Heterocycles by Cycloaddition. IV.1) Cycloaddition Reactions of Mesoionic Compounds with a 7-Azabicyclo[2.2.1]heptadiene, and Double Fragmentation of the Adducts

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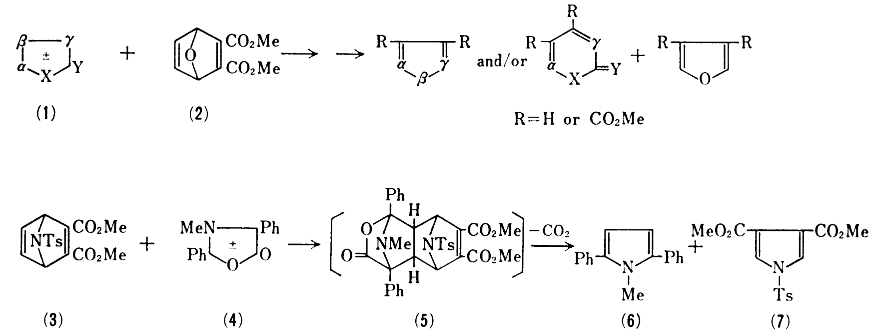
Cycloaddition of some five-membered mesoionic compounds with dimethyl 7-tosyl-7-azabicyclo[2.2.1]-hepta-2,5-diene-2,3-dicarboxylate occurs only across the unsubstituted double bond. Pyrolysis of the adducts resulted in a double fragmentation reaction to give two five-membered aromatic heterocycles. A dithiolone adduct gave the *S*-oxide, which was pyrolyzed to the corresponding thiopyran-2-one.

In an effort to extend the synthetic value of mesoionic compounds, we have reported that the cycloaddition-double fragmentation reactions of mesoionic compounds (**1**) with a 7-oxabicyclo[2.2.1]heptadiene (**2**) provides an attractive route for the preparation of many five- and six-membered aromatic heterocycles.2) In these reactions, some mesoionic compounds gave adducts (or fragmentation products) with a high periselectivity, while others gave products resulting from cycloaddition across both the two double bonds of **2**. Since it was established that the approach of mesoionic compounds to **2** occurs from above the surface of the oxygen bridge,2—4) a bulky substituent at the 7-position may be expected to cause a higher periselectivity than with **2** due to the steric effect of the substituent. With this in mind, we studied the reactions of mesoionic compounds with dimethyl 7-*p*-toluenesulfonyl-7-azabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**3**), and report here the results.

The reaction of mesoionic 3-methyl-2,4-diphenyl-5-oxazolone (**4**) with the azabicycloheptadiene **3** proceeded at a slower rate than with the oxabicycloheptadiene **2**, and gave 1-methyl-2,5-diphenylpyrrole (**6**) and dimethyl 1-(*p*-toluenesulfonyl)pyrrole-3,4-dicarboxylate (**7**). This result shows that the cycloaddition of the oxazolone **4** took place selectively across the unsubstituted double bond to give an intermediate adduct (**5**), which spontaneously underwent double fragmentation under the reaction conditions to carbon dioxide, **6**, and **7**. This behavior is in contrast to the reaction of **4** with the oxa analog **2**, which afforded products resulting from addition of **4** on both the substituted and the unsubstituted double bonds.

The reaction of mesoionic 2,5-diphenyl-1,3-dithiol-4-one (**8a**) with **3** in benzene under reflux gave the 1 : 1 adduct, dimethyl 9-oxo-1,8-diphenyl-12-*p*-toluenesulfonyl-12-aza-10,11-dithiatetracyclo-[6.2.1.1.^{3,6}-0^{2,7}]dodec-4-ene-4,5-dicarboxylate (**9a**). The base peak of the mass spectrum of the adduct at *m/e* 236, and the lack of NMR signal assignable to olefinic protons show that the addition took place across the unsubstituted double bond of **3**. Assignment of the *exo*, *exo* configuration among the four possible stereoisomers (**9a** and **ixa**--**ixc**) is based on the NMR spectrum: the lack of coupling between the bridgehead and the angular protons (H_a and H_c; H_b and H_d) eliminates structures **ixb** and **ixc**, and small or no chemical shift difference of the two methoxycarbonyl (0.03 ppm) and two bridgehead protons (H_a and H_b; 0 ppm) as well as a considerable one between the two angular protons (H_c and H_d; 0.45 ppm) are compatible only with the *exo*, *exo* configuration **9a**. A larger chemical shift difference of the two bridgehead protons than that of the two angular methine protons would be expected for configuration **ixa**. Pyrolysis of the adduct **9a** in toluene under reflux afforded 2,5-diphenylthiophene (**10**) and the pyrrole **7**. The treatment of the dithiolone adduct **9** with *m*-chloroperbenzoic acid gave the corresponding *S*-oxide (**11a**). The oxide oxygen was probably introduced anti to the aza bridge because it exerted only a small effect on the chemical shift values of the angular and the bridgehead protons. The *S*-oxide was fairly stable thermally, but was pyrolyzed in refluxing diethylbenzene with an extrusion of SO to give 3,6-diphenylthiopyran-2-one (**12a**) and the pyrrole **7**. The *S*-oxide **11a** was only partly decomposed after refluxing in xylene for a long time though the yield of the thiopyranone **12a** was higher (70%) than that in diethylbenzene (29%) when based on con-



Scheme 1.

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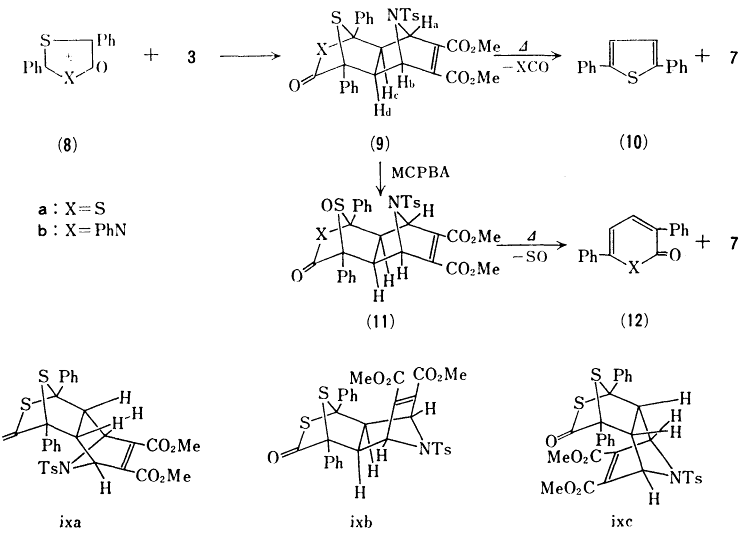

Scheme 2.

sumed *S*-oxide.

As previously reported,[2] the reaction of mesoionic 2,3,5-triphenyl-4-thiazolone (**8b**) with the oxabicycloheptadiene **2** gave adducts resulting from addition across both the substituted and the unsubstituted double bonds as well as other minor products. The reaction of **8a** with the aza analog **3** proceeded sluggishly in benzene under reflux, but afforded the cycloadduct, dimethyl *exo,exo*-9-oxo-1,8,10-triphenyl-12-*p*-toluenesulfonyl-10,12-diaza-11-thiatetracyclo[6.2.1.1.^{3,6}0^{2,7}]-dodec-4-ene-4,5-dicarboxylate (**9b**) resulting from the addition only on the unsubstituted double bond. The proposed structure and configuration of **9a** are based on spectral data (See Experimental). When the thiazolone adduct **9b** was pyrolyzed in diphenyl ether under reflux, the thiophene **10** and the pyrrole **7** were formed. The thiazolone adduct **9b** gave the corresponding (*anti*-) *S*-oxide (**11b**) on treatment with *m*-chloroperbenzoic acid. The mass spectrum of **11b** was rather complex although it showed weak peaks expected for double fragmentation products (*m/e* 337 and 323). The pyrolysis of **11b** in xylene under reflux gave complex products, from which neither the expected pyridone (**12b**) nor the pyrrole **7** could be isolated.

The above survey shows that the periselectivity of the mesoionic compounds to a bicycloheptadiene system is improved as expected by introducing a bulky substituent into the 7-position. At the outset of the present work, it was also anticipated that the double fragmentation of the adduct with **3** might be more facilitated than that of the adduct with **2** due to the pronounced aromaticity of the pyrrole ring and to the repulsive acceleration between the two bridge groups.[5] This expectation was not realized. This is probably due to the fact that the double fragmentation steps are not concerted but rather are two consecutive processes consisting of the initial extrusion of X=C=O or SO to give an unstable intermediate ylide, and its fragmentation to stable products.[6] Since the main purpose of the present work was improvement of the periselectivity, reaction conditions were not optimized. However, the high yields of products based on consumed starting materials suggest that this cycloaddition-double fragmentation reaction should constitute an attractive synthetic method of many heterocycles by appropriate selection of reaction partners.

Experimental

Mps were determined on a hot stage and are not corrected. UV and IR (KBr) spectra were recorded on a Hitachi EPS-3T and a Hitachi EPI-G3 spectrophotometer. PMR ($CDCl_3$, TMS internal standard) and mass (70 eV, direct inlet) spectra were measured with a JEOL JNM-4H-100 (100 MHz) and a Hitachi RMU-6 spectrometer. Solvents were concentrated *in vacuo*. The identity of a compound was established on the basis of mp, mixed mp, and IR and NMR spectral determinations.

*Reaction of the Oxazolone **4** with the Diene **3**.* A mixture of the diene **3**[7] (1.4 mmol) and the oxazolone **4**[8] (1.4 mmol) in benzene (50 cm^3) was stirred at 40 °C under a nitrogen atmosphere for 28 h. The solvent was concd and the residue was chromatographed (silica gel/$CHCl_3$) to give, besides the unreacted diene **3** (27%), 1-methyl-2,5-diphenylpyrrole **6** (55%), mp 206—207 °C, lit,[9] 204—205 °C, identical with an authentic specimen,[2] and dimethyl 1-tosylpyrrole-3,4-dicarboxylate **7** (56%), mp 116.5—117.5 °C; UV_{max} (MeOH) 237 ($\log\varepsilon$ 4.35) and 275^{sh} nm (2.98); IR 1747, 1730, 1720, 1709, 1378, 1275, 1192, 1176, and 1160 cm^{-1}; PMR δ=7.74 and 7.27 (AA'BB', each 2, J=8 Hz, ArH), 7.58 (s, 2, =CH), 3.80 (s, 6, OMe), and 2.41 ppm (s, 3, CMe); MS *m/e* (rel intensity), 337 (38, M$^+$), 306 (23, M$^+$−OMe), 155 (68, Ts$^+$), 151 (25, M$^+$−Ts−OMe), and 91 (100, $MeC_6H_4^+$). Found: C, 53.50; H, 4.46; N, 4.00%. Calcd for $C_{15}H_{15}NO_6S$: C, 53.41; H, 4.48; N, 4.15%.

*Adduct (**9a**) of the Dithiolone **8a** and the Diene **3**.* A soln of the diene **3** (1.1 mmol) and the dithiolone **8a**[10] (1.1 mmol) in benzene (50 cm^3) was refluxed under nitrogen for 11 h. The solvent was concd and the residue was recrystd (MeOH) to give needles of the adduct **9a** (95%), mp 154—155 °C (dec); UV (MeOH) end absorption; IR 1748, 1714, 1350, and 1165 cm^{-1}; PMR δ=7.52—7.14 (m, 14, ArH), 4.67 (s, 2, bridgehead H), 3.76 and 3.73 (s, each 3, OMe), 3.66 and 3.21 (d, each 1, J=6.5 Hz, angular H), and 2.41 ppm (s, 3, CMe); MS *m/e* (rel intensity) 337 (12, **7**$^+$), 236

(100, **10**$^+$), 155 (23, Ts$^+$), 121 (22, PhCS$^+$), 91 (48, MeC$_6$H$_4$$^+$), and 60 (37, COS$^+$). Found: C, 60.54; H, 4.21; N, 2.14%. Calcd for $C_{32}H_{27}NO_7S_3$: C, 60.65; H, 4.29; N, 2.21%.

*Pyrolysis of the Adduct **9a**.* A suspension of the adduct **9a** (160 mg) in toluene (25 cm^3) was heated under reflux for 100 h. The soln was concd and the residue was chromatographed (silica gel/acetone : cyclohexane : ligroin=1 : 3 : 6) to give 2,5-diphenylthiophene (**10**)[2] (67%), mp 154—155 °C, lit,[11] 152—153 °C, the pyrrole **7** (64%), and unchanged adduct **9a** (31%), all identical with authentic specimens.

S-*Oxide (**11a**).* A soln of the adduct **9a** (0.28 mmol) and *m*-chloroperbenzoic acid (80% purity, 0.32 mmol) in dichloromethane (20 cm^3) was stirred at room temp for 23 h. The soln was washed (aq NaOH; water), dried (Na$_2$SO$_4$), and concd, and the residue was recrystd (CHCl$_3$-Et$_2$O) to give prisms of the *S*-oxide **11a** (87%), mp 238—239 °C (dec); UV (MeOH) end absorption; IR 1750^{sh}, 1716, 1706^{sh}, 1350, 1164, and 1086 cm^{-1}; PMR δ=7.70—7.38 (m, 12, ArH), 7.25 (AA′ part of AA′BB′, 2, J=8 Hz, ArH), 4.78 and 4.57 (d, each 1, J=1.7 Hz, bridgehead H), 3.72 (s, 6, OMe), 3.65 and 3.05 (d, each 1, J=8 Hz, angular H), and 2.42 ppm (s, 3, CMe); MS *m/e* (rel intensity) 337 (19, **7**$^+$), 264 (27, **12a**$^+$), 236 (100, **10**$^+$), 155 (36, Ts$^+$), 121 (19, PhCS$^+$), and 91 (81, MeC$_6$H$_4$$^+$). Found: C, 59.19; H, 4.13; N, 2.03%. Calcd for $C_{32}H_{27}NO_8S_3$: C, 59.15; H, 4.19; N, 2.16%.

Pyrolysis of the S-*Oxide **11a**.* The *S*-oxide **11a** (85 mg) was heated in diethylbenzene (10 cm^3) under reflux for 10 h. The soln was concd, and the residue was chromatographed (silica gel/CHCl$_3$) to give 3,6-diphenylthiopyran-2-one (**12a**)[2] (29%), mp 187—187.5 °C, lit,[12] 183.5—184 °C, the pyrrole **7** (23%), and unchanged **11a** (24%), all identical with authentic specimens. When the *S*-oxide **11a** was heated in xylene under reflux for 95 h, **12a** (18%), **7** (4%), and **11a** (75%) were isolated.

*Adduct (**9b**) of the Thiazolone **8b** and the Diene **3**.* A soln of the thiazolone **8b**[13] (1.1 mmol) and the diene **3** (1.1 mmol) in benzene (50 cm^3) was refluxed for 98 h. The soln was concd and the residue was recrystd (PhH-hexane) to give prisms of **9b** (52%), mp 215—216 °C; UV (MeOH) end absorption; IR 1737, 1715, 1699^{sh}, 1350, and 1166 cm^{-1}; PMR δ=7.58—7.03 (m, 17, ArH), 6.82—6.65 (m, 2, ArH), 4.95 and 4.67 (d, each 1, J=1.7 Hz, bridgehead H), 3.81 and 3.76 (s, each 3, OMe), 3.66 and 3.16 (d, each 1, J=7 Hz, angular H), and 2.40 ppm (s, 3, CMe); MS *m/e* (rel intensity) 355 (8, M$^+$−**7**), 337 (27, **7**$^+$), 263 (23, M$^+$−**7**−PhNH), 236 (92, **10**$^+$), 155 (49, Ts$^+$), 121 (19, PhCS$^+$) 119 (47, PhNCO$^+$), and 91 (100, MeC$_6$H$_4$$^+$). Found: C, 67.50; H, 4.63; N, 3.62%. Calcd for $C_{41}H_{35}N_2O_7S_2$ (**9b**+1/2 PhH): C, 67.28; H, 4.82; N, 3.83%. Found (after prolonged heating *in vacuo*): C, 66.45; H, 4.60; N, 3.77%. Calcd for $C_{38}H_{32}N_2O_7S_2$: C, 65.88; H, 4.66; N, 4.04%.[14] From the mother liquor of recrystallization, the unchanged diene **3** (35%) was recovered.

*Pyrolysis of the Adduct **9b**.* A suspension of the adduct **9b** (0.1 g) in diphenyl ether (20 cm^3) was heated under reflux for 30 min. The solvent was removed and the residue was chromatographed (silica gel/CHCl$_3$) to give the thiophene **10** (88%) and the pyrrole **7** (82%), both identical with authentic specimens.

S-*Oxide (**11b**).* A soln of the adduct **9b** (0.29 mmol) and *m*-chloroperbenzoic acid (0.32 mmol) in dichloromethane (10 cm^3) was stirred overnight at room temp. The soln was washed (aq NaOH; water), dried (Na$_2$SO$_4$), concd, and the residue was recrystd (CHCl$_3$-Et$_2$O) to give the *S*-oxide **11b** (83%) as prisms, mp 182—184 °C (dec); UV (MeOH) 225 nm^{sh} (log ε 4.505); IR 1722, 1713^{sh}, 1350, 1166, and 1087 cm^{-1}; PMR δ=7.68—6.92 (m, 19, ArH), 4.98 and 4.65 (d, each 1, J=1.7 Hz, bridgehead H), 3.80 and 3.72 (s, each 3, OMe), 3.67 and 3.15 (d, each 1, J=8 Hz, angular H), and 2.41 ppm (s, 3, CMe); MS *m/e* (rel intensity) 506 (21), 431 (16), 337 (7, **7**$^+$), 323 (13, **12b**$^+$), 180 (21, PhCNPh$^+$), 155 (34, Ts$^+$), 119 (12, PhNCO$^+$), 91 (100, MeC$_6$H$_4$$^+$), and 77 (43, Ph$^+$). Found: C, 64.20; H, 4.49; N, 3.73%. Calcd for $C_{38}H_{32}N_2O_8S_2$: C, 64.39; H, 4.55; N, 3.95%.

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14) Repeated analyses gave poor agreement with the calculated value. PMR measurement showed that many cycloadducts of thiazolone **8b** strongly hold solvents of crystallization (benzene, ether, *etc.*), which are liberated only after prolonged heating *in vacuo*.[2] The adduct **9b** could not be completely freed of solvent by heating below its dec p.