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REACTIONS OF 4-METHOXY-2-(4-METHOXYPHENYL)-9-OXO-CYCLOHEPTA[*b*]PYRYLIUM PERCHLORATE WITH ACTIVE METHYLENE COMPOUNDS

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Abstract - 4-Methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium perchlorate (**1**) reacted with active methylene compounds to give two types of products. The reactions with nitromethane and cyano-substituted active methylene compounds occurred at the 4-position to yield 4-methylene-substituted 4,9-dihydrocyclohepta[*b*]pyran-9-ones (**2**, **3a**-**d**). On the other hand, the reactions with active methylene compounds having an acetyl group took place at the 9a-position to give the ring-opened 6,7-dimethylenecyclohepta-2,4-dien-1-ones (**4a**-**d**). In the reactions with malonic acid diesters, 2*H*-cyclohepta[*b*]furan-2-ones (**5a**,**b**) were obtained by the attack at the 9a-position, ring-opening, and recyclization. Compound (**5a**) reacted with *in situ*-generated enamines to afford azulene derivatives (**6a**-**e**).

INTRODUCTION

In the chemistry of six-membered oxygen heterocycles, there are many reports on the reactions of monocyclic pyrylium salts, while the reactions of bicyclic chromylium and flavylium salts are not necessarily numerous except for a few examples.[1-3] The chemical behaviors of pyrylium salts are very interesting, because their positive charge is usually written on the ring oxygen atom and is able to be on the carbon atom at the 2-, 4-, and 6-position by resonance. Consequently, pyrylium salts react with nucleophiles to

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Dedicated to Professor Leo A. Paquette on the occasion of his 70th birthday.

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produce a variety of products.

Previously, we reported the synthesis of 2-aryl-4-methoxy-9-oxocyclohepta[*b*]pyrylium perchlorates by the reactions of 3-acetyltropolone with benzaldehydes in trimethyl orthoformate in the presence of perchloric acid.[4] These 9-oxocyclohepta[*b*]pyrylium salts have a methoxy group at the 4-position which is a good leaving group. It was found that these 9-oxocyclohepta[*b*]pyrylium salts reacted with hydrazines to give two types of products, 4,9-dihydrocyclohepta[*b*]pyran-4,9-dione 4-hydrazones and 5-aryl-3-tropolonyl-pyrazoles.[5] In the present paper, we describe that the reactions of 2-aryl-9-oxocyclohepta[*b*]pyrylium salts with carbon nucleophiles gave a variety of products.

RESULTS AND DISCUSSION

Reaction of 4-Methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium Perchlorate (1) with Nitromethane.

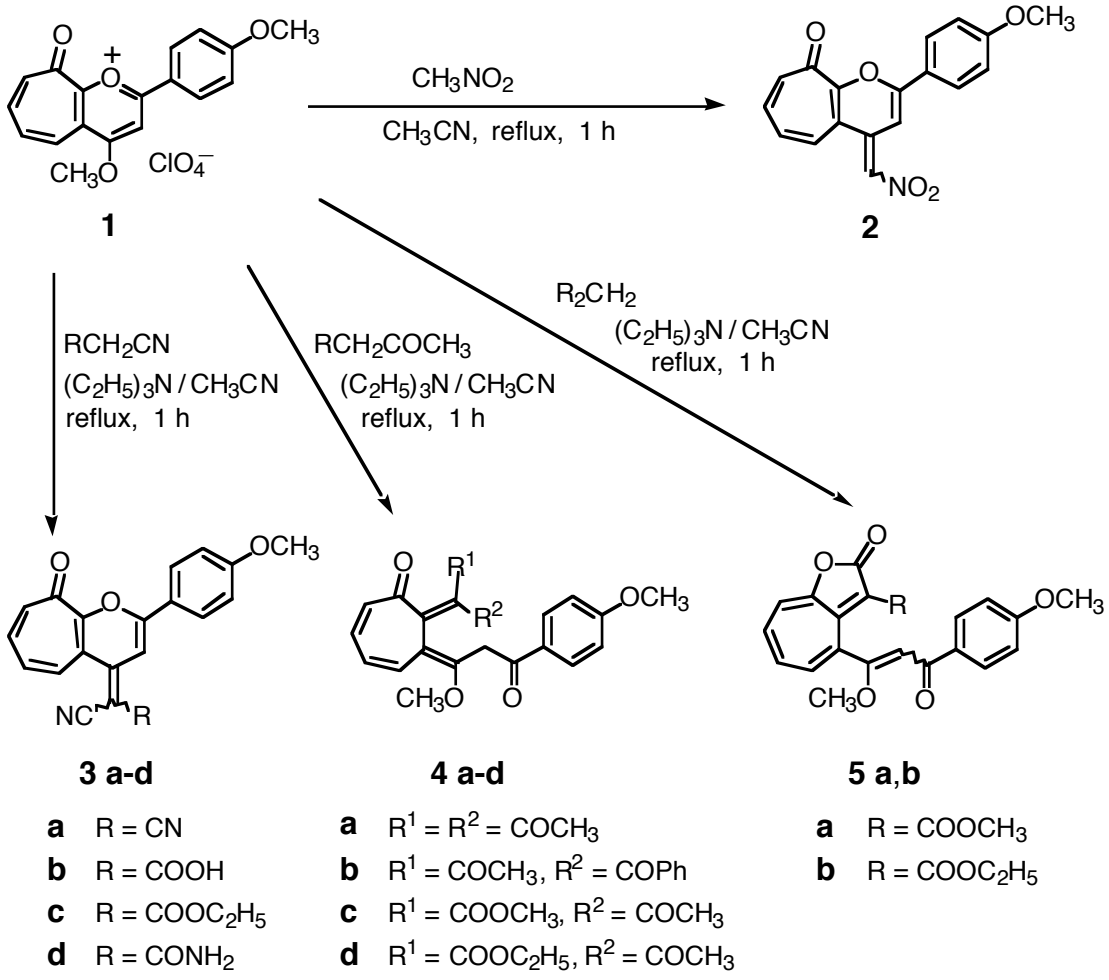
When a solution of 4-methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium perchlorate (**1**) and nitromethane in acetonitrile was refluxed for 1 h in the presence of triethylamine, 2-(4-methoxyphenyl)-4-nitromethylene-4,9-dihydrocyclohepta[*b*]pyran-9-one (**2**) was obtained as red needles in 50% yield. Its structure was established by an elemental analysis ($C_{18}H_{13}NO_5$) and spectral data. In the IR spectrum, a characteristic carbonyl absorption was observed at 1627 cm^{-1}. The ^1H NMR spectrum was measured in deuteriochloroform containing 10% deuteriotrifluoroacetic acid, because the product (**2**) is less soluble in organic solvent. The 3-H proton of the pyran was observed at 8.80. In this case, it was found that the nucleophilic attack occurred at the 4-position of a resonance form (**1C**) of 9-oxocyclohepta[*b*]pyrylium salt (**1**) to produce 4-nitromethylene derivative (**2**), as shown in Scheme 2.

Reaction of 9-Oxocyclohepta[*b*]pyrylium Salt (1) with Active Methylene Compounds Having a Cyano Group.

The reaction of 9-oxocyclohepta[*b*]pyrylium salt (**1**) with malononitrile was carried out under refluxing for 1 h in acetonitrile in the presence of triethylamine to give 4-dicyanomethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (**3a**) in 50% yield. Its structure was also determined by an elemental analysis ($C_{20}H_{12}N_2O_3$) and spectral data. The IR spectrum showed the three caracteristic absorptions at 2219 and 2185 cm^{-1} for the two cyano groups and at 1605 cm^{-1} for the carbonyl group. In the ^1H NMR spectrum in deuteriochloroform containing 10% deuteriotrifluoroacetic acid, the 3-H proton in the pyran ring was observed at 7.37. In a similar manner, the reactions with cyanoacetic acid, ethyl cyanoacetate, and cyanoacetamide gave the corresponding 4-carboxycyanomethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (**3b**) (40%), 4-cyanoethoxycarbonylmethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (**3c**) (43%), and 4-carbamoylcyanomethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (**3d**) (32%), respectively.

As a plausible mecahism is shown in Scheme 2, it was thought that the reactions of 9-oxocyclohepta[*b*]-pyrylium salt (**1**) with cyano-substituted active methylene compounds took place at the 4-position of a

resonance structure (**1C**) to form intermediates (**I**), from which methanol was eliminated to afford the products (**3a**-**d**).

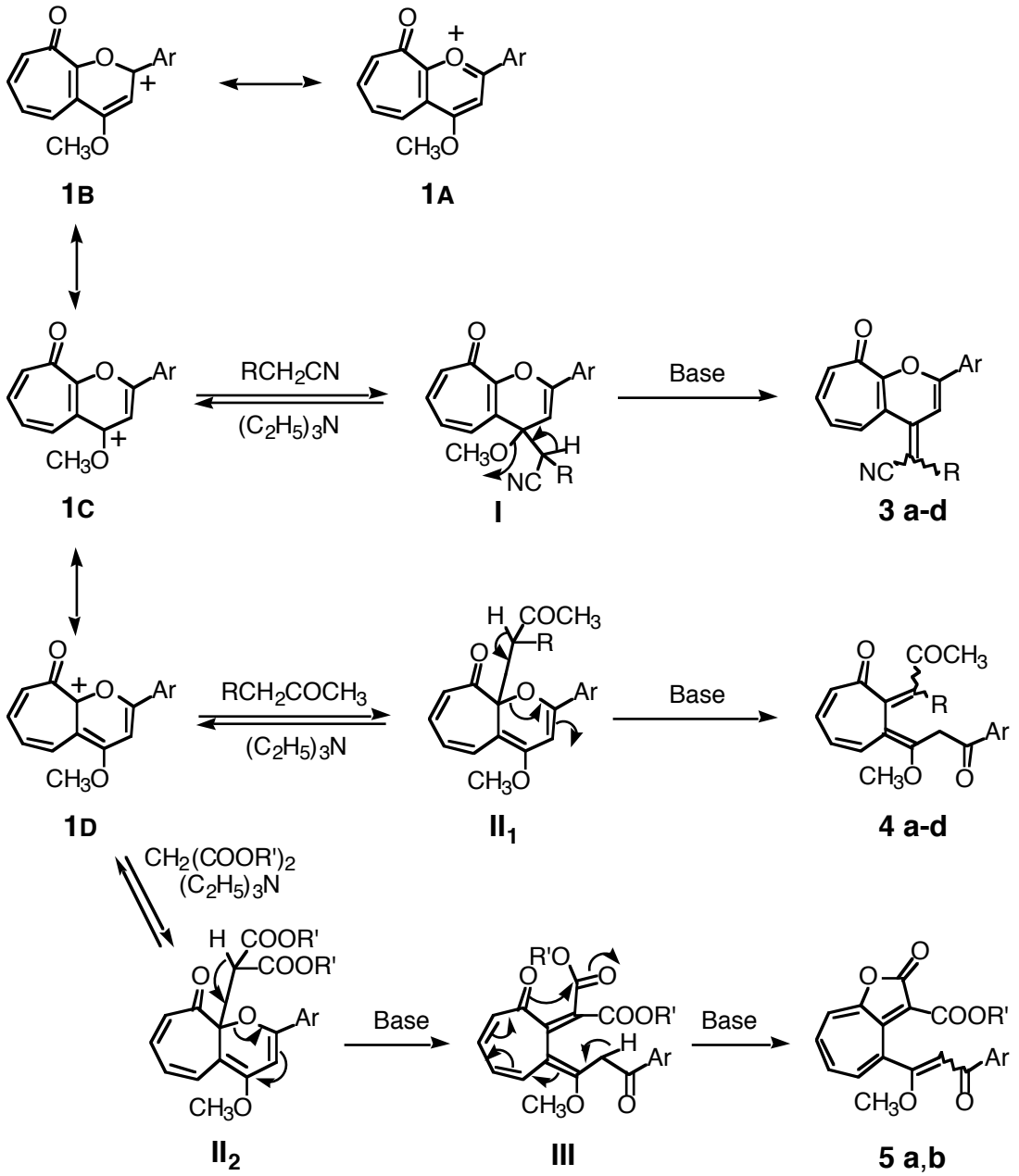


Scheme 1

Reaction of 9-Oxocyclohepta[*b*]pyrylium Salt (1) with Active Methylene Compounds Having an Acetyl Group.

A solution of 9-oxocyclohepta[*b*]pyrylium salt (**1**) and 2,4-pentanedione in acetonitrile was refluxed for 1 h in the presence of triethylamine to afford 2-diacetylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)-methylene]tropone (**4a**) in 76% yield. An elemental analysis ($C_{23}H_{22}NO_6$) and the spectral data supported its structure. In the IR spectrum, the three carbonyl absorptions were observed at 1669, 1600, and 1570 cm^{-1}. The ^1H NMR spectrum in deuteriochloroform showed two singlet signals at 1.97 and 2.19 for the two acetyl groups. The two singlet signals at 3.24 and 3.86 were assigned to the 1' - and 4" -methoxy group, respectively. The two doublet signals for the methylene protons were observed at 3.39 and 3.66 as AB system (J = 14.1 Hz). Similarly, the pyrylium salt (**1**) reacted with benzoylacetone, methyl

acetoacetate, and ethyl acetoacetate to yield 2-acetylbenzoylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)-methylene]tropone (**4b**) (75%), 2-acetylmethoxycarbonylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)methylene]tropone (**4c**) (78%), and 2-acetylethoxycarbonylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)methylene]tropone (**4d**) (65%), respectively.



Scheme 2

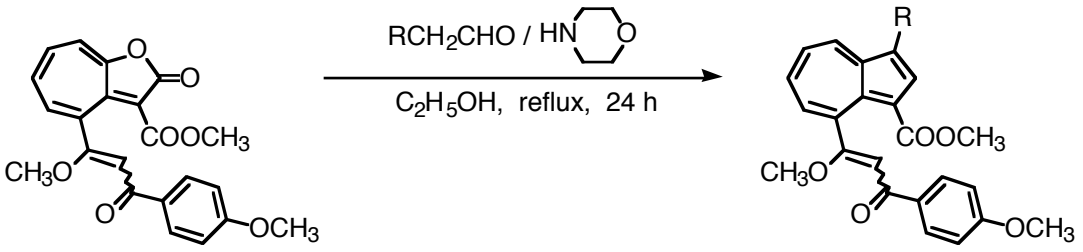
As shown in Scheme 2, the reactions might be initiated by nucleophilic attack of the active methylene

compounds at the 9a-position of a resonance form (**1D**) of the pyrylium salts (**1**) followed by ring-opening of the pyrylium ring ($\mathbf{II}_1$) to give the products (**4a**-**d**).

Reaction of 9-Oxocyclohepta[*b*]pyrylium Salt (1) with Malonic Acid Esters.

The reaction of 9-oxocyclohepta[*b*]pyrylium salt (**1**) with dimethyl malonate was carried out in acetonitrile under refluxing for 1 h in the presence of triethylamine to afford methyl 4-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]-2*H*-cyclohepta[*b*]furan-2-one-3-carboxylate (**5a**) in 91% yield. Its structure was confirmed by an elemental analysis ($C_{22}H_{18}O_7$) and spectral data. In the IR spectrum, the three characteristic carbonyl absorptions were observed at □ 1754, 1717, and 1643 cm^{-1}. The ^1H NMR spectrum showed the three singlet signals at □ 3.62, 3.83, and 3.92 for the methoxyl group and one singlet signal at □ 6.52 for the olefinic proton. In a similar manner, the reaction with diethyl malonate gave ethyl 4-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]-2*H*-cyclohepta[*b*]furan-2-one-3-carboxylate (**5b**) in 80% yield.

In these reactions, the nucleophilic attack of the malonic acid esters might be occurred at the 9a-position to form an intermediate ($\mathbf{II}_2$) as well as the reactions with acetyl-substituted active methylene compounds. The intermediate ($\mathbf{II}_2$) would collapsed to the second intermediates (**III**) which corresponds to the products (**4a**-**d**). Then, one of the ester functional groups in the intermediates (**III**) is subject to cyclization by a carbonyl function in the seven-membered ring to give 2*H*-cyclohepta[*b*]furan-2-one derivatives (**5a**,**b**). This is well known as a step in the azulene formation from reactive troponoids.



5 a **6 a-e**

a R = H
b R = CH_3
c R = CH_2CH_3
d R = $CH_2CH_2CH_3$
e R = $CH(CH_3)_2$

Scheme 3

It is known that 2*H*-cyclohepta[*b*]furan-2-ones are versatile intermediates for the synthesis of azulenes.[6,7] To an ethanolic solution of the 2*H*-cyclohepta[*b*]furan-2-one derivative (**5a**) were added acetaldehyde and diethylamine. The mixed solution was refluxed for 48 h to afford methyl 8-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]azulene-1-carboxylate (**6a**) in 26% yield. In a similar manner, the reactions using propionaldehyde, butyraldehyde, valeraldehyde, and isovaleraldehyde in the presence of morpholine gave

respectively the corresponding methyl 3-alkyl-8-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]azulene-1-carboxylate (**6b**-**e**) in 54-94% yields.

CONCLUSION

We examined the reactions of 9-oxocyclohepta[*b*]pyrylium salt (**1**) with a vaiety of active methylene compounds in the presence of triethylamine. It was found that the reactions with cyano-substituted nucleophiles occurred at the 4-position to give products (**3a**-**d**), while the reactions with acetyl- and alkoxycarbonyl-substituted nucleophiles took place at the 9a-position. The latter gave two-types of products (**4a**-**d**) and (**5a**,**b**). It is thought that azulenes (**6a**-**e**) derived from compound (**5a**) are useful key intermediates for the synthesis of novel ring systems because of their reactive enone functional group. These results will be reported elsewhere.

EXPERIMENTAL

The melting points were determined with Yanagimoto MP JP-3 apparatus and are uncorrected. The IR spectra were taken on a JASCO IRA-1 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded with JEOL JNM-EX 90 spectrometer (90 MHz for ^{1}H and 22.5 MHz for ^{13}C). The MS spectra were obtained by a JEOL JMX-DX 303HF instrument. Elemental analyses were performed by the Instrumental Analysis Center, Kumamoto University.

Reaction of 4-Methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium Perchlorate (1) with Nitromethane.

To a soluiton of 4-methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium perchlorate (**1**) (394 mg, 1.0 mmol) and nitromethane (73 mg, 1.0 mmol) in acetonitrile (10 mL) was added triethylamine (0.2 mL, 1.5 mmol). The mixed solution was refluxed for 1 h and cooled to rt to give 2-(4-methoxyphenyl)-4-nitromethylene-4,9-dihydrocyclohepta[*b*]pyran-9-one (**2**) (162 mg, 50%) as red needles (from acetic acid); mp 238-239 °C; IR (KBr) 1627 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$ + 10% CF_3COOD) 3.95 (3H, s, OCH_3), 7.10 (2H, d, *J* = 9.0 Hz, 3'-,5'-H), 7.34-7.82 (3H, m), 8.05 (2H, d, *J* = 9.0 Hz, 2'-,6'-H), 8.60 (1H, d, *J* = 9.0 Hz, 5-H), 8.80 (1H, s, 3-H). *Anal*. Calcd for $C_{18}H_{13}NO_5$: C, 66.87; H, 4.05; N, 4.33. Found: C, 66.65; H, 4.32; N, 4.39.

Reaction of 4-Methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium Perchlorate (1) with Active Methylene Compounds Having a Cyano Group.

To a solution of 9-oxocyclohepta[*b*]pyrylium salt (**1**) (197 mg, 0.5 mmol) and cyano-substituted active methylene compound (1.0 mmol) in acetonitrile (10 mL) was added triethylamine (0.2 mL, 1.5 mmol). After refluxing for 1 h, the mixture was worked up, as described above, to give the corresponding products (**3a**-**d**).

4-Dicyanomethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (3a).

This compound (**3a**) was obtained from the reaction with malononitrile as yellow needles (from acetic acid); yield 82 mg (50%); mp 249-250 °C; IR (KBr) ν 2219 (CN), 2185 (CN), 1605 cm^{-1} (C=O); ^1H NMR ($CDCl_3$ + 10% CF_3COOD) δ 3.95 (3H, s, OCH_3), 7.10 (2H, d, *J* = 9.1 Hz, 3'-,5'-H), 7.37 (1H, s, 3-H), 7.56-7.74 (3H, m), 8.05 (2H, d, *J* = 9.1 Hz, 2'-,6'-H), 8.35 (1H, d, *J* = 10.9 Hz, 5-H). *Anal.* Calcd for $C_{20}H_{12}N_2O_3$: C, 73.16; H, 3.68; N, 8.53. Found: C, 72.97; H, 3.72; N, 8.42.

4-Carboxycyanomethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (3b). This compound (**3b**) was obtained from the reaction with cyanoacetic acid as yellow needles (from acetic acid); yield 69 mg (40%); mp 281-283 °C; IR (KBr) ν 3172 (OH), 2216 (CN), 1729 (C=O), 1601 cm^{-1} (C=O); ^1H NMR ($CDCl_3$ + 10% CF_3COOD) δ 3.94 (3H, s. OCH_3), 7.09 (2H, d, *J* = 9.0 Hz, 3'-,5'-H), 6.97-7.92 (4H, m), 7.35 (1H, s, 3-H), 7.93 (2H, *J* = 9.0 Hz, 2'-,6'-H), 8.33 (1H, d, *J* = 11.0 Hz, 5-H). *Anal.* Calcd for $C_{20}H_{13}NO_5$: C, 69.16; H, 3.77; N, 4.03. Found: C, 68.89; H, 3.88; N, 4.08.

4-Cyanoethoxycarbonylmethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (3c). This compound (**3c**) was obtained from the reaction with ethyl cyanoacetate as yellow needles (from acetic acid); yield 81 mg (43%); mp 235-236 °C; IR (KBr) ν 2192 (CN), 1683 (C=O), 1618 cm^{-1} (C=O); ^1H NMR ($CDCl_3$ + 10% CF_3COOD) δ 1.43 (3H, t, *J* = 7.1 Hz, OCH_2CH_3), 3.94 (3H, s, OCH_3), 4.40 (2H, q, *J* = 7.1 Hz, OCH_2CH_3), 7.08 (2H, d, *J* = 9.0 Hz, 3'-,5'-H), 7.39-7.94 (4H, m), 8.02 (2H, d, *J* = 9.0 Hz, 2'-,6'-H), 8.69 (1H, s, 3-H). *Anal.* Calcd for $C_{22}H_{17}NO_5$: C,70.39; H, 4.57; N, 3.73. Found: C, 70.19; H, 4.66; N, 3.81.

4-Carbamoylcyanomethylene-2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-9-one (3d). This compound (**3d**) was obtained from the reaction with cyanoacetamide as yellow needles (from acetic acid); yield 52 mg (32%); mp 239-240 °C; IR (KBr) ν 3312 (NH), 2180 (CN), 1677 (C=O), 1592 cm^{-1} (C=O); ^1H NMR ($CDCl_3$ + 10% CF_3COOD) δ 3.95 (3H, s, OCH_3), 7.09 (2H, d, *J* = 9.1 Hz, 3'-,5'-H), 7.37-7.86 (4H, m), 8.00 (2H, d, *J* = 9.1 Hz, 2'-,6'-H), 8.69 (1H, s, 3-H). *Anal.* Calcd for $C_{20}H_{14}N_2O_4$: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.60; H, 4.14; N, 7.88.

Reaction of 4-Methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium Perchlorate (1a) with Active Methylene Compounds Having an Acetyl group.

To a solution of 9-oxocyclohepta[*b*]pyrylium salt (**1**) (197 mg, 0.5 mmol) and acetyl-substituted active methylene compound (1.0 mmol) in acetonitrile (10 mL) was added triethylamine (0.2 mL, 1.5 mmol). After refluxing for 1 h, the mixture was worked up, as described above, to give the corresponding products (**4a**-**d**).

2-Diacetylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)methylene]tropone (4a). This compound (**4a**) was obtained from the reaction with 2,4-pentanedione as reddish orange needles (from ethanol); yield 150 mg (76%); mp 135-137 °C; IR (KBr) ν 1669 (C=O), 1600 (C=O), 1570 cm^{-1}

(C=O); ^{1}H NMR ($CDCl_3$) □1.97 (3H, s, $COCH_3$), 2.19 (3H, s, $COCH_3$), 3.24 (3H, s, 1'-OCH_3), 3.39 (1H, d, *J* = 14.1 Hz, 2'-$CH_□$), 3.66 (1H, d, *J* = 14.1 Hz, 2'-$CH_□$), 3.86 (3H, s, 4"-OCH_3), 6.91 (2H, d, *J* = 9.0 Hz, 3"-, 5"-H), 7.01-7.10 (4H, m), 7.92 (2H, d, *J* = 9.0 Hz, 2"-,6"-H); ^{13}C NMR ($CDCl_3$) □17.3 ($CO\mathit{C}H_3$), 30.5 ($CO\mathit{C}H_3$), 47.5 (CH_3), 50.8 (OCH_3), 55.2 (OCH_3), 105.1 (=C<), 113.4 (=CH-), 115.6 (=C<), 130.0 (=C<), 130,8 (=CH-), 131,0 (=C<), 131.8 (=CH-), 131.9 (=CH-), 135.9 (=CH-), 138.4 (=CH-), 142.7 (=C<), 157.0 (=C<), 163.5 (C=O), 183.2 (C=O), 192.3 (C=O), 199.0 (C=O). *Anal*. Calcd for $C_{23}H_{22}O_6$: C, 70.04; H, 5.62. Found: C, 69.82; H, 5.64.

2-Acetylbenzoylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)methylene]tropone (4b). This compound (**4b**) was obtained from the reaction with 1-benzoylacetone and purified by using a preparative thin layer chromatography on a Wakogel B-10 plate (30 x 30 cm) with chloroform-ethanol (10 : 1) as reddish orange oil; yield 171 mg (75%); IR ($CHCl_3$) □1665 (C=O), 1600 (C=O), 1576 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) □1.86 (3H, s, $COCH_3$), 3.66 (3H, s, 1'-OCH_3), 3.66-3.70 (2H, m, CH_2), 3.82 (3H, s, 4"-OCH_3), 6.74-6.91 (5H, m), 7.12-7.52 (4H, m), 7.92-8.02 (4H, m); ^{13}C NMR ($CDCl_3$) □17.9 ($CO\mathit{C}H_3$), 48.4 (CH_2), 50.5 (OCH_3), 55.2 (OCH_3), 109.4 (=C<), 111.8 (=C<), 113.5 (=CH-), 126.7 (=CH-), 128.0 (=CH-), 128.1 (=CH-), 129.8 (=C<), 130.0 (=C<), 130.8 (=CH-), 131.6 (=CH-), 131.9 (=CH-), 135.4 (=CH-), 137.9 (=CH-), 139.0 (=C<), 143.6 (=C<), 158.1 (=C<), 163.6 (C=O), 182.9 (C=O), 192.6 (C=O), 193.7 (C=O); MS (EI) m/z (%) 456 (M^+, 10), 135 (100). HRMS Calcd for $C_{28}H_{24}O_6$: M, 456.1572. Found: M^+, 456.1567.

2-Acetylmethoxycarbonylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)methylene]-tropone (4c). This compound (**4c**) was obtained from the reaction with methyl acetoacetate as reddish orange needles (from ethanol); yield 160 mg (78%); mp 152-153 °C; IR (KBr) □1724 (C=O), 1664 (C=O), 1621 (C=O), 1599 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) □2.16 (3H, s, $COCH_3$), 3.25 (3H, s, 1'-OCH_3), 3.39 (1H, d, *J* = 14.3 Hz, 2'-$CH_□$), 3.61 (1H, d, *J* = 14.3 Hz, 2'-$CH_□$), 3.74 (3H, s, $COOCH_3$), 3.85 (3H, s, 4"-OCH_3), 6.90 (2H, d, *J* = 8.9 Hz, 3"-,5"-H), 7.00-7.15 (4H, m), 7.90 (2H, d, *J* = 8.9 Hz, 2"-,6"-H); ^{13}C NMR ($CDCl_3$) □17.7 ($CO\mathit{C}H_3$), 46.7 (CH_2), 51.0 (OCH_3), 51.5 (OCH_3), 55.2 ($COO\mathit{C}H_3$), 105.5 (=C<), 107.5 (=C<), 113.4 (=CH-), 130.1 (=CH-), 130.3 (=C<), 130.6 (=C<), 130.9 (=CH-), 131.6 (=CH-), 134.8 (=CH-), 137.5 (=CH-), 140.9 (=C<), 160.7 (=C<), 163.4 (C=O), 167.3 (C=O), 184.2 (C=O), 192.4 (C=O). *Anal*. Calcd for $C_{23}H_{22}O_7$: C, 67.31; H, 5.40. Found: C, 67.13; H, 5.26.

2-Acetylethoxycarbonylmethylene-3-[1-methoxy-1-(4-methoxyphenacyl)methylene]-tropone (4d). This compound (**4d**) was obtained from the reaction with ethyl acetoacetate as reddish orange needles (from ethanol); yield 138 mg (65%); mp 108-109 °C; IR (KBr) □1709 (C=O), 1669 (C=O), 1624 (C=O), 1599 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) □1.28 (3H, t, *J* = 7.0 Hz, $OCH_2C\mathit{H}_3$), 2.17 (3H, s, $COCH_3$), 3.26 (3H, s, 1'-OCH_3), 3.38 (1H, d, *J* = 13.7 Hz, 2'-$CH_□$), 3.59 (1H, d, *J* = 13.7 Hz, 2'-$CH_□$), 3.85 (3H, s, 4"-OCH_3), 4.22 (2H, q, *J* = 7.0 Hz, $OC\mathit{H}_2CH_3$), 6.85 (2H, d, *J* = 9.0 Hz, 3"-, 5"-H), 6.86-7.11 (4H, m), 7.90 (2H, d, *J* = 9.0 Hz, 2"-,6"-H); ^{13}C NMR ($CDCl_3$) □13.9 ($OCH_2\mathit{C}H_3$), 17.8

($CO\underline{C}H_3$), 46.7 (CH_2), 51.2 (OCH_3), 55.4 (OCH_3), 60.6 ($O\underline{C}H_2CH_3$), 105.6 (=C<), 107.9 (=C<), 113.5 (=CH-), 129.9 (=CH-), 130.6 (=C<), 130.9 (=C<), 131.1 (=CH-), 131.6 (=CH-), 134.7 (=CH-), 137.4 (=CH-), 141.0 (=C<), 160.9 (=C<), 163.5 (C=O), 166.9 (C=O), 184.6 (C=O), 192.6 (C=O). *Anal.* Calcd for $C_{24}H_{24}O_7$: C, 67.91; H, 5.70. Found: C, 68.04; H, 5.81.

Reaction of 4-Methoxy-2-(4-methoxyphenyl)-9-oxocyclohepta[*b*]pyrylium Perchlorate (1) with Malonic Acid Esters.

To a solution of 9-oxocyclohepta[*b*]pyrylium salt (**1**) (197 mg, 0.5 mmol) and malonic acid ester (1.0 mmol) in acetonitrile (10 mL) was added triethylamine (0.2 mL, 1.5 mmol). After refluxing for 1 h, the mixture was worked up, as described above, to give the corresponding products (**5a**-**c**).

Methyl 4-[1-Methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]-2*H*-cyclohepta[*b*]furan-2-one-3-carboxylate (5a). This compound (**5a**) was obtained from the reaction with dimethyl malonate as reddish orange needles (from ethanol); yield 179 mg (91%); mp 225-226 °C; IR (KBr) 1754 (C=O), 1717 (C=O), 1643 cm^{-1} (C=O); ^{1}H NMR (DMSO-d_6) 3.62 (3H, s, $COOCH_3$), 3.83 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 6.52 (1H, s, 2'-H), 6.99 (2H, d, J = 9.0 Hz, 3"-,5" -H), 7.29-7.63 (4H, m), 7.91 (2H, d, J = 9.0 Hz, 2"-,6" -H); ^{13}C NMR (DMSO-d_6) 51.7 (OCH_3), 55.3 (OCH_3), 57.2 (COO-$\underline{C}H_3$), 97.1 (=CH-), 100.5 (=C<), 113.5 (=CH-), 118.7 (=CH-), 130.0 (=CH-), 130.5 (=C<), 131.1 (=C<), 132.4 (=CH-), 136.1 (=CH-), 136.7 (=C<), 140.0 (=CH-), 148.0 (=C<), 156.8 (=C<), 162.6 (=C<), 164.5 (C=O), 168.3 (C=O), 185.5 (C=O). *Anal.* Calcd for $C_{22}H_{18}O_7$: C, 67.00; H, 4.60. Found: C, 67.04; H, 4.74.

Ethyl 4-[1-Methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]-2*H*-cyclohepta[*b*]furan-2-one-3-carboxylate (5b). This compound (**5b**) was obtained from the reaction with diethyl malonate as reddish orange needles (from ethanol); yield 163 mg (80%); mp 110-112 °C; IR (KBr) 1724 (C=O), 1664 (C=O), 1620 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) 1.16 (3H, t, J = 7.0 Hz, $OCH_2C\underline{H}_3$), 3.83 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 4.19 (2H, q, J = 7.0 Hz, $OC\underline{H}_2CH_3$), 6.31 (1H, s, 2'-H), 6.85 (2H, d, J = 9.0 Hz, 3"-,5" -H), 7.08-7.40 (4H, m), 7.85 (2H, d, J = 9.0 Hz, 2"-,6" -H); ^{13}C NMR ($CDCl_3$) 13.9 ($OCH_2\underline{C}H_3$), 55.3 (OCH_3), 56.6 (OCH_3), 61.0 ($O\underline{C}H_2CH_3$), 97.7 (=CH-), 102.4 (=C<), 113.5 (=CH-), 117.7 (=CH-), 129.9 (=C<), 130.3 (=CH-), 131.3 (=C<), 131.6 (=CH-), 135.2 (=CH-), 136.7 (=C<), 139.9 (=CH-), 148.4 (=C<), 158.2 (=C<), 162.9 (=C<), 165.1 (C=O), 168.9 (C=O), 186.6 (C=O). *Anal.* Calcd for $C_{23}H_{20}O_7$: C, 67.64; H, 4.94. Found: C, 67.72; H, 4.91.

Reaction of Methyl 4-[1-Methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]-2*H*-cyclohepta-[*b*]furan-2-one-3-carboxylate (5a) with Enamines.

To a suspended solution of 2*H*-cyclohepta[*b*]furan-2-one derivative (**5a**) (394 mg, 1.0 mmol) in ethanol (10 mL) were added aldehyde (3.0 mmol) and morpholine (261 mg, 3.0 mmol) [diethlylamine (219 mg, 3.0 mmol) for **6a**]. Then, the solution was refluxed for 24 h (48 h for **6a**). After removal of the solvent, the residue was dissolved in benzene. The benzene solution was washed with water and dried over sodium

sulfate. The oily residue was twice chromatographed on a column (Merck's silica gel 60, 30 g) with chloroform to give the corresponding azulenes (**6a**-**e**).

Methyl 8-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]azulene-1-carboxylate (6a). This compound (**6a**) was obtained from the reaction of **5a** using acetaldehyde and diethylamine as blue oil; yield 98 mg (26%); IR ($CHCl_3$) 1710 (C=O), 1655 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 4.00 (3H, s, $COOCH_3$), 6.35 (1H, s, 2'-H), 6.79 (2H, d, *J* = 9.0 Hz, 3"-, 5"-H), 7.21 (1H, d, *J* = 4.2 Hz, 3-H), 7.25-7.61 (3H, m), 7.77 (2H, d, *J* = 9.0 Hz, 2"-,6"-H), 8.18 (1H, d, *J* = 4.2 Hz, 2-H), 8.40 (1H, d, *J* = 8.5 Hz, 4-H); ^{13}C NMR ($CDCl_3$) 51.3 (OCH_3), 55.3 (OCH_3), 56.5 (OCH_3), 98.9 (=CH-), 113.3 (=CH-), 118.8 (=C<), 126.1 (=C<), 129.4 (=CH-), 129.9 (=CH-), 130.0 (=CH-), 132.3 (=C<), 137.4 (=CH-), 138.4 (=CH-), 141.0 (=CH-), 144.4 (=C<), 145.6 (=C<), 162.6 (=C<), 172.5 (C=O), 187.9 (C=O); MS (EI) m/z (%) 376 (M^+, 10), 135 (100). HRMS. Calcd for $C_{23}H_{20}O_5$: M, 376.1310. Found: M^+, 376.1227.

Methyl 3-Methyl-8-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]azulene-1-carboxylate (6b). This compound (**6b**) was obtained from the reaction using propionaldehyde and morpholine as blue needles (from benzene); yield 367 mg (94%); mp 141-142 °C; IR (KBr) 1705 (C=O), 1658 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 2.56 (3H, s, CH_3), 3.77 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 3.98 (3H, s, $COOCH_3$), 6.30 (1H, s, 2'-H), 6.76 (2H, d, *J* = 9.0 Hz, 3"-,5"-H), 7.25-7.54 (3H, m), 7.73 (2H, d, *J* = 9.0 Hz, 2"-,6"-H), 8.01 (1H, s, 2-H), 8.27 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C NMR ($CDCl_3$) 12.6 (CH_3), 51.2 (OCH_3), 55.2 (OCH_3), 56.4 (OCH_3), 98.8 (=CH-), 113.1 (=CH-), 117.0 (=C<), 124.6 (=C<), 125.8 (=CH-), 128.5 (=CH-), 129.9 (=CH-), 132.2 (=C<), 135.0 (=CH-), 137.1 (=CH-), 141.7 (=CH-), 141.9 (=C<), 143.6 (=C<), 162.4 (=C<), 165.8 (=C<), 172.4 (C=O), 188.0 (C=O). *Anal.* Calcd for $C_{24}H_{22}O_5$: C, 73.83; H, 5.68. Found: C, 74.05; H, 5.71.

Methyl 3-Ethyl-8-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]azulene-1-carboxylate (6c). This compound (**6c**) was obtained from the reaction using butyraldehyde and morpholine as blue oil; yield 372 mg (92%); IR ($CHCl_3$) 1706 (C=O), 1652 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 1.35 (3H, t, *J* = 7.5 Hz, CH_2CH_3), 2.91 (2H, q, *J* = 7.5 Hz, CH_2CH_3), 3.76 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.97 (3H, s, $COOCH_3$), 6.30 (1H, s, 2'-H), 6.76 (2H, d, *J* = 8.9 Hz, 3"-, 5"-H), 7.25-7.53 (3H, m), 7.73 (2H, d, *J* = 8.9 Hz, 2"-, 6"-H), 8.07 (1H, s, 2-H), 8.33 (1H, d, *J* = 8.7 Hz, 4-H); ^{13}C NMR ($CDCl_3$) 14.7 (CH_2CH_3), 20.1 (CH_2CH_3), 51.2 (OCH_3), 55.2 (OCH_3), 56.3 (OCH_3), 98.8 (=CH-), 113.1 (=CH-), 117.2 (=C<), 124.6 (=C<), 127.8 (=CH-), 128.6 (=CH-), 129.8 (=CH-), 132.3 (=C<), 134.4 (=CH-), 137.1 (=CH-), 139.9 (=C<), 141.0 (=CH-), 143.6 (=C<), 162.4 (=C<), 165.9 (=C<), 172.5 (C=O), 188.0 (C=O); MS (EI) m/z (%) 404 (M^+, 30), 135 (100). HRMS. Calcd for $C_{25}H_{24}O_5$: M, 404.1624. Found: M^+, 404.1600.

Methyl 3-Propyl-8-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]azulene-1-carboxylate (6d). This compound (**6d**) was obtained from the reaction using valeraldehyde and morpholine as

blue oil; yield 345 mg (83%); IR ($CHCl_3$) 1705 (C=O), 1658 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 0.98 (3H, t, J = 7.4 Hz, $CH_2CH_2CH_3$), 1.74 (2H, m, $CH_2CH_2CH_3$), 2.91 (2H, q, J = 7.5 Hz, $CH_2CH_2CH_3$), 3.77 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.97 (3H, s, $COOCH_3$), 6.30 (1H, s, 2'-H), 6.76 (2H, d, J = 9.0 Hz, 3"-, 5" -H), 7.24-7.61 (3H, m), 7.74 (2H, d, J = 9.0 Hz, 2"-, 6" -H), 8.05 (1H, s, 2-H), 8.33 (1H, d, J = 9.0 Hz, 4-H); ^{13}C NMR ($CDCl_3$) 14.2 ($CH_2CH_2CH_3$), 23.9 ($CH_2CH_2CH_3$), 29.2 ($CH_2CH_2CH_3$), 51.3 (OCH_3), 55.3 (OCH_3), 56.4 (OCH_3), 98.9 (=CH-), 113.2 (=CH-), 117.3 (=C<), 124.7 (=C<), 128.7 (=CH-), 130.0 (=CH-), 131.0 (=CH-), 132.3 (=C<), 134.7 (=CH-), 137.2 (=CH-), 140.9 (=CH-), 141.5 (=C<), 143.7 (=C<), 162.5 (=C<), 166.6 (=C<), 172.7 (C=O), 188.1 (C=O). HRMS. Calcd for $C_{26}H_{26}O_5$: M, 418.1781. Found: M^+, 418.1781.

Methyl 3-(1-Methylethyl)-8-[1-methoxy-3-(4-methoxyphenyl)-3-oxopropenyl]azulene-1-carboxylate (6e). This compound (**6e**) was obtained from the reaction of **5a** using isovaleraldehyde and morpholine as blue oil; yield 218 mg (54%); IR ($CHCl_3$) 1702 (C=O), 1642 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 1.32 [6H, d, J = 7.4 Hz, $CH(CH_3)_2$], 2.98 [1H, sept, J = 7.4 Hz, $CH(CH_3)_2$], 3.75 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.97 (3H, s, $COOCH_3$), 6.30 (1H, s, 2'-H), 6.75 (2H, d, J = 9.0 Hz, 3"-,5" -H), 7.31 (2H, d, J = 9.0 Hz, 2"-,6" -H), 7.51-7.85 (3H, m), 8.11 (1H, s, 2-H), 8.31 (1H, d, J = 9.5 Hz, 4-H); ^{13}C NMR ($CDCl_3$) 14.6 [$CH(CH_3)_2$], 20.0 [$CH(CH_3)_2$], 51.2 (OCH_3), 55.2 (OCH_3), 56.3 (OCH_3), 98.8 (=CH-), 113.0 (=CH-), 114.3 (=C<), 124.6 (=C<), 127.7 (=CH-), 128.5 (=CH-), 129.8 (=CH-), 132.1 (=C<), 134.1 (=C<), 134.4 (=C<), 137.1 (=CH-), 137.9 (=CH-), 139.9 (=CH-), 143.6 (=C<), 162.3 (=C<), 172.4 (C=O), 187.9 (C=O); MS (EI) m/z (%) 418 (M^+, 30), 135 (100). HRMS. Calcd for $C_{26}H_{26}O_5$: M, 418.1781. Found: M^+, 418.1700.

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