CYCLOADDITION REACTIONS OF 1-ETHOXYCARBONYL-1H-AZEPINE AND 1-ETHOXYCARBONYL-1H-1,2-DIAZEPINE WITH 3,4,5,6-TETRACHLORO-1,2-BENZOQUINONE

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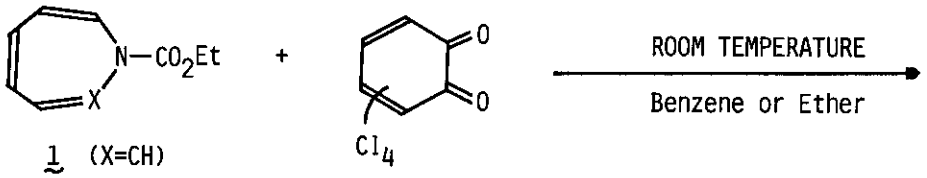
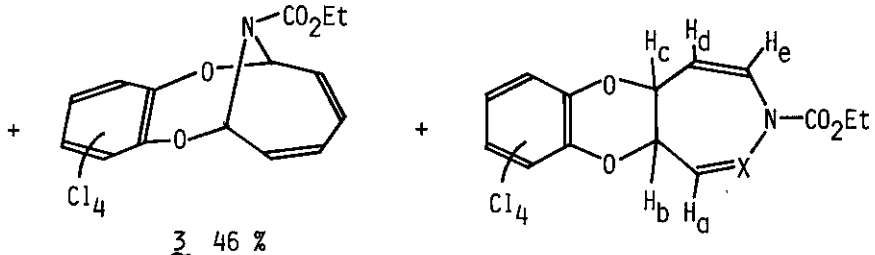
Abstract: The reaction of 1-ethoxycarbonyl-1H-azepine (1) with 3,4,5,6-tetrachloro-1,2-benzoquinone at room temperature afforded a [6+4] type cycloadduct 3 as a major product in addition to two [4+2] type cycloadducts 4 and 5. Upon heating, 3 rearranged to 5 in a fairly good yield. In the same reaction with 1-ethoxycarbonyl-1H-1,2-diazepine (2), a [4+2] type cycloadduct 6 was formed. The low electron density at the 2 and 7 positions of 1 is considered to be one reason for the formation of the [6+4] type cycloadduct 3.

The cycloaddition reactions of heterocyclic compounds have received considerable attention, not only from the point of view of synthetic utility but also examination of the electronic nature of the heterocyclic compounds. As a part of our research, previously, we have published some results of the cycloaddition reactions of 1-ethoxycarbonyl-1H-azepine (1) and 1-ethoxycarbonyl-1H-1,2-diazepine (2) with 2-pyrone derivatives[1] and the addition reactions of 1 and 2 with some chlorosilane derivatives.[2] Recently, Kanematsu et al.,[3,4,5] Gockel et al.,[6] and Murphy et al.[7] reported the cycloaddition reactions of azepine derivatives with phencyclone, cyclopropene derivatives, and nitrosobenzene, respectively. These facts prompted us to report our recent results of the cycloaddition reactions of 1 and 2 with 3,4,5,6-tetrachloro-1,2-benzoquinone (o-chloranil)[8-13] which is typical of the class of dienes displaying reverse electron demand in Diels-Alder reactions.[8]



1 (X=CH)

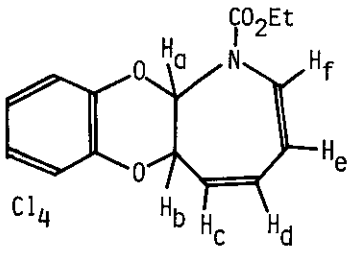
2 (X=N)



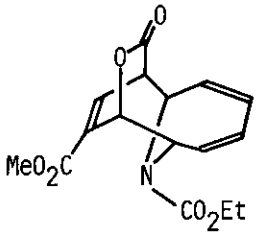
3 46 %

4 (X=CH) 15 %

6 (X=N) 10 %



5 7 %



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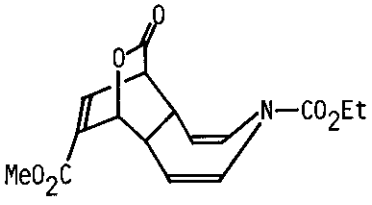

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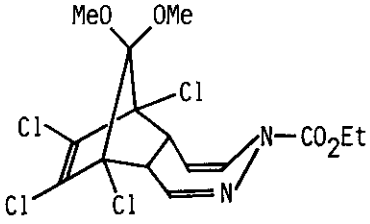

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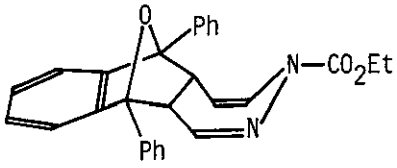

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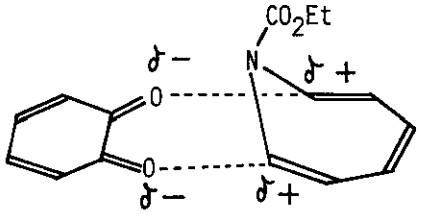

1-Ethoxycarbonyl-1H-azepine (1) was allowed to react with o-chloranil in benzene or ether at room temperature for 70 min to yield three types of colorless crystals of 1:1 adducts 3, 4, and 5 in the yields of 46, 15, and 7 %, respectively. 1-Ethoxycarbonyl-1H-1,2-diazepine (2) was also allowed to react with o-chloranil in benzene or ether at room temperature for 3.5 h to yield colorless crystals of a 1:1 adduct 6 in a 10 % yield. The adducts 4 and 5 were thermally stable recovering completely even after heating at 180°C for 24 h in benzene in a sealed tube. On the other hand, the adduct 3 was converted to 5 in a 84 % yield by heating at 90°C for 6 h. The adduct 6 was not changed at all by heating at 130°C for 15 h, but turned to black polymers after heating at 180°C for 10 h. The physical data of these adducts are as follows.[14]

3; mp 156-157°C. IR (KBr): 1720 cm^{-1}. Mass (m/e, %): 411 (M^+, 9), 165 (100), 92 (82). NMR ($CDCl_3$), δ ppm: 1.29 (t, CH_3, J=7.0 Hz), 4.20 (q, CH_2, J=7.0 Hz), 6.04 (bs, 4H), 6.83 (d, 2H, J=4.5 Hz).

4; mp 165-166°C. IR (KBr): 1735 cm^{-1}. Mass (m/e, %): 411 (M^+, 9), 165 (31), 152 (98), 80 (100). NMR ($CDCl_3$), δ ppm: 1.36 (t, CH_3, J=7.0 Hz), 4.30 (q, CH_2, J=7.0 Hz), 4.97 (bs, 4H), 7.06 (d, 2H, J=9.0 Hz).

5; mp 200-202°C. IR (KBr): 1730 cm^{-1}. Mass (m/e, %): 411 (M^+, 8), 165 (100), 152 (48), 92 (84). NMR ($CDCl_3$), δ ppm: 1.36 (t, CH_3, J=7.0 Hz), 4.31 (q, CH_2, J=7.0 Hz), 5.11 (bs, H_b), 5.28 (dd, H_e, J_{de}=7.5, J_{ef}=8.6 Hz), 5.39 (bd, H_c, J_{bc}=2.1, J_{cd}=11.9 Hz), 5.91 (ddd, H_d, J_{cd}=11.9, J_{de}=7.5, J_{bd}=2.1 Hz), 6.63 (bs, H_a), 6.87 (d, H_f, J_{ef}=8.6 Hz).

6; mp 183-184°C. IR (KBr): 1740 cm^{-1}. Mass (m/e, %), 412 (M^+, 11), 166 (65), 107 (50), 94 (100), 81 (71). NMR ($CDCl_3$), δ ppm: 1.40 (t, CH_3, J=7.0 Hz), 4.40 (q, CH_2, J=7.0 Hz), 4.93 (ddd, H_c, J_{cd}=6.5, J_{ac}=2.5, J_{bc}=2.1 Hz), 5.22 (dd, H_b, J_{ab}=2.5, J_{bc}=2.1 Hz), 5.30 (dd, H_d, J_{cd}=6.5, J_{de}=10.3 Hz), 7.07 (dd, H_a, J_{ab}=2.5, J_{ac}=2.5 Hz), 7.49 (d, H_e, J_{de}=10.3 Hz).

The 1:1 nature of these adducts was shown by their Mass spectrometry and elemental analysis. All of these adducts showed no carbonyl absorption except those bands due to their ester groups in their IR spectra, suggesting that 1 and 2 reacted with o-chloranil at its oxygen atoms to form the ether linkages. The NMR spectra of 3 and 4 indicated these adducts are symmetric compounds, suggesting that the 2 and 7 positions or the 4 and 5 positions of 1 were involved in these reactions. The chemical shift (6.04 ppm) and the broad singlet nature of the olefinic protons of 3 resembled closely those features of the olefinic protons of

the skeletally analogous compound 7[1] and the azepine dimers.[15,16] Similarly, the chemical shift (7.06 ppm) and the coupling constant (9.0 Hz) of the olefinic protons of 4 had a likeness to those parameters of the resembled compound 8,[1] the adduct of 1 with chlorosilane derivatives,[2] and an isobenzofuran derivative.[17] The broad singlet peak at 4.97 ppm of 4 was considered to contain the absorptions due to the other two olefinic protons and the two methine protons. On the basis of these spectroscopic data the structures of 3 and 4 were determined as shown in the figure. The electronegativity of the ether oxygen atoms accounts for the observed lower field resonance of the bridgehead protons of the chloranil adducts 3 and 4 as compared to the adducts 7 and 8.

The structure of 5 was mainly assigned on the basis of its NMR data, employing the double resonance technique which showed that there were four olefinic protons (H_c-H_f) attached to a conjugated double bond and two methine protons (H_a and H_b) attached to the carbons adjacent to the double bond. The coupling constants between the olefinic protons suggested that this compound contained a seven-membered ring.[1,2,18,19] As for the stereochemistry of the bridgehead protons, Dreiding models revealed that the dihedral angle between H_a and H_b was approximately 60° for cis-addition and approximately 170° for trans-addition. Thus, the small coupling constant between H_a and H_b (ca. 2 Hz) indicates that the addition reaction occurred in a cis mode.[19] The thermal transformation of 3 to 5 confirmed the structures of 3 and 5 because this migration is quite reasonably attributed to a thermally allowed 1,5-carbon shift.[20]

The NMR spectrum of the adduct 6 was complicated, but the double resonance technique revealed that the protons were arranged in the order H_a-H_b-H_c-H_d-H_e, with the corresponding coupling constants listed previously. The chemical shifts of the two olefinic protons (H_a and H_e) were reasonable for protons attached to the carbons adjacent to nitrogen atoms. The coupling constant between H_d and H_e (J_{de}=10.3 Hz) which is larger than that between H_a and H_b (J_{ab}=2.5 Hz) indicated that H_d was more reasonable as the olefinic proton rather than H_b. Thus, the structure of 6 was determined as illustrated in the figure. The small coupling constant between H_b and H_c (J_{bc}=2.1 Hz) indicated that the cis-addition occurred based on the same reason for the formation of 5. The structure of 6 was further confirmed by the resemblance of its NMR spectrum to those spectra of the skeletally analogous compounds 9,[21] 10,[22] and the adduct of 2 with a cyclopentadienone derivative.[23] The low field shift of the bridgehead protons of 6 in the NMR

spectrum compared to the compounds 9 and 10 can be explained by the same reason given for the formation of the adducts 3 and 4.

The adducts 4 and 6 were formed as a result of the reverse electron demand [4+2] type cycloaddition reactions.[9] The adduct 5 could be regarded as the secondary product thermally derived from 3. Considering that the thermal transformation of 3 required prolonged heating, and the cycloaddition proceeded at room temperature, however, it seemed to be more reasonable to consider 5 as the primary product of [4+2] type cycloaddition. Cycloaddition reactions to 2 and 3 positions of azepine derivatives are rather rare, and the only report in the literature involves the reaction with dichlorocarbene.[24] The adduct 3 is a product of a [6+4] type addition reaction. It is well known that the azepine derivatives proceed [4+2] or [6+4] type addition reactions,[1-6] but the yields of the [6+4] type addition products seem to be low[3] with an exceptional case of azepine dimer.[15,16] As for o-chloranil, many cycloaddition reactions have been studied,[8-13] but to our knowledge, there is no example of the [6+4] type cycloaddition. With these facts in mind, it is rather interesting that the reaction of 1 with o-chloranil gave the [6+4] type cycloadduct as the main product. We tentatively suggest that this selectivity is a result of the electronic attraction between the oxygen atoms of o-chloranil and the carbons in the 2 and 7 positions of 1. The oxygen atoms of carbonyl groups are well known to be charged negatively and a molecular orbital calculation has shown that the azepine has the lowest electron density at the carbons in the 2 and 7 positions.[25,26]

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22) S. Iida, A Thesis for Masterate, Tohoku University (1975) and the references cited therein. The NMR data of the compound 10 are as follows. NMR ($CDCl_3$), δ ppm: 1.26 (t, CH_3), 3.57 (q, 1H), 3.85 (q, 1H), 4.14 (q, CH_2), 5.12 (q, 1H), 6.59 (d, 1H), 7.25 (d, 1H), 7.1-7.8 (Ph, 14H).

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