A CONVENIENT, ONE-POT AZULENE SYNTHESIS FROM 2*H*-CYCLOHEPTA[*b*]FURAN-2-ONES WITH VINYL ETHER AND ITS ANALOGUES III.[1] ORTHOESTERS AS A REAGENT[2]

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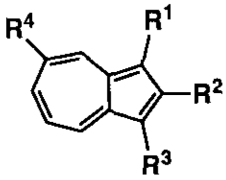
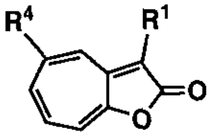
Abstract - 2-Alkoxy and 2,4-dialkoxyazulene derivatives were synthesized in one-pot and in good yields by the reaction of 2*H*-cyclohepta[*b*]furan-2-ones with orthoesters on heating either neat or in an aprotic solvent at 160-190 °C.

In a preceding paper,[3] we reported a facile synthetic method for variously functionalized azulene derivatives (**1** and **2**) utilizing the reaction of 2*H*-cyclohepta[*b*]furan-2-ones (**3** and **4**) with vinyl ether derivatives. This method was further developed to a new azulene synthesis using acetals of some aldehydes and ketones instead of vinyl ether derivatives as a reagent.[1]



1a-n: R^4=H
2a-k: R^4=iPr



3a-e: R^4=H
4a-e: R^4=iPr

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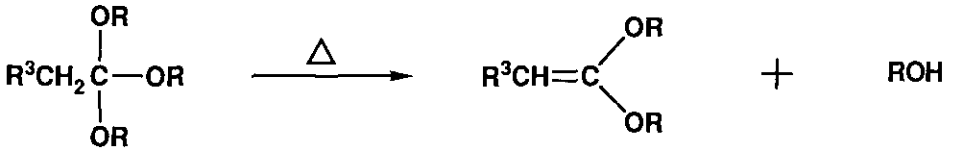
Table 1. Synthesis of Azulene Derivatives by the Reaction of **3** or **4** with **5**.

Reagent		Azulene Derivatives[5-20]				Color / Form		mp	Yield
			R^1	R^2	R^3			(°C)	(%)
3a	**5a**	**1a**[5]	H	OMe	H	reddish violet	needles	64-65	24
3b	**5a**	**1b**[5]	COOMe	OMe	H	reddish orange	needles	73-74	87
3d	**5a**	**1c**[6]	COMe	OMe	H	reddish orange	needles	50-51	96
3e	**5a**	**1d**	CN	OMe	H	reddish orange	prisms	104-105	95
3a	**5c**	**1e**[7]	H	OEt	Me	violet	needles	78-79	47
3c	**5c**	**1f**[8]	COOEt	OEt	Me	reddish violet	oil	---	97
3d	**5c**	**1g**[9]	COMe	OEt	Me	reddish violet	prisms	53-54	90
3e	**5c**	**1h**[10]	CN	OEt	Me	reddish violet	prisms	111-112	98
3a	**5d**	**1i**	H	OMe	Et	reddish violet	oil	---	87
3d	**5d**	**1k**[11]	COMe	OMe	Et	reddish violet	oil	---	70
3e	**5d**	**1l**[12]	CN	OMe	Et	reddish violet	needles	89-90	99
3a	**5e**	**1m**	H	OMe	Pr	reddish violet	oil	---	34
3b	**5e**	**1n**	COOMe	OMe	Pr	reddish violet	oil	---	83
4a	**5a**	**2a**[13]	H	OMe	H	reddish violet	oil	---	11
4c	**5b**	**2b**	COOEt	OEt	H	reddish orange	needles	52-53	94
4d	**5b**	**2c**[14]	COMe	OEt	H	reddish orange	prisms	106-107	94
4e	**5b**	**2d**[15]	CN	OEt	H	reddish orange	prisms	83-84	98
4c	**5c**	**2e**[16]	COOEt	OEt	Me	reddish violet	oil	---	94
4d	**5c**	**2f**[17]	COMe	OEt	Me	reddish violet	prisms	73-74	95
4d	**5c**	**2g**	CN	OEt	Me	reddish orange	needles	111-112	96
4b	**5d**	**2h**[18]	COOMe	OMe	Et	reddish violet	oil	---	88
4d	**5d**	**2i**[19]	COMe	OMe	Et	reddish violet	oil	---	77
4e	**5d**	**2j**	CN	OMe	Et	reddish violet	prisms	98-99	96
4b	**5e**	**2k**[20]	COOMe	OMe	Pr	reddish violet	oil	---	61

In this communication, we wish to report another convenient method of preparing azulenes (**1**, **2**, **9**, and **10**) having alkoxyl groups on the C-2 or C-2,4 positions in one-pot by the reaction of **3**, **4**, **7**, or **8** with several orthoesters (**5**). These orthoesters are expected to generate the corresponding dialkyl acetals (**6**) of ketenes at



5a - e **6a - e**

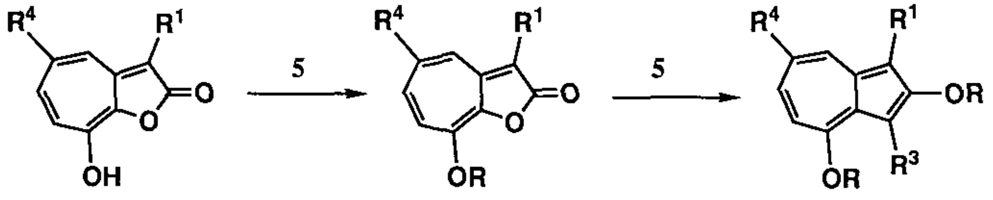
Table 2. Synthesis of Azulene Derivatives by the Reaction of **7** or **8** with **5**.

Reagent		Azulene Derivatives[21-30]				Color / Form		mp	Yield
			R^1	OR	R^3			(°C)	(%)
7b	**5a**	**9a**[21]	COOMe	OMe	H	reddish orange	needles	141-142	69
7c	**5a**	**9b**	COOEt	OEt	H	reddish orange	needles	119-120	80
7d	**5b**	**9c**	COMe	OEt	H	reddish orange	needles	108-109	89
7e	**5b**	**9d**[22]	CN	OEt	H	reddish orange	needles	106-107	88
7c	**5c**	**9e**[23]	COOEt	OEt	Me	violet	needles	85-86	99
7d	**5c**	**9f**	COMe	OEt	Me	reddish violet	prisms	85-86	83
7e	**5c**	**9g**[24]	CN	OEt	Me	reddish violet	prisms	141-142	88
7c	**5d**	**9h**	COOEt	OMe	Et	reddish violet	oil	---	63
7d	**5d**	**9i**	COMe	OMe	Et	reddish violet	prisms	58-89	51
7e	**5d**	**9j**[25]	CN	OMe	Et	reddish violet	prisms	120-121	96
7c	**5e**	**9k**	COOEt	OMe	Pr	reddish violet	oil	---	58
8c	**5b**	**10a**[26]	COOEt	OEt	H	reddish orange	needles	62-63	86
8d	**5b**	**10b**[27]	COMe	OEt	H	reddish orange	prisms	90-91	99
8e	**5b**	**10c**	CN	OEt	H	reddish orange	needles	123-124	90
8c	**5c**	**10d**[28]	COOEt	OEt	Me	reddish violet	oil	---	89
8d	**5c**	**10e**	COMe	OEt	Me	reddish violet	prisms	100-101	91
8e	**5c**	**10f**[29]	CN	OEt	Me	reddish violet	needles	108-109	87
8d	**5d**	**10g**	COMe	OMe	Et	reddish violet	oil	---	16
8e	**5d**	**10h**[30]	CN	OMe	Et	reddish violet	needles	75-76	72

high reaction temperatures by the elimination of one molar alcohol. Orthoesters used in this study are trimethyl orthoacetate (**5a**), triethyl orthoacetate (**5b**), triethyl orthopropionate (**5c**), trimethyl orthobutyrate (**5d**), and trimethyl orthovalerate (**5e**).

Thus, cyclohepta[b]furan-2-ones[4] (**3a-e** and **4a-e**) having various functional groups (**a**: R^1=H, **b**: R^1=COOMe, **c**: R^1=COOEt, **d**: R^1=COMe, **e**: R^1=CN) on C-3 are heated either neat or in an aprotic solvent (THF, toluene, benzene) with 3-6 equivalents of orthoesters (**5**) at 160-190 °C for 20-60 h in a Pyrex sealed tube. After evaporation of the unreacted reagents and solvent in vacuo, azulenes produced are easily separated by silica gel column chromatography (benzene as an eluent). The reactions of **3** or **4** with orthoesters (**5**) gave 2-alkoxyazulene derivatives (**1** and **2**). The structures of these azulenes were established on the basis of the ^{1}H nmr (see References) and other spectral data. The structures, properties, and yields of azulenes obtained by this method are shown in Table 1. The formation of the present azulenes is believed to proceed via [8+2] cycloadducts of cyclohepta[b]furanones (**3** and **4**) with dialkyl acetals (**6**) of ketenes, in a manner similar to that proposed in a previous paper.[1]

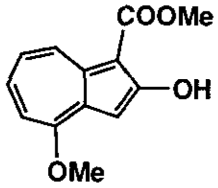
Smilarly, the reaction of 8-hydroxycyclohepta[b]furan-2-ones[31] (**7** and **8**) with orthoester (**5**) directly afforded azulenes (**9** and **10**) having two alkoxyl groups on C-2 and C-4 positions via 8-alkoxy derivatives[32] (**11** and **12**, R=Me or Et). The product yields and structures of 8-alkoxyazulenes (**9** and **10**) are listed in Table 2.



7b-e: R^4=H   **11**: R^4=H   **9a-k**: R^4=H

8c-e: R^4=iPr   **12**: R^4=iPr   **10a-h**: R^4=iPr

Alkoxyazulenes (**9** and **10**) have been found to be versatile starting materials for synthesis of various, useful azulenes. For example, when the dialkoxyazulene derivative (**9a**) was treated with 75% sulfuric acid at 90 °C, hydrolysis occurred only at 2-position to give monohydroxy compound (**13**,[33] brown needles, mp 90-92 °C) in a 80% yield. On the other hand, treatment of **9b** with N-chlorosuccinimide in benzene at room temperature gave 3-chloroazulene derivative (**14**,[34] reddish violet needles, mp 102-103 °C) in a 60% yield. The reaction of **14** with o-aminobenzenethiol in ethanol at 120 °C for 20 h gave ethyl 6-ethoxyazuleno[1,2-b][1,4]-benzothiazine-11-carboxylate (**15**,[35] dark violet needles, mp 128-130 °C) in a 53% yield.



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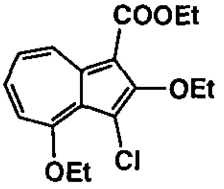

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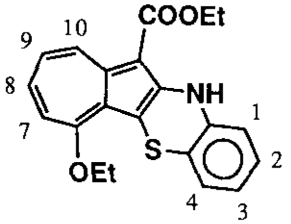

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We thank Professor Hiroshi Yamamoto (Okayama Univ.) for his helpful discussions and to National Science Council of the Republic of China for financial support (NSC 79-0208-M002-23 to P.-W. Yang).

REFERENCES

1) Part II: T. Nozoe, H. Wakabayashi, S. Ishikawa, C.-P. Wu, and P.-W. Yang, Heterocycles, 1990, **31**, 17.
2) Presented at the 57th National Meeting of the Chemical Society of Japan, Sendai, 1988, Abstr. No. E214.

3) T. Nozoe, P.-W. Yang, C.-P. Wu, T.-S. Huang, T.-H. Lee, H. Wakabayashi, H. Okai, and S. Ishikawa, Heterocycles, 1989, **29**, 1225.

4) T. Nozoe, K. Takase, T. Nakazawa, and S. Fukuda, Tetrahedron, 1971, **27**, 3357.

5) T. Nozoe, K. Takase, and N. Shimazaki, Bull. Chem. Soc. Jpn, 1964, **37**, 1644; T. Nozoe, P.-W. Yang, H. Ogawa, and T. Toda, Bull. Chem. Soc. Jpn, 1968, **41**, 2095.

6) **1c**: ^1H Nmr (300 MHz, $CDCl_3$) δ =2.63 (3H, s, $COCH_3$), 4.08 (3H, s, OCH_3), 6.66 (1H, s, H-3), 7.37 (1H, t, J=10 Hz, H-6), 7.53 (2H, m, J=10 Hz, H-5,7), 8.13 (1H, d, J=10 Hz, H-4), 9.66 (1H, d, J=10 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =31.9 (q), 58.0 (q), 99.3 (d), 112.1 (s), 128.5 (d), 130.6 (d), 133.9 (d), 135.1 (d), 135.1 (d), 140.7 (s), 143.8 (s), 170.1 (s), and 195.4 (s).

7) **1e**: ^1H Nmr (270 MHz, $CDCl_3$) δ =1.49 (3H, t, J=7.3 Hz, $OCH_2C\underline{H}_3$), 2.45 (3H, s, CH_3), 4.27 (2H, q, J=7.3 Hz, $OC\underline{H}_2CH_3$), 6.71 (1H, s, H-3), 7.08 (2H, t, J=10 Hz, H-5,7), 7.32 (1H, t, J=10 Hz, H-6), 7.96 (1H, d, J=10 Hz, H-4 or 8), 8.01 (1H, d, J=10 Hz, H-8 or 4).

8) **1f**: ^1H Nmr (270 MHz, $CDCl_3$) δ =1.46 (6H, t, J=7.3 Hz, $OCH_2C\underline{H}_3$), 2.48 (3H, s, CH_3), 4.43 (2H, q, J=7.3 Hz, $OC\underline{H}_2CH_3$), 4.46 (2H, q, J=7.3 Hz, $OC\underline{H}_2CH_3$), 7.36 (1H, t, J=10 Hz, H-5), 7.43 (1H, t, J=10 Hz, H-7), 7.59 (1H, t, J=10 Hz, H-6), 8.21 (1H, d, J=10 Hz, H-4), 9.33 (1H, d, J=10 Hz, H-8); ^{13}C nmr (67.8 MHz, $CDCl_3$) δ =8.7 (q), 14.6 (q), 15.9 (q), 59.8 (t), 70.9 (t), 105.4 (s), 116.5 (s), 125.9 (d), 127.6 (d), 132.4 (d), 134.2 (d), 135.6 (d), 138.8 (s), 140.2 (s), 164.9 (s), and 167.3 (s).

9) **1g**: ^1H Nmr (300 MHz, $CDCl_3$) δ =1.44 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 2.42 (3H, s, CH_3), 2.66 (3H, s, $COCH_3$), 4.30 (2H, q, J=6.9 Hz, $OC\underline{H}_2CH_3$), 7.25 (1H, t, J=10 Hz, H-5), 7.37 (1H, t, J=10 Hz, H-7), 7.48 (1H, t, J=10 Hz, H-6), 8.06 (1H, d, J=10 Hz, H-4), and 9.51 (1H, d, J=10 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =9.8 (q), 15.7 (q), 31.2 (q), 70.1 (t), 113.8 (s), 114.3 (s), 126.5 (d), 129.3 (d), 132.0 (d), 135.3 (d), 135.8 (d), 139.1 (s), 140.0 (s), 1167.3 (s), and 195.5 (s).

10) **1h**: ^1H Nmr (200 MHz, $CDCl_3$) δ =1.15 (3H, t, J=7.5 Hz, $OCH_2C\underline{H}_3$), 2.82 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 4.44 (3H, s, OCH_3), 7.26 (1H, t, J=10 Hz, H-5), 7.33 (1H, t, J=10 Hz, H-7), 7.48 (1H, t, J=10 Hz, H-6), 8.05 (1H, d, J=10 Hz, H-4), and 8.21 (1H, d, J=10 Hz, H-8).

11) **1k**: ^1H Nmr (200 MHz, $CDCl_3$) δ =1.24 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 2.68 (3H, s, $COCH_3$), 2.93 (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 4.07 (3H, s, OCH_3), 7.25 (1H, t, J=10 Hz, H-5), 7.36 (1H, t, J=10 Hz, H-7), 7.48 (1H, t, J=10 Hz, H-6), 8.12 (1H, d, J=10 Hz, H-4), and 9.55 (1H, d, J=10 Hz, H-8).

12) **1l**: ^1H Nmr (200 MHz, $CDCl_3$) δ =1.55 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 2.34 (3H, s, OCH_3), 4.81 (2H, q, J=7.0 Hz, $C\underline{H}_2CH_3$), 7.32 (2H, m, H-5,7), 7.49 (1H, t, J=10 Hz, H-6), 8.02 (1H, d, J=10 Hz, H-4), and 8.20 (1H, d, J=10 Hz, H-8); ^{13}C nmr (50.2 MHz, $CDCl_3$) δ =14.5 (q), 16.6 (t), 59.3 (q, OCH_3), 79.5 (s, C-1), 117.7 (s, CN), 120.5 (s), 126.9 (d), 127.3 (d), 130.7 (d), 131.2 (d), 134.7 (d), 136.9 (s), 143.6 (s), and 166.9 (s, C-2).

13) **2a**: ^1H Nmr (270 MHz, $CDCl_3$) δ =1.35 (6H, d, J=7.0 Hz, $CH(C\underline{H}_3)_2$), 3.16 (1H, m, J=7.0 Hz, $C\underline{H}(CH_3)_2$), 4.02 (3H, s, OCH_3), 6.74 (2H, s, H-1,3), 7.13 (1H, t, J=10 Hz, H-7), 7.35 (1H, dd, J=10 and 1.5 Hz, H-6), 7.98 (1H, d, J=10 Hz, H-8), 8.07 (1H, d, J=1.5 Hz, H-4).

14) **2c**: ^1H Nmr (200 MHz, $CDCl_3$) δ =1.39 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.55 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 2.67 (3H, s, $COCH_3$), 3.18 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.33 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.56 (1H, s, H-3), 7.33 (1H, t, J=10 Hz, H-5), 7.50 (1H, dd, J=10 and 1.5 Hz, H-6), 8.02 (1H, d, J=10 Hz, H-4), and 9.83 (1H, d, J=1.5 Hz, H-8).

15) **2d**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.36 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.52 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 3.14 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.35 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.57 (1H, s, H-3), 7.37 (1H, t, J=10 Hz, H-5), 7.52 (1H, dd, J=10 and 1.2 Hz, H-6), 8.02 (1H, d, J=10 Hz, H-4), and 8.27 (1H, d, J=1.2 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =14.6 (q), 24.4 (q), 38.8 (d), 67.1 (t), 83.9 (s), 98.1 (d), 116.3 (s), 128.3 (d), 131.7 (d), 132.3 (d), 133.8 (d), 142.5 (s), 142.7 (s), 149.5 (s), and 169.3 (s).

16) **2e**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.38 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.44 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$), 1.46 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$), 2.14 (3H, s, CH_3), 3.14 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.31 (2H, q, J=7.2 Hz, $OC\underline{H}_2CH_3$), 4.45 (2H, q, J=7.2 Hz, $OC\underline{H}_2CH_3$), 7.27 (1H, t, J=10 Hz, H-5), 7.50 (1H, dd, J=10 and 1.7 Hz, H-6), 8.06 (1H, d, J=10Hz, H-4), and 9.45 (1H, d, J=1.7 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =8.59 (q), 14.6 (q), 1 5.9 (q), 24.6 (q), 39.2 (d), 59.6 (t), 70.8 (t), 104.2 (s), 115.5 (s), 125.7 (d), 130.8 (d), 134.4 (d), 134.5 (d), 138.8 (s), 140.1 (s), 148.6 (s), 165.0 (s), and 167.6 (s).

17) **2f**: ^{1}H Nmr (200 MHz, $CDCl_3$) δ =1.38 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.50 (3H, t, J= 7.0 Hz, $OCH_2C\underline{H}_3$), 2.39 (3H, s, CH_3), 2.71 (3H, s, $COCH_3$), 3.16 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.36 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 7.31 (1H, t, J=10 Hz, H-5), 7.52 (1H, dd, J=10 and 1.6 Hz, H-6), 8.06 (1H, d, J=10 Hz, H-4), and 9.72 (1H, d, J=1.6 Hz, H-8); ^{13}C nmr (50.2 MHz, $CDCl_3$) δ =10.0 (q, CH_3), 16.1 (q, CH_3), 24.8 (q, CH_3), 31.6 (q, $COCH_3$), 39.4 (d, CH), 70.5 (t, OCH_2), 113.3 (s), 113.8 (s), 126.8 (d), 130.8 (d), 134.8 (d), 136.2 (d), 139.5 (s), 140.5 (s), 151.1 (s, C-7), 168.0 (s, C-2), and 195.7 (s).

18) **2h**: ^{1}H Nmr (270 MHz, $CDCl_3$) δ =1.24 (3H, t, J=7.3 Hz, $CH_2C\underline{H}_3$), 1.40 (6H, d, J=6.6 Hz, $CH(C\underline{H}_3)_2$), 2.94 (2H, q, J=7.3 Hz, $C\underline{H}_2CH_3$), 3.17 (1H, m, J=6.6 Hz, $C\underline{H}(CH_3)_2$), 3.99 (3H, s, OCH_3), 4.10 (3H, s, OCH_3), 7.31 (1H, t, J=10 Hz, H-5), 7.55 (1H, ddd, J=10, 1.5, and 0.7 Hz, H-6), 8.13 (1H, dd, J=10 and 0.7 Hz, H-4), and 9.43 (1H, d, J=1.5 Hz, H-8).

19) **2i**: ^{1}H Nmr (200 MHz, $CDCl_3$) δ =1.28 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 1.37 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 2.71 (3H, s, $COCH_3$), 2.98 (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 3.15 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.12 (3H, s, OCH_3), 7.31 (1H, t, J=10 Hz, H-5), 7.53 (1H, dd, J=10 and 1.8 Hz, H-6), 8.11 (1H, d, J=10 Hz, H-4), and 9.74 (1H, d, J=1.8 Hz, H-8).

20) **2k**: ^{1}H Nmr (270 MHz, $CDCl_3$) δ =0.97 (3H, t, J=7.3 Hz, $CH_2CH_2C\underline{H}_3$), 1.40 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.65 (2H, m, J=7.3 Hz, $CH_2C\underline{H}_2CH_3$), 2.88 (2H, m, J=7.3 Hz, $C\underline{H}_2CH_2CH_3$), 3.17 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.00 (3H, s, OCH_3), 4.09 (3H, s, OCH_3), 7.30 (1H, t, J=10 Hz, H-5), 7.54 (1H, ddd, J=10, 1.8, and 0.7 Hz, H-6), 8.13 (1H, dd, J=10 and 0.7 Hz, H-4), and 9.42 (1H, d, J=1.8 Hz, H-8).

21) **9a**: ^{1}H Nmr (270 MHz, $CDCl_3$) δ =3.95 (3H, s, $COOCH_3$), 4.07 (3H, s, OCH_3), 4.11 (3H, s, OCH_3), 6.98 (1H, s, H-3), 7.06 (1H, d, J=10 Hz, H-5), 7.26 (1H, t, J=10 Hz, H-7), 7.47 (1H, t, J=10 Hz, H-6), 9.39 (1H, d, J=10 Hz, H-8).

22) **9d**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.51 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 1.56 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 4.34 (2H, q, J=6.9 Hz, $OC\underline{H}_2CH_3$), 4.35 (2H, q, J=6.9 Hz, $OC\underline{H}_2CH_3$), 6.83 (1H, s, H-3), 7.10 (1H, d, J=10 Hz, H-5), 7.19 (1H, t, J=10 Hz, H-7), 7.50 (1H, t, J=10 Hz, H-6), and 8.24 (1H, d, J=10 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =14.7 (q, CH_3), 14.8 (q, CH_3), 65.0 (t, CH_2), 66.8 (t,

CH_2), 83.5 (s, C-1), 97.1 (d, C-3), 112.8 (d), 116.5 (s, CN), 123.2 (d), 131.2 (s), 132.8 (d), 133.7 (d), 140.1 (s), 160.3 (s, C-4), and 166.8 (s, C-2).

23) **9e**: ^{1}H Nmr (270 MHz, $CDCl_3$) δ =1.44 (6H, t, J=7.3 Hz, $OCH_2C\underline{H}_3$), 1.52 (3H, t, J=7.3 Hz, $OCH_2C\underline{H}_3$), 2.60 (3H, s, CH_3), 4.16 (4H, m, J=7.3 Hz, $OC\underline{H}_2CH_3$), 4.43 (2H, q, J=7.3 Hz, $OC\underline{H}_2CH_3$), 6.78 (1H, d, J=10 Hz, H-5), 7.05 (1H, t, J=10 Hz, H-7), 7.35 (1H, td, J=10 and 1.0 Hz, H-6), 9.32(1H, dd, J=10 and 1.0 Hz, H-8).

24) **9g**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.51 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 1.55 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 2.51 (3H, s, CH_3), 4.23 (2H, q, J=6.9 Hz, $OC\underline{H}_2CH_3$), 4.73 (2H, q, J=6.9 Hz, $OC\underline{H}_2CH_3$), 6.80 (1H, d, J=10 Hz, H-5), 7.00 (1H, t, J=10 Hz, H-7), 7.33 (1H, t, J=10 Hz, H-6), and 8.11 (1H, d, J=10 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =11.8 (q, CH_3), 14.6 (q, CH_3), 15.3 (q, CH_3), 64.9 (t, OCH_2), 67.6 (t, OCH_2), 80.0 (s, C-1), 110.5 (d, C-5), 115.9 (s, CN), 118.2 (s, C-3), 121.5 (d, C-7), 127.6 (s, C-3a), 131.5 (d, C-8), 133.5 (d, C-6), 140.6 (s, C-8a), 162.9 (s, C-4), and 164.7 (s, C-2).

25) **9j**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.14 (3H, t, J=7.4 Hz, $CH_2C\underline{H}_3$), 2.98 (2H, q, J=7.4 Hz, $C\underline{H}_2CH_3$), 4.05 (3H, s, OCH_3), 4.40 (3H, s, OCH_3), 6.86 (1H, d, J=10 Hz, H-5), 7.05 (1H, t, J=10 Hz, H-7), 7.39 (1H, t, J=10 Hz, H-6), and 8.15 (1H, d, J=10 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =16.1 (q, CH_3), 19.0 (t, CH_2), 55.9 (q, OCH_3), 59.3 (q, OCH_3), 78.1 (s, C-1), 109.8 (d, C-5), 118.1 (s, CN), 121.7 (s, C-7), 122.5 (d, C-3), 126.9 (s, C-3a), 131.7 (d, C-8), 133.4 (d, C-6), 140.7 (s, C-8a), 163.2 (s, C-4), and 165.4 (s, C-2).

26) **10a**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.36 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.44 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 1.53 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 1.54 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 3.10 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.31 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 4.35 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 4.38 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 6.87 (1H, s, H-3), 7.06 (1H, d, J=11 Hz, H-5), 7.42 (1H, dd, J=11 and 1.2 Hz, H-6), and 9.46 (1H, d, J=1.2 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =14.5 (q), 14.8 (q), 15.0 (q), 24.7 (q), 38.8 (d), 59.3 (t), 64.8 (t), 66.4 (t), 96.2 (d), 101.5 (s), 112.3 (d), 131.8 (d), 132.2 (s), 134.3 (d), 139.3 (s), 144.6 (s), 158.5 (s), 165.5 (s), and 167.1 (s).

27) **10b**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.35 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.53 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 1.56 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 2.65 (3H, s, $COCH_3$), 3.12 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.32 (2H, q, J=6.9 Hz, $OC\underline{H}_2CH_3$), 4.35 (2H, q, J=6.9 Hz, $OC\underline{H}_2CH_3$), 6.80 (1H, s, H-3), 7.08 (1H, d, J=11 Hz, H-5), 7.43 (1H, dd, J=11 and 1.6 Hz, H-6), and 9.80 (1H, d, J=1.6 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =14.9 (q), 15.0 (q), 24.7, (q), 31.9 (d), 38.8 (q), 64.8 (t), 66.4 (t), 95.9 (d), 110.9 (s), 112.7 (d), 132.2 (d), 133.3 (s), 136.0 (d), 139.0 (s), 146.7 (s), 158.9 (s), 167.6 (s), and 195.3 (s).

28) **10d**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.34 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.44 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$), 1.45 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$), 1.52 (3H, t, J=7.2 Hz, $OCH_2C\underline{H}_3$), 2.60 (3H, s, CH_3), 3.04 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.18 (2H, q, J=7.0 Hz, $OC\underline{H}_2CH_3$), 4.20 (2H, q, J=7.2 Hz, $OC\underline{H}_2CH_3$), 4.43 (2H, q, J=7.2 Hz, $OC\underline{H}_2CH_3$), 6.83 (1H, d, J=11.2 Hz, H-5), 7.35 (1H, dd, J=11.2 and 1.8 Hz, H-6), and 9.45 (1H, d, J=1.8 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =12.3 (q), 14.5 (q), 14.6 (q), 15.7 (q), 24.5 (q), 38.2 (d), 59.4 (t), 64.8 (t), 70.7 (t), 104.6 (d), 111.0 (d), 117.2 (s), 127.6 (d), 133.6 (d), 135.2 (d), 138.1 (s), 142.3 (s), 162.6 (s), 165.2 (s), and 165.3 (s).

29) **10f**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.32 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 1.51 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 1.53 (3H, t, J=6.9 Hz, $OCH_2C\underline{H}_3$), 2.50 (3H, s, CH_3), 3.02 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.21 (2H, q, J=6.9 Hz, $OC\underline{H_2}CH_3$), 4.73 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 6.79 (1H, d, J=11 Hz, H-5), 7.28 (1H, dd, J=11 and 1.8 Hz, H-6), and 8.09 (1H, d, J=1.8 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =11.6 (q), 14.6 (q), 15.3 (q), 24.3 (q), 37.8 (d), 64.7 (t), 67.5 (t), 79.4 (d), 110.5 (s), 114.6 (s), 118.5 (s), 127.5 (s), 131.6 (d), 131.8 (d), 140.8 (s), 141.9 (s), 161.5 (s), and 164.7 (s).

30) **10h**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ =1.13 (3H, t, J=7.3 Hz, $CH_2C\underline{H}_3$), 1.33 (6H, d, J=6.9 Hz, $CH(C\underline{H}_3)_2$), 2.97 (2H, q, J=7.3 Hz, $C\underline{H_2}CH_3$), 3.04 (1H, m, J=6.9 Hz, $C\underline{H}(CH_3)_2$), 4.03 (3H, s, OCH_3), 4.40 (3H, s, OCH_3), 6.78 (1H, d, J=11 Hz, H-5), 7.34 (1H, dd, J=11 and 1.8 Hz, H-6), and 8.13 (1H, d, J=1.8 Hz, H-8); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ =16.2 (q), 18.9 (t), 24.3 (q), 37.8 (d), 55.8 (q), 59.3 (q), 79.4 (s), 109.8 (d), 118.4 (d), 121.3 (s), 126.7 (s), 131.7 (d), 131.9 (d), 140.9 (s), 142.2 (s), 161.8 (s), and 165.5 (s).

31) K. Takase, Bull. Chem. Soc. Jpn, 1964, **37**, 1460; T. Nozoe, K. Takase, M. Kato, and T. Nogi, Tetrahedron, 1971, **27**, 6023.

32) T. Yanagisawa, S. Wakabayashi, T. Tominaga, M. Yasunami, and K. Takase, Chem. Pharm. Bull., 1988, **36**, 641.

33) **13**: ^{1}H Nmr (270 MHz, $CDCl_3$) δ =4.03 (3H, s, $COOCH_3$), 4.11 (3H, s, OCH_3), 6.96 (1H, s, H-3), 7.07 (1H, d, J=10.5 Hz, H-5), 7.25 (1H, t, J=10.5 Hz, H-7), 7.47 (1H, t, J=10.5 Hz, H-6), 8.90 (1H, d, J=10.5 Hz, H-8), 10.6 (1H, br, OH).

34) **14**: ^{1}H Nmr (270 MHz, $CDCl_3$) δ =1.45 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 1.49 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 1.64 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 4.34 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 4.36 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 4.44 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 7.03 (1H, d, J=10.0 Hz, H-5), 7.19 (1H, t, J=10.0 Hz, H-7), 7.54 (1H, t, J=10.0 Hz, H-6), 9.40 (1H, d, J=10.0 Hz, H-8).

35) **15**: ^{1}H Nmr (270 MHz, C_6D_6) δ =1.06 (3H, t, J=7.0 Hz, $CO_2CH_2C\underline{H}_3$), 1.21 (3H, t, J=7.0 Hz, $OCH_2C\underline{H}_3$), 3.40 (2H, q, J=7.0 Hz, $CO_2C\underline{H_2}CH_3$), 4.14 (2H, q, J=7.0 Hz, $OC\underline{H_2}CH_3$), 5.87 (1H, dd, J=10.0 and 0.5 Hz, H-7), 5.95 (1H, dd, J=8.0 and 1.5 Hz, H-4), 6.41 (1H, td, J=8.0 and 1.5 Hz, H-2), 6.44 (1H, td, J=10.0 and 0.5 Hz, H-8), 6.47 (1H, td, J=8.0 and 1.5 Hz, H-3), 6.54 (1H, td, J=10.0 and 0.5 Hz, H-9), 6.71 (1H, dd, J=8.0 and 1.5 Hz, H-1), 8.62 (1H, dd, J=10 and 0.5 Hz, H-10), 9.44 (1H, br, NH).

Received, 14th November, 1990