Heterocycles by Cycloaddition. Part 7.[1] Cycloaddition Reactions of Mesoionic Dithiolones with Fulvenes

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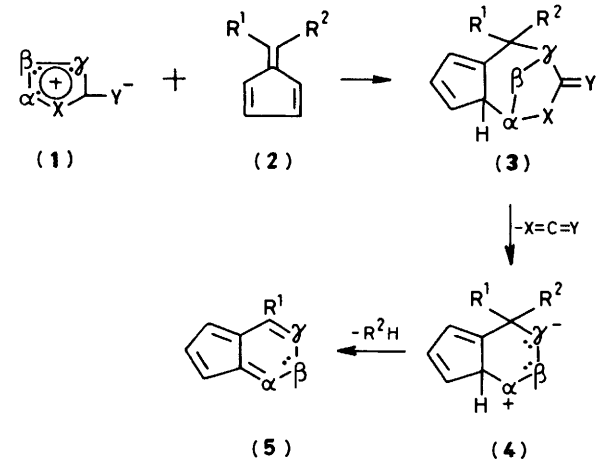
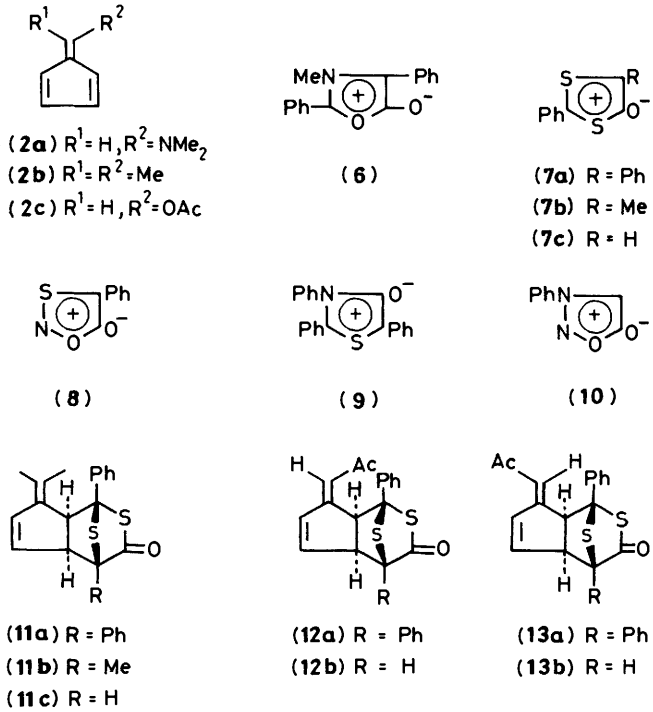
The reactions of fulvenes with several mesoionic compounds have been investigated. The mesoionic dithiolones (**7**) gave regio- and stereo-selective [4π + 2π] cycloadducts (**11**)—(**13**) across the endocyclic double bonds of fulvenes, but no periselectivity was observed with unsymmetrical fulvenes. Several other mesoionic ring systems failed to react or gave complex reaction products.

Mesoionic compounds have been widely used as building blocks for a variety of heterocycles. The 1,3-dipolar cycloaddition–extrusion reactions of mesoionic ring systems with alkenes and alkynes afford a valuable synthetic route to a variety of five-membered heterocycles.[2] The synthetic value of these systems can be enhanced further by taking advantage of secondary reactions of the ylide intermediates which are formed by extrusion reactions of the primary cycloadducts. In this way, they serve further as starting compounds for six-,[3,4] seven-,[3] and even nine[5] and ten-[6] membered heterocycles.

However, all the cycloaddition reactions of the five-membered mesoionic compounds (**1**) reported to date concern [2π + 4π] cycloaddition, and no examples of the [4π + 6π] type have been described. In this report, we describe the reactions of several mesoionic compounds with fulvenes. Fulvenes are capable of acting as an ene, a diene, or a triene system toward cycloaddition.[7,8] The present investigation was undertaken in order to see if fulvenes and mesoionic compounds can undergo cycloaddition by the theoretically possible [4π + 6π] mode. When such a cycloaddition mode is possible, and when a fulvene substituent on the 6-position is a good leaving group, the cycloadduct (**3**) may afford a fully conjugated condensed heterocycle (**5**) by extrusion and elimination reactions (see Scheme). It was hoped that the sequence of reactions described above would afford an attractive general synthetic pathway for a variety of condensed heterocycles which are isoelectronic with azulenes. After the completion of the present work,[9] Friedrichsen and his co-workers[10] independently reported the reactions of mesoionic oxazol-5-ones with fulvenes. The present work is thus complementary to the work of Friedrichsen *et al.*, and it gives additional information concerning the stereo-, regio-, and peri-selectivity of reactions of this type.



Scheme.



Results and discussion

As the fulvene component, 6-dimethylaminofulvene (**2a**) was selected first in the hope that dimethylamine would be eliminated readily from the cycloaddition–extrusion intermediate (**4**) to give a fully conjugated system. However, reaction of the fulvene (**2a**) with the mesoionic oxazol-5-one (**6**), 1,3-dithiol-4-one (**7a**), or 1,3,2-oxathiazol-5-one (**8**), at room temperature or under reflux in toluene, always resulted in complex product mixtures. Mesoionic compounds generally react preferentially with electron deficient olefins,[2] whereas dimethylaminofulvene (**2a**) should be regarded as a considerably electron-excessive system.

The reactions of 6,6-dimethylfulvene (**2b**) with several mesoionic compounds were investigated next because it was felt that the presence of the readily removable dimethylamino group might complicate the reaction. The reactions of the fulvene (**2b**) with the mesoionic oxazolone (**6**) or thiazol-4-one (**9**) at room temperature again resulted in a complex mixture, and the reaction with 3-phenylsydnone (**10**) did not take place even under reflux in toluene. Friedrichsen *et al.* have reported the isolation of products in low yield by the reaction of the fulvene

(**2b**) and the oxazolone (**6**) in the presence of manganese dioxide or dimethyl acetylenedicarboxylate.[10b] The reaction of dimethylfulvene (**2b**) with the mesoionic 2,5-diphenyldithiolone (**7a**) occurred at room temperature to give a single 1:1 adduct. Similar 1:1 adducts were formed by the reaction of the fulvene (**2b**) with 5-methyl-2-phenyl- and 2-phenyl-dithiolone (**7b**) and (**7c**). The n.m.r. spectra of the adducts (Tables 1 and 2) are consistent with the [4π + 2π] adducts (**11**) across the 1,2-double bond of the fulvene. In every case, one methyl group of the exocyclic isopropylidene group of the adduct is strongly shielded (δ 0.6) by the phenyl substituent. The signal of the 5-H olefin proton of the diphenyl adduct (**11a**) appears at a higher magnetic field than those of the monophenyl adducts (**11b**) and (**11c**). These features show that the reaction took place regioselectively to give the single adduct (**11a—c**) in which the exocyclic isopropylidene group takes a *syn* configuration with the 5-phenyl group of the dithiolones. The relatively small coupling (*ca.* 6 Hz) between the two angular protons (4a-H and 7a-H) would favour the *exo* configuration. Conclusive evidence in support of the *exo* configuration was provided by the n.m.r. spectrum of the adduct (**11c**): the small coupling constant (*J* 0.9 Hz) between the bridgehead 4-H proton and the angular 4a-H proton is consistent only with the *exo* configuration. A larger value (*ca.* 3—5 Hz) would be expected if the adduct had the *endo* configuration.[11]

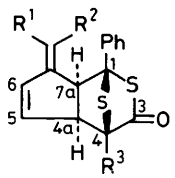
The reaction between 6-acetoxyfulvene (**2c**) and several mesoionic compounds was then tried in order to elucidate the periselectivity with an unsymmetrical fulvene. It was also hoped that the presence of a readily removable and electron-withdrawing acetoxy substituent might facilitate a mesoionic HOMO–fulvene LUMO interaction,[7] and lead to reaction types different from those observed with dimethylfulvene. The reaction of 6-acetoxyfulvene (**2c**) with either the oxathiazolone (**8**) or 3-phenylsydnone (**10**) resulted in a complex mixture. During the reaction of the fulvene (**2c**) with the mesoionic oxazolone (**6**), the colour of the reaction mixture changed to deep reddish violet. However, attempts at isolation of the coloured material were unsuccessful.

The reaction of 6-acetoxyfulvene (**2c**) and the mesoionic diphenyldithiolone (**7a**) gave a mixture of 1:1 adducts (88% yield). Repeated recrystallisation of the mixture gave two isomeric products, both of which are adducts of dithiolone across the endocyclic double bond of the fulvene. They were assigned structures (**12a**) and (**13a**) on the basis of n.m.r. spectra (Tables 1 and 2). The acetoxy proton of one isomer (**12a**), and the exocyclic olefinic proton of the other (**13a**), respectively, are considerably shielded by the nearby phenyl substituent. The deshielding of the 6-H of (**13a**) by the *syn*-acetoxy group further supports this assignment. Although recrystallisation gave the *syn*-acetoxy isomer (**12a**) as the major adduct, n.m.r. analysis of the reaction mixture showed that the two isomers are formed in almost equal amounts.

The reaction of 6-acetoxyfulvene (**2c**) and the mesoionic 2-phenyldithiolone (**7c**) which was prepared *in situ*, likewise afforded two isomers in low yields. Though n.m.r. measurement of the reaction mixture showed the formation of the two isomers in almost equal amounts, only one isomer could be isolated in an analytically pure form. The small coupling constant between the bridgehead and angular protons supports the *exo*-configuration of the two adducts, and *syn*-configuration was assigned to the isolated adduct (**12b**) on the basis of considerations similar to those described above. Although it was not isolated in a pure form, the n.m.r. spectrum of the other isomer showed that it has the *exo-anti* configuration (**13b**) (see Experimental section and Tables 1 and 2).

In summary, the present results show that the mesoionic dithiolones always react with fulvenes regioselectively at the endocyclic double bond by an *exo*-[4π + 2π] mode, and that the 6-substituents of the fulvenes exert little influence on the periselectivity between the two endocyclic double bonds. These

Table 1. ^{1}H N.m.r. spectra of the adducts (δ)



	R^3	4a	5	6	7a	R^1	R^2	*J*(4a,7a) (Hz)	*J*(4,4a)[a] (Hz)
(**11a**)	*c*	4.24	5.16	6.51	4.16	1.56	0.58	*b*	—
(**11b**)	1.63	3.65	5.70	6.68	4.05	1.57	0.56	5.8	—
(**11c**)	4.13	3.97	5.59	6.64	3.97	1.59	0.58	*b*	0.9
(**12a**)	*c*	4.29	5.28	6.22	4.41	7.00	1.60	5.9	—
(**12b**)	4.12	3.99	5.67	6.28	4.19	7.03	1.60	5.7	0.9
(**13a**)	*c*	4.34	5.32	6.51	4.34	1.96	5.67	*b*	—
(**13b**)	4.15	3.97	5.73	6.59	4.10	1.94	5.70	6.0	0.6

a Accuracy: ±0.2 Hz. *b* Coupling constant could not be determined due to the close proximity of the two signals. *c* Multiplets around δ 7.0—7.6.

Table 2. ^{13}C N.m.r. spectra of the adducts (δ)

	1	3	4	4a	5	6	7a	R^1	R^2
(**11a**)	79.8	203.3	77.1	58.5	128.0	136.6	63.8	21.0	20.8
(**11c**)	83.2	204.5	64.3	54.3	128.7	136.7	61.4	21.1	20.9
(**12a**)	79.7	203.0	76.2	59.3	130.6	135.4	62.5		20.2 166.7
(**12b**)	82.1	203.7	63.8	54.9	130.9	135.4	60.0		20.1 166.6
(**13a**)	81.2	202.9	75.6	58.9	131.4	134.4	61.6	20.5 167.0	

results are in contrast with the results observed in the reaction of arylidenecyclopentadienes with mesoionic oxazolones, where cycloaddition took place preferentially on the endocyclic double bond which is *anti* to the aryl group but with complete loss of regioselectivity.[10a]

Experimental

M.p.s were determined with a Yanagimoto hot-stage apparatus and are uncorrected. U.v. spectra were recorded with a Hitachi EPS-3T, and i.r. (KBr) spectra with a Hitachi 345 spectrophotometer. ^{1}H- and ^{13}C-n.m.r. spectra were obtained on a JEOL FX90Q spectrometer (90 and 22.5 MHz respectively) with 8K sampling points for solutions in deuteriochloroform (tetramethylsilane as internal standard). N.m.r. assignments given in Tables 1 and 2 are based on ^{1}H–^{1}H decoupling, off-resonance decoupling, or ^{1}H–^{13}C selective decoupling measurements. Mass spectra were measured with a JEOL 01 SG spectrometer. Chromatographic separations were performed on Merck Kieselgel 60 or PF254. Yields are based on isolated products with sufficient purity.

Reactions of 6,6-*Dimethylfulvene* (**2b**) *with Mesoionic Dithiolones* (**7**).—(*a*) A solution of 2,5-diphenyldithiolone (**7a**) (1.08 g, 4 mmol) and the fulvene (**2b**) (0.62 g, 5.8 mmol) in benzene (70 ml) was allowed to stand for 28 h at room temperature in the dark under an atmosphere of argon. The solution was concentrated, the residue was triturated with benzene, and the product was recrystallised from cyclohexane to give colourless prisms of 7-*isopropylidene*-1,4-*diphenyl*-4,4a,7,7a-*tetrahydro*-1,4-*epithiocyclopenta*[d]*thiopyran*-3(1H)-*one* (**11a**) (0.74 g, 49%), m.p. 160—162 °C (Found: C, 73.3; H, 5.4. $C_{23}H_{20}OS_2$ requires C, 73.35; H, 5.35%); $\nu_{max.}$ 1 700 cm^{-1} (CO); *m/z* 376 (1%, M^+), 316 (2, M − SCO), 270 (100, M − **2b**), and 121 (99, PhCS$^+$).

(*b*) Similar treatment of the fulvene (**2b**) (1.4 mmol) and 2-phenyl-5-methyldithiolone (**7b**) (1.6 mmol) gave the corresponding *4-methyl derivative* (**11b**) as colourless leaflets (0.14 g, 32%), m.p. 188—189 °C (Found: C, 68.75, H, 5.75. $C_{18}H_{18}OS_2$ requires C, 68.75, H, 5.75%); $\nu_{max.}$ 1 695 cm^{-1} (CO); *m/z* 314 (6%, M^+) 254 (1, M − SCO), 208 (92, M − **2b**), 180 (15, M − **2b** − CO), 121 (100, PhCS$^+$), and 106 (4, **2b**).

(*c*) To a refluxing solution of thiobenzoylthioglycollic acid (6 mmol) and the fulvene (**2b**) (6 mmol) in anhydrous benzene (20 ml), a solution of dicyclohexylcarbodi-imide (6.6 mmol) in benzene (10 ml) was added over a period of 10 min, and the resulting mixture was refluxed for another 4 h. The mixture was then filtered and the filtrate concentrated and recrystallised from benzene to give the 4-*unsubstituted product* (**11c**) as colourless needles (27%; 38% by n.m.r. determination), m.p. 191—191.5 °C (Found: C, 67.65; H, 5.45. $C_{17}H_{16}OS_2$ requires C, 67.95; H, 5.35%); $\nu_{max.}$ 1 712 and 1 698sh cm^{-1} (CO); *m/z* 300 (18%, M^+), 240 (8, M − SCO), 194 (52, M − **2b**), 121 (100, PhCS$^+$), and 106 [22, (**2b**)$^+$].

Reactions of 6-*Acetoxyfulvene* (**2c**) *with Mesoionic Dithiolones* (**7a**) *and* (**7c**).—(*a*) A solution of the fulvene (**2c**) (4.1 mmol) and diphenyldithiolone (**7a**) (3.7 mmol) in benzene (50 ml) was allowed to stand for 2 days at room temperature. The solution was concentrated and the residue was triturated with methanol and recrystallised repeatedly from benzene–cyclohexane to give colourless prisms of 7-*acetoxymethylene*-1,4-*diphenyl*-4,4a,7,7a-*tetrahydro*-1,4-*epithiocyclopenta*[d]*thiopyran*-3(1H)-*one* (**12a**) (31%), m.p. 202—203 °C (decomp.) (Found: C, 67.9; H, 4.55. $C_{23}H_{18}O_3S_2$ requires C, 67.95; H, 4.45%); $\nu_{max.}$ 1 750 and 1 705 cm^{-1} (CO); *m/z* 406 (2%, M^+), 346 (27, M − COS), 270 [100, (**7a**)$^+$], and 121 (100, PhCS$^+$). The mother liquor of recrystallisation was fractionated by chromatography (silica–dichloromethane) and the fraction with a shorter retention time was recrystallised from benzene to give colourless prisms of the anti-*isomer* (**13a**) (3.1%), m.p. 193—195 °C (Found: C, 67.8; H, 4.4. $C_{23}H_{18}O_3S_2$ requires C, 67.95; H, 4.45%); $\nu_{max.}$ 1 760 and 1 700 cm^{-1} (CO); *m/z* 406 (< 1%, M^+), 346 (14, M − COS), 270 [89, (**7a**)$^+$], and 121 (100, PhCS$^+$). The n.m.r. spectrum of the above reaction mixture (dioxane internal standard) showed it to be a mixture of (**12a**) (42%) and (**13a**) (45%).

(*b*) A benzene solution (20 ml) of the fulvene (**2c**) (6 mmol) and 2-phenyldithiolone (**7c**), prepared *in situ* as described above from thiobenzoylthioacetic acid (6 mmol), was heated under reflux for 2 h. The reaction mixture was then chromatographed on silica (toluene). The first fraction was recrystallised from benzene–cyclohexane to give colourless needles of the syn-*isomer* (**12b**) (12%), m.p. 144—145 °C (Found: C, 61.85; H, 4.37. $C_{17}H_{14}O_3S_2$ requires C, 61.8; H, 4.25%); $\nu_{max.}$ 1 757 and 1 716 cm^{-1} (CO); *m/z* 330 (13%, M^+), 270 (9, M − SCO), 194 [66, (**7c**)$^+$], and 121 (100%, PhCS$^+$). Chromatographic separation and recrystallisation gave another crude product which was assigned as the anti-*isomer* (**12b**) on the basis of n.mr. data (Tables 1 and 2). Though the n.m.r. determination of the crude reaction mixture showed it to be a mixture of the *syn*- and the *anti*-isomer in a ratio of 7:6 (total yield: 58%), attempted isolation of the *anti*-isomer (**13b**) in an analytically pure form was unsuccessful.

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