Synthesis of Five-membered 2-Heteroaryl 2-Heteroaromatic Carboxylates and Attempted Cyclization to Bisheteroaryl[2,3-*b*:3',2'-*d*]pyran-2-one

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2-Heteroaryl 2-heteroaromatic carboxylates were prepared by reactions of 2-heteroaromatic carbonyl chlorides and 2(5*H*)-furanone, 2(5*H*)-thiophenone, and 1-methyl-2(5*H*)-pyrrolone in triethylamine. The ^{1}H nmr spectra of the esters showed that the electronic effect of both heteroaromatic rings did not cause any sizable shift from each other except for 1-methyl-2-pyrrolyl 1-methyl-2-pyrrolecarboxylate (**5c**). Attempts to cyclize the esters to heteroaryl-fused pyran-2-ones were unsuccessful. The results may be explained by the most stable conformation of the esters in which two heteroatoms are anti along the C-O bond of the ester group.

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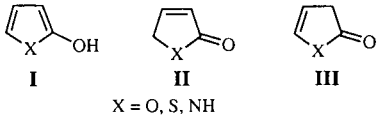
2-Heteroarylcarboxylic acids have stronger acidities than benzoic acid but their chemistry is known to be quite similar to that of benzoic acid [1]. Therefore, various derivatives of 2-heteroarylcarboxylic acids can be prepared by following the procedures applied to derivatives of benzoic acid. On the other hand, 2-hydroxyheteroaryl compounds do not exist as phenols do [2,3]. That is, 2-hydroxyfuran, 2-hydroxythiophene, and 2-hydroxypyrrole do not exist in the free hydroxy form such as **I**. Instead, they have the forms of 2(5*H*)-furanone (X = O), 2(5*H*)-thiophenone (X = S), and 2(5*H*)-pyrrolone (X = NH) such as **II** [4]. Pyrrolone structure **III** is also feasible and **II** and **III** are in equilibrium [5].



I **II** **III**

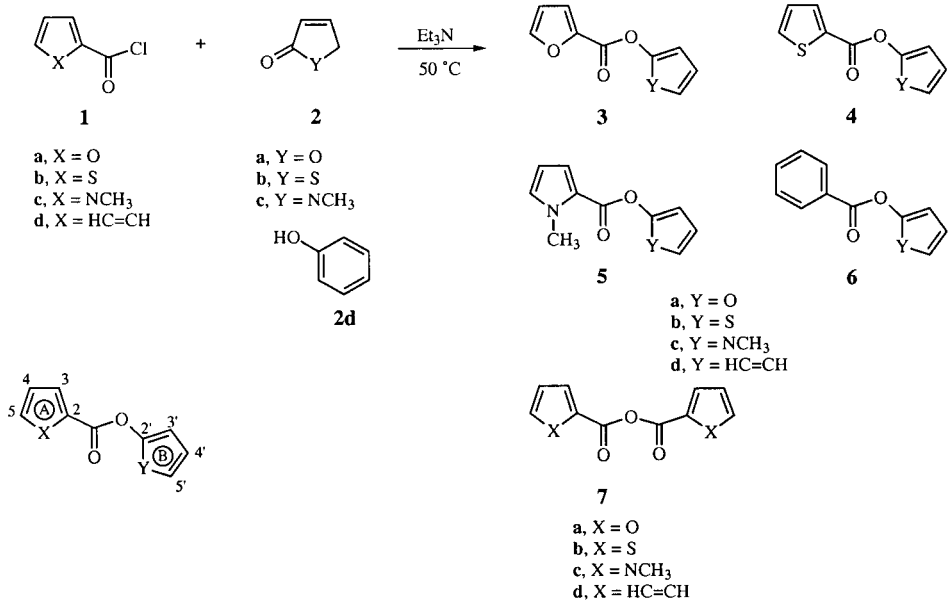
X = O, S, NH

In solution, however, and in the presence of a suitable acid or base, the amount of **I** may become significant. Structure **I** can be considered as a phenol-analogue of the 5-membered heterocycle [2]. Free hydroxy compounds can undergo various kinds of reactions which are typical of phenolic compounds.

We have been interested in the preparation of 2-heteroaryl 2-heteroaromatic carboxylates because not only are they a new type of compound but they may undergo cyclization leading to 2*H*-pyran-2-one to which two heterocyclic rings are fused. We report herein the preparation of the esters, their spectroscopic characteristics, and our attempts to cyclize them to form bisheteroaryl[2,3-*b*:3',2'-*d*]-2*H*-pyran-2-ones **9**.

Results and Discussion.

We followed the typical procedure for esterification in order to prepare the esters **3-6**. Heating a mixture of 2-furoyl chloride (**1a**) and 2(5*H*)-furanone (**2a**) in pyri-



dine at 30° for 1-3 hours, however, gave only 2-furoic anhydride (**7a**). Similarly, 1-methyl-2-pyrroloyl chloride (**1c**) gave **7c** after 3 hours of heating with **2a**. On the other hand, 2-thienoyl chloride (**1b**) and benzoyl chloride (**1d**) did not give anhydrides **7b** and **7d**, respectively, under similar conditions with **2a**. Instead esters **3b** (66%) and **4b** (37%) which were derived from 2(5*H*)-thiophenone (**2b**) could be prepared under these conditions.

The esterification took place most effectively when triethylamine was employed as the base as well as the solvent. For most cases, the exothermic reactions took place at an early stage of the reaction and cooling with an ice-water bath was necessary. Otherwise, polymerization of **2a-c** took place, which lowered the yields of **3-5**. The mixture was then heated in an oil bath at 50° for 3 hours to ensure completion. The yields listed in Table IV were after purification by distillation under vacuum. Fractional extraction or separation by column chromatography was attempted for those reactons which produced low yields, but it was difficult to remove the impurities completely.

The anhydride **7a** is a known compound [6] and the structure of compound **7c** was readily confirmed by spectroscopic method by comparing it with the spectra of **7a**. The anhydrides have symmetric structures and there are only three signals in the aromatic region corresponding for 3-H, 4-H, and 5-H in each ^{1}H nmr spectrum [7]. The ir spectrum of **7a** shows very strong peaks at 1790 and 1730 cm^{-1} whereas **7c** shows peaks at 1760 and 1700 cm^{-1}, indicating the presence of the anhydride linkage. The mass spectrum of **7a** did not show a molecular ion, instead the peak corresponding to 2-furoic acid (m/z 112) was the largest fragment. On the other hand, **7c** showed a molecular ion at m/z 232 (30%).

It is conceivable that an enolate ion or an enol form of **2** should be formed prior to reaction with **1**. Tautomerism of **2a** and **2c** may not be feasible in pyridine and therefore, esterification does not take place. We examined the possble equilibrium between **I** and **II** in pyridine and in triethylamine by ^{1}H nmr spectroscopy. In the case of **2b** an equilibrium constant of approximately 4 x 10^{-3} could be obtained in triethylamine by the ratio of the integrations of the peaks corresponding to form **I** [at δ 6.18 (dd, 1H), 6.22 (s, 1H), 6.63 (dd, 1H), and 6.77 (dd, 1H)] and form **II** [at δ 4.16 (t, 2H), 6.40 (dt, 1H), and 7.58 (dt, 1H)]. It was difficult to observe enol form **2a** or **2c** by nmr in pentadeuteriopyridine or in deuteriochloroform in the presence of triethylsilane.

We also explored the use of the Baeyer-Villiger oxidation of the 2-diheteroaryl ketones **8** to transform them into esters **3** and **4**. Ketones **8** were prepared by typical Friedel-Crafts acylation [8,9] and the oxidation was attempted with *m*-chloroperbenzoic acid in carbon tetrachloride solution. However, the transformation of **8a** and **8b** to **3a** and **4b**, respectively, did not take place after reflux for 3 days.

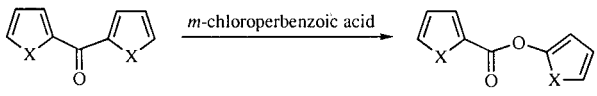
In order to compare the effects of the 5-membered heteroaromatic rings to that of phenyl rings we prepared benzoates **6a-d** and examined their nmr spectra. Esters **3-6** showed quite remarkable spectroscopical characteristics. As shown in Table I, the proton chemical shift values

Table I

^{1}H and ^{13}C NMR Chemical Shift Values of the Acyl-aryl (A) Rings of Compounds **3-6** in Chloroform-*d*, (ppm)

Compound	3-H	4-H	5-H	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	2-C	3-C	4-C	5-C	C=O
3a	7.41	6.60	7.70	3.6	0.8	1.7	142.3	120.6	112.4	147.9	154.0
3b	7.43	6.61	7.70	3.6	0.8	1.7	142.8	120.1	112.3	147.6	155.0
3c	7.40	6.60	7.69	3.6	0.8	1.7	143.7	119.7	112.1	147.4	155.2
3d	7.38	6.59	7.67	3.5	0.8	1.6	144.0	119.4	112.2	147.1	156.9
4a	7.98	7.17	7.71	3.9	1.3	5.0	130.7	135.5	128.2	134.6	157.9
4b	8.00	7.19	7.70	3.9	1.3	5.0	131.4	135.2	128.2	134.2	158.9
4c	7.98	7.18	7.67	3.8	1.3	5.0	131.6	135.0	128.1	133.9	159.1
4d	7.99	7.18	7.67	3.7	0.8	5.0	132.9	134.7	128.0	133.5	160.6
5a [a]	7.14	6.13	6.85	4.0	1.5	2.5	119.3	119.8	108.2	131.3	156.5
5b [a]	7.14	6.13	6.82	4.0	1.8	2.5	120.0	119.5	108.4	131.1	157.3
5c [a]	7.21	6.28	6.98	4.0	1.8	2.5	120.3	119.2	108.2	130.9	158.1
5d [a]	7.18	6.16	6.82	4.0	2.0	2.5	122.9	119.0	108.1	130.5	159.5
6a	8.18	7.52	7.66	8.0	7.5	2.4	128.0	130.4	128.7	134.2	162.7
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	
6b	8.19	7.51	7.64	7.8	7.1	1.8	128.3	130.2	128.7	133.9	163.3
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	
6c	8.16	7.50	7.62	7.8	7.4	1.4	128.6	129.8	128.4	133.6	163.3
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	
6d	8.20	7.50	7.60	8.0	7.5	2.4	129.6	130.2	128.6	133.6	165.2
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	

[a] ^{1}H and ^{13}C CH_3 signals (ppm), respectively at: **5a**, 3.85 and 36.2; **5b**, 3.88 and 36.5; **5c**, 3.91 and 36.6; **5d**, 3.90 and 36.7. [b] *Ortho*-H. [c] *Meta*-H. [d] *Para*-H. [e] $J_{2,3}$. [f] $J_{3,4}$. [g] $J_{2,4}$. [h] *Ipso*-C. [i] *Ortho*-C. [j] *Meta*-C. [k] *Para*-C.



8
a, X = O
b, X = S

3a
4b

esters. As shown in Table II, the $\Delta\delta$ for 3'-H, 4'-H, and 5'-H is less than 0.03 ppm for these series. However, the pyrroloyl esters showed quite remarkable deviations in different directions: shifted upfield by 0.05-0.14 ppm in cases of 2-furyl (**5a**), 2-thienyl (**5b**), and phenyl (**5d**) esters, but downfield by 0.03-0.10 ppm in the case of 2-pyrrolyl (**5c**) ester.

Table II

^{1}H and ^{13}C NMR Chemical Shift Values of the Oxygen-aryl (B) Rings of **3-6** in Chloroform-*d*, (ppm)

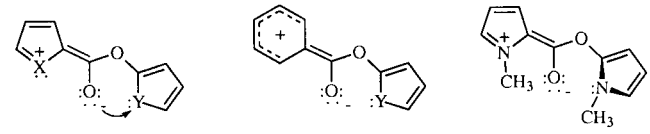
Compound	3'-H	4'-H	5'-H	$J_{3',4'}$	$J_{3',5'}$	$J_{4',5'}$	2'-C	3'-C	4'-C	5'-C	C=O
3a	6.02	6.41	7.11	3.3	1.1	2.1	150.3	92.7	111.2	135.5	154.0
4a	6.00	6.40	7.11	3.4	0.9	2.0	150.6	92.7	111.2	135.5	157.9
5a	5.90	6.35	7.06	3.3	1.2	2.2	150.7	92.3	110.8	135.1	156.5
6a	6.04	6.43	7.13	3.4	1.0	1.9	151.2	92.6	111.3	135.5	162.7
3b	6.84	6.88	6.95	3.9	1.7	5.8	151.2	113.8	123.4	118.3	155.0
4b	6.81	6.88	6.94	3.7	1.6	5.7	151.7	113.7	123.4	118.3	158.9
5b	6.72	6.81	6.84	3.8	1.5	5.9	151.6	113.0	123.0	117.6	157.3
6b	6.85	6.88	6.94	4.0	1.5	5.6	152.0	113.5	123.3	118.2	163.3
3c [a]	5.97	6.09	6.40	3.8	2.0	3.1	135.3	94.8	105.4	115.9	155.2
4c [a]	5.94	6.07	6.39	3.8	2.0	3.0	136.0	95.0	105.7	116.0	159.1
5c [a]	5.97	6.17	6.45	3.7	2.0	3.1	136.0	94.8	105.5	115.8	158.1
6c [a]	5.96	6.08	6.38	3.7	1.9	3.1	136.1	94.7	105.5	115.8	163.3
3d	7.21	7.42	7.27	3.7	7.4	2.0	150.1	121.6	129.5	126.0	156.9
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	
4d	7.22	7.43	7.27	7.7	7.4	1.2	150.5	121.6	129.5	126.0	160.6
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	
5d	7.17	7.37	7.21	7.8	7.8	1.9	150.4	121.8	129.2	125.4	159.5
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	
6d	7.20	7.40	7.25	7.5	7.4	1.3	150.9	121.7	129.5	125.9	165.2
	[b]	[c]	[d]	[e]	[f]	[g]	[h]	[i]	[j]	[k]	

[a] ^{1}H CH_3' and ^{13}C CH_3' signals (ppm), respectively at: **3c**, 3.46 and 31.7; **4c**, 3.50 and 32.0; **5c**, 3.44 and 31.7; **6c**, 3.43 and 31.7. [b] *Ortho*-H'. [c] *Meta*-H'. [d] *Para*-H'. [e] $J_{2',3'}$. [f] $J_{3',4'}$. [g] $J_{2',4'}$. [h] *Ipso*-C'. [i] *Ortho*-C'. [j] *Meta*-C'. [k] *Para*-C'.

of 3-, 4-, and 5-H of the acid part (A ring) did not show any significant difference due to the nature of the alcohol part (B ring). This may be an indication that the effect of the heteroatom in the B ring, whether it is inductive or resonance, does not propagate to the A ring through -CO-O- bonds linking the two heterocycles. For example, the chemical shift values of the protons in the furan (A) ring in **3a-d** are δ 7.41 (±0.03), 6.60 (±0.01), and 7.69 (±0.02) for 3-, 4-, and 5-H, respectively. Similarly, the chemical shift values in **4a-d** are 7.99 (±0.01), 7.18 (±0.01), and 7.69 (±0.02) for 3-, 4-, and 5-H, respectively. In the case of 1-methyl-2-pyrrolecarboxylates **5a-d**, the average chemical shift values are 7.16 (±0.11), 6.18 (±0.10), and 7.17 (±0.04) for 3-, 4-, and 5-H, respectively. The deviations in the pyrroloyl esters are much larger than the other series because of the large δ values observed in **5c**. The electronic effect of the B ring also does not cause a recognizable effect on the chemical shifts of the phenyl protons of the benzoates **6a-d**.

The nature of the A ring does not cause any significant effect on the chemical shift values of the protons of the B ring in case of furoyl (**3**), thienoyl (**4**), and benzoyl (**6**)

Apparently, the effects of 2-furoyl, 2-thienoyl, and benzoyl groups do not transmit through the ester bond effectively because the contribution of the resonance structures such as **IV** should not be significant if X is O or S due to the highly electronegative character of the O atom and the size of the S atom prohibiting effective overlapping of the non-bonding orbital with the adjacent carbon atom. A resonance structure such as **V** is also unlikely to be effective because the benzene ring would have to lose aromaticity. The result is the upfield shift of 3'-H, 4'-H, and 5'-H in **5a**, **5b**, and **5d**.



IV **V** **VI**

In contrast, the conjugation of the lone-pair electrons on the nitrogen atom in the 2-pyrroloyl esters (**5**) makes the carbonyl oxygen atom negatively charged, which in turn makes the B ring rich in electron density as shown in **VI**. In the case of **5c** the methyl group in the B ring makes

the ring slightly skewed and the effect of conjugation of the A ring cannot be exercised to an approximately equal extent to the other three cases. Therefore, the slight downfield shift in **5c** may be the result of the electron-withdrawing effect of the ester group.

The ^{13}C chemical shift values show interesting trends. As shown in Table I, the peaks corresponding to 2-C of the A ring which is bonded to the carbonyl carbon move downfield as the B ring changes from 2-furyl (**a**) to 2-thienyl (**b**) to 1-methyl-2-pyrrolyl (**c**) to phenyl (**d**). The deviation ranges 1.7, 2.2, 3.6, and 1.6 ppm for the series of **3**, **4**, **5**, and **6**, respectively. Contrastingly, those of 3-C, 4-C, and 5-C shift upfield as the B ring changes similarly. Furthermore, the deviation is rather small: 0.6-1.2 ppm for 3-C; 0.1-0.2 ppm for 4-C; and 0.6-1.1 ppm for 5-C. It is not surprising that the chemical shift values of 4-C are essentially similar because the position can be considered as *meta* to the ester group. However, it is unusual that chemical shift values of 3-C (*ortho*) and 5-C (*para*) show a very similar trend. This may be a result of conformations such as **VII** or **VIII** in which C_2=C_3 of the A ring and C=O take an *s-trans* form [9]. The diamagnetic anisotropic effect of the carbonyl group may not effectively affect the chemical shift of 3-C in such a conformation.

The rationale for the conformation may be supported by the essentially close chemical shift values of each series of the carbons in the B ring regardless of the position as shown in Table II. That is, the effect of the A ring is insignificant to the chemical shifts of the carbons in the B ring.

The ^{13}C chemical shift values of the carbonyl carbons listed in Table II show excellent correlation with the aromaticity indices of the A ring with a correlation coefficient of 0.998-1.000 (Table III) [10]. As shown in Figure 1 the slope is the largest with 2-furyl (**a**, 67.24) and the smallest with 1-methyl-2-pyrrolyl (**c**, 61.55). 2-Thienyl (**b**) and phenyl (**d**) show very close values, 64.37 and 63.72, respectively, indicating that thiophene is most similar to benzene in its physical properties. However, the correlation is poor with other values of the aromaticity indices in the literature [11]. Plot of the chemical shift against diamagnetic susceptibility also shows poor correlation, but the similar plots with values of the ring current [10] and the resonance energy of the A ring [10] show very good correlation.

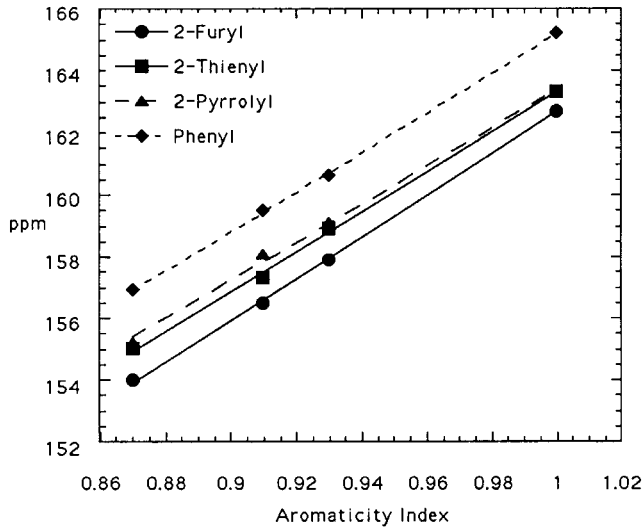


Figure 1. Plot of the chemical shift values of ^{13}C=O of **3-6** vs aromaticity index.

In contrast to Figure 1 the correlation of the ^{13}C chemical shift values of the carbonyl carbon listed in Table I with the same values for the B ring (plot not shown) is poor in the pyrrole series (**5**, r = 0.917) and fair with the other series (**3**, **4**, and **6**, r = 0.971-0.976). The slope was less than one third of magnitude of that in Figure 1. The low correlation with the pyrrole series may be due to the electron-donating nature of the pyrrole ring through resonance, which is in contrast to electron-withdrawing properties of the other rings.

The esters **3-5** were subjected to various conditions for ring closure. Much effort was concentrated on photochemical cyclization because there are ample examples of cyclization of 1,2-diheteroarylethylene to bisheteroarylobenzene [12-15] and 2-heteroaroyl anilide to heteroarylopyridone or quinolone [16-18]. The reaction was attempted with a 450 watt medium pressure mercury lamp equipped with or without Pyrex filter and in solution of either ethanol or hexane. The progress of the reaction was intermittently monitored by tlc and gc for a 24 hour period, but no notable change was apparent. Bubbling nitrogen or oxygen gas didn't make any difference. Addition of iodine also didn't initiate any reaction.

Table III

Correlation Coefficients of the Plots of ^{13}C=O Chemical Shift Values of the Esters vs Various Physical Constants of the Heterocycles

Series	IA_1 [a] (r)	IA [b] (r)	IA [c] (r)	RC [d] (r)	E [e] (r)	DS [f] (r)
a	0.87 (1.000)	0.06 (0.975)	0.530 (0.902)	0.46 (0.991)	8 (0.999)	8.9 (0.901)
b	0.93 (0.999)	0.67 (0.980)	0.815 (0.897)	0.75 (0.995)	20 (0.999)	13.0 (0.913)
c	0.91 (0.998)	0.38 (0.979)	0.850 (0.933)	0.59 (0.986)	15 (0.993)	10.2 (0.902)
d	1.00 (1.000)	1.00 (0.973)	1.000 (0.913)	1.00 (0.988)	36 (0.998)	13.7 (0.894)

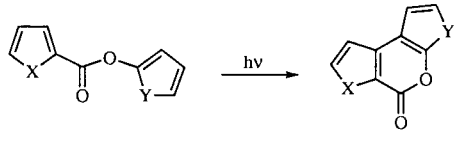
[a] Aromaticity indices from reference [10]. [b] Aromaticity indices from reference [10]. [c] Combined aromaticity indices from reference [11]. [d] Ring current from reference [10]. [e] Resonance energy from reference [10]. [f] Diamagnetic susceptibility from reference [10].

Table IV

Mass, UV, and IR Spectral Data of **3-5**

Compound	M+ (%)	Base peak	Other fragment (%)	λ_{max}, nm (log ε)	$\nu_{C=O}$ cm^{-1}
3a	178 (9)	95	112 (1), 96 (6), 83 (2)	214 (3.87), 257 (4.12)	1750
3b	194 (9)	95	178 (3), 112 (11), 111 (8), 96 (6)	259 (4.13)	1730
3c	191 (74)	95	192 (8), 96 (66), 67 (5)	215 (3.90), 255 (4.13)	1730
4a	194 (0.2)	111	128 (16), 112 (6), 83 (6)	250 (4.03), 276 (3.96)	1730
4b	210 (11)	111	113 (12), 112 (16), 83 (15)	248 (4.03), 278 (3.96)	1700
4c	207 (100)	207	191 (70), 113 (82), 112 (85) 111 (43), 97 (19), 96 (52) 95 (50), 83 (50)	250 (4.04)	1730
5a	191 (1)	108	142 (18), 109 (34), 80 (36)	213 (3.62), 238 (3.89) 277 (4.23)	1720
5b	207 (20)	108	180 (14), 142 (29), 109 (54) 80 (63)	239 (3.87), 282 (4.27)	1710
5c	204 (64)	108	144 (21), 142 (64), 109 (47) 96 (26), 80 (38)	239 (3.87), 273 (4.21)	1710
6a	188 (5)	105	83 (5)	232 (4.13), 273 (3.57)	1750
6b	204 (45)	105	96 (9), 83 (35)	234 (4.20), 275 (3.78)	1710
6c	201 (100)	105	96 (45), 95 (40), 83 (45)	231 (4.15), 276 (3.40)	1730

Starting materials were recovered over 80% in cases of X and Y where O, S, and HC=CH, but no material related to **9** could be isolated. In cases of X and/or Y were NCH_3 polymeric material was formed which could not be identified.



3-6 **9**

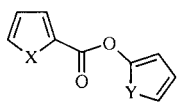
The unfavorable cyclization of the ester seems to be due to the most stable conformation of the ester mentioned earlier. There are eight possible conformations for the heteroaryl ester illustrated as **VII-XIV**. PCMODEL calculation indicates that the conformers such as **VII-X** in which the two rings are anti along the C-O single bond are more stable than the syn conformers **XI-XIV** by *ca.* 10 kcal/mole. Among the anti conformers the order of stability is **VII > VIII > IX > X** by the same calculation. The rotational energy barriers along CO-O bond calculated by PCMODEL are very high for **3-6**. Although the

Table V

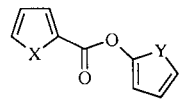
Yields, Boiling Points, and Analytical Data of **3-6**

Compound	(Formula)	Yield %	Bp, °C (mmHg)	Found (%) (Required) C	H	N	S
3a	($C_9H_6O_4$)	70	82 (0.02)	60.5 (60.7)	3.5 (3.4)		
3b	($C_9H_6O_3S$)	78	102-106 (0.03) 56-59 [a]	55.9 (55.7)	3.2 (3.1)		16.3 (16.5)
3c	($C_{10}H_9NO_3$)	73	102-112 (0.01)	62.9 (62.8)	5.0 (4.9)	7.1 (7.3)	
3d	($C_{11}H_8O_3$)	45	110 (0.1)	[b]			
4a	($C_9H_6O_3S$)	43	90 (0.03) 53-55 [a]	55.4 (55.7)	3.3 (3.1)		16.6 (16.5)
4b	($C_9H_6O_2S_2$)	65	110-114 (0.01)	51.7 (51.4)	2.8 (2.9)		30.1 (30.5)
4c	($C_{10}H_9NO_2S$)	33	122.5 (0.05)	57.8 (58.0)	4.1 (4.4)	6.6 (6.8)	15.8 (15.5)
4d	($C_{11}H_8O_2S$)	58	46-50 [a]	[b]			
5a	($C_{10}H_9NO_3$)	76	95-100 (0.02)	62.8 (62.7)	4.7 (4.7)	7.2 (7.3)	
5b	($C_{10}H_9NO_2S$)	62	120-124 (0.05)	58.2 (58.0)	4.4 (4.4)	7.0 (6.8)	15.2 (15.5)
5c	($C_{11}H_{12}N_2O_2$)	62	86-90 (0.05)	64.8 (64.7)	5.8 (5.9)	13.5 (13.7)	
5d	($C_{12}H_{11}NO_2$)	93	121-125 (0.075)	71.8 (71.6)	5.4 (5.5)	7.1 (7.0)	
6a	($C_{11}H_8O_3$)	44	92 (0.05)	70.4 (70.2)	4.2 (4.3)		
6b	($C_{11}H_8O_2S$)	77	110-117 (0.03)	65.0 (64.7)	4.2 (4.0)		15.4 (15.7)
6c	($C_{12}H_{11}NO_2$)	68	114-124 (0.025)	71.8 (71.6)	5.5 (5.5)	6.7 (7.0)	
6d	($C_{13}H_{10}O_2$)	83	90 (0.025) 70-71 C [a]	[c]			

[a] Melting point. [b] Known compound in the literature [19] and elemental analysis was not attempted. [c] Commercially available compound and elemental analysis was not attempted.



VII



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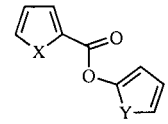
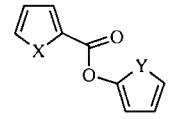


IX



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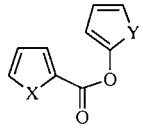

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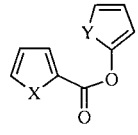

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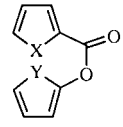

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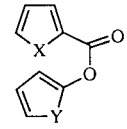

XIV

calculation is in the gas phase and it may be much lower in solution, the unfavorable cyclization may be due to the hindered conformational requirement.

EXPERIMENTAL

Melting points were determined on a Fischer MEL-TEMP apparatus and are uncorrected. PCMODEL calculations were performed on a Macintosh Quadra 610 with molecular modeling software from Serena Software, Bloomington, Indiana. Nuclear magnetic resonance (nmr) spectra were recorded on a Bruker DPX 400 MHz FT NMR spectrometer in the Central Laboratory of Kangwon National University with deuteriochloroform as the solvent at 400 MHz for ^1H and 100 MHz for ^{13}C and were referenced to tetramethylsilane. Infrared (ir) spectra were recorded on a JASCO Model IR Report-100 spectrophotometer as potassium bromide pellets or neat. Ultraviolet and visible (uv) spectra were obtained in ethanol on a UVIKON 941 Plus double-beam spectrophotometer. Electron-impact mass spectra (ms) were obtained using a JEOL JMS-AX505WA mass spectrometer in the Research Center for New-Biomaterials in Agriculture, Seoul National University, Suwon. Elemental analyses were performed by the M-H-W Laboratories, Phoenix, Arizona.

Starting Materials.

All 2-heteroaryl carbonyl chlorides were prepared prior to use from the corresponding carboxylic acids and thionyl chloride. 2(5*H*)-Furanone (**2a**) and 2(5*H*)-thiophenone (**2b**) were purchased from the Aldrich Chemical Co., and used as delivered. All solvents were purified according to the literature.

1-Methyl-2(5*H*)-pyrrolone (**2c**) and 1-Methyl-2(3*H*)-pyrrolone (**2c'**).

To a suspension of barium carbonate (3.00 g) in water (900 ml) 1-methylpyrrole (13.40 ml, 0.150 mole) was added and followed by addition of hydrogen peroxide (30%, 14.00 g, 0.150 mole). The resulting mixture was heated to reflux for 4 hours. The excessive oxidant was destroyed by adding finely ground lead dioxide while the solution was boiling. The solution was cooled, filtered, and then evaporated under vacuum while maintaining the bath temperature at 40-50° to produce a syrupy residue. The residue was treated with dioxane and filtered. The filtrate was evaporated under reduced pressure and the residue which was a red liquid was distilled at 60° at 1.1 mm Hg to give a 2:1 mixture of **2c** and its isomer **2c'** in 17% yield; ir (neat): 3065 (vw, C=C-H), 2900 (w, CH_3), 1740 (s) and 1690 (vs, C=O) cm^{-1}; ^1H nmr for **2c**: δ 3.01 (s, 3H, CH_3), 3.96 (app s, 2H, CH_2), 6.13 (dt, 1H, 3-H), 7.03 (dt, 1H, 4-H); ^1H nmr for **2c'**: δ 2.99 (s, 3H, CH_3), 3.05 (app s, 1H, CH_2), 5.26 (dt, 1H, 4-H), 6.32 (dt, 1H, 5-H).

Anal. Calcd. for C_5H_7NO (97.12): C, 61.8; H, 7.3; N, 14.4. Found: C, 62.0; H, 7.4; N, 14.2.

Preparation of Esters **3-6**. An Illustrated Procedure with 2-Furyl Furoate (**3a**).

A mixture of **2a** (1.00 ml, 0.014 mole), triethylamine (5.00 ml, 0.036 mole), and 2-furoyl chloride (15.5 ml, 0.016 mole) was stirred in a 50 ml-round-bottomed flask cooling with an ice-water bath for 5 minutes. The bath was replaced with an oil-bath and the solution was heated at 50° for 3 hours. After cooling, dried diethyl ether was added and filtered the mixture. The filtrate was evaporated under reduced pressure and the residual liquid was distilled at 82° under 0.02 mm Hg to give **3a** in 70% yield.

Reaction of 2-Furoyl Chloride (**1a**) with 2(5*H*)-Furanone (**2a**): Furoic Anhydride (**7a**).

A mixture of pyridine (0.5 ml) and **1a** (0.58 ml, 5.88 mmoles) was cooled in an ice-water bath to 0° and **2a** (0.42 ml, 5.92 mmoles) was added. The mixture became a solid mass. Pyridine (0.5 ml) was added and the mixture was stirred at room temperature under the stream of nitrogen for 24 hours. The mixture was fractionated into water (10 ml) and diethyl ether (10 ml). The ethereal layer was separated, dried over anhydrous magnesium sulfate, and filtered. Evaporation of the solvent gave **7a** as a colorless solid, 0.41 g (34%), mp 71-70° (lit [6] 73°).

1-Methyl-2-pyrroloic Anhydride (**7c**).

This compound was obtained by a similar method to **7a**, 45%, mp 41-44°; ir (neat): 3100 (vw), 2970 (vw), 1760 (s), 1700 (s), 1405 (m), 1350 (m), 1205 (m), 1035 (ms), 1000 (s), 745 (ms) cm^{-1}; ^1H nmr: δ 3.98 (s, 3 H, NCH_3), 6.10 (dd, 1H, 4-H, $J_{4,5}$ = 2.4 Hz, $J_{4,3}$ = 4.1 Hz), 6.93 (app t, 1H, 5-H, $J_{5,4}$ = 2.2 Hz, $J_{5,3}$ = 2.0 Hz), 7.11 (dd, 1H, 3-H, $J_{3,4}$ = 4.1 Hz, $J_{3,5}$ = 2.0 Hz); ms: m/z (%) 232 (30, M^+), 125 (16), 108 (100), 80 (10).

Anal. Calcd. for $C_{12}H_{12}N_2O_3$ (232.24): C, 62.1; H, 5.2; N, 12.1. Found: C, 62.3; H, 5.3; N, 12.0.

Acknowledgment.

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