

Endo-adduct 1d can be used as starting material for other 7-oxabicyclo[2.2.1]heptane systems. Catalytic hydrogenation over 10% Pd/C gave the saturated nitro compound 4a, which on prolonged hydrogenation



4 a R_1 = NO_2 , R_2 = H
b R_1 = NH_2 , R_2 = H
c R_1 = R_2 = O
d R_1 = R_2 = OMe
e R_1 = NO_2 , R_2 = $(CH_2)_2CO_2Me$



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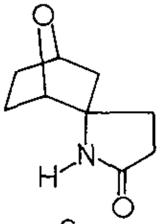

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afforded amine 4b. Nef reaction (9) of 4a gave in 80% yield 7-oxabicyclo[2.2.1]heptan-2-one (4c; IR: 1760 cm^{-1}, C=O). Dimethyl acetal 4d was obtained if a methanolic solution of the sodium nitronate of 4a was poured into $MeOH/H_2SO_4$ at -30°C (10). A similar Nef reaction of 1d gave methyl furylacetate 5. The presence of a hydrogen atom adjacent to the nitro group allows the introduction of substituents at this position. Michael reaction of 4a with methyl acrylate in the presence of Triton-B (11) yielded crystalline 4e (mp: 59.5 - 60.5°C), which upon subsequent hydrogenation afforded spiro compound 6 (mp: 165 - 166°C; IR 1700 cm^{-1}, C=O) in 70% yield from 4a.

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7. Use of a water-soluble diene clearly demonstrated the influence of the solvent on the Diels-Alder reaction of maleic acid. Reaction of maleic acid with one equivalent of furfuryl alcohol in D_2O gave, after 18 hr at r.t., 40% conversion. However - according to NMR - no detectable products were formed in a similar reaction in DMSO-d_6. The conversion, based on maleic acid in the reaction carried out in D_2O, gives a poor illustration of the actual reaction rate of the Diels-Alder reaction, because furfuryl alcohol polymerized to a considerable extent under the reaction conditions. After 18 hr furfuryl alcohol could not be detected in the reaction medium.

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