CONTRIBUTIONS TO THE STUDY OF ROTATIONAL ISOMERISM IN DERIVATIVES OF FURAN, THIOPHENE, AND PYRROLE BEARING CARBONYL-CONTAINING SUBSTITUENTS (REVIEW)

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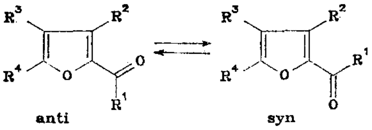
During the past 12 years, we have been engaged in a comprehensive study (chiefly by infrared and nuclear magnetic resonance techniques) of rotational isomerism in carbonyl-containing derivatives of furan, thiophene, and pyrrole. In this review, we draw together the spectroscopic aspects of this work and discuss the conclusions by individual ring system and functional group type.

FURAN

1. 2-Aldehydes and 2-Ketones

Infrared Studies. In the last 15 years there have been many investigations by physical methods (notably ^{1}H NMR [1-5], ^{13}C NMR [6], microwave [7], and IR spectroscopy [8-10], and dipole moment measurement [11, 12]) into the conformational preferences of heterocyclic 2-carbaldehydes, and it is now accepted that solutions of furan-2-carbaldehyde in nonpolar solvents contain syn- and anti-forms with the former predominating.



$R^1=R^2=R^3=R^4=H$

Early studies [8] of the IR carbonyl doublet of furan-2-carbaldehyde (1700 and 1681 cm^{-1}; CCl$_4$ solution at 293 K) in solutions of different concentrations over a range of temperature excluded both intramolecular association and the occurrence of a "hot transition" as the cause of the band splitting. The components of the doublet were assigned as being the characteristic absorptions of the syn- and anti-forms, espectially since "evidence" [13] against the operation of Fermi resonance was at that time known. Later studies [9, 10], however, mainly with isotopically labeled aldehydes, show that the doublet does not reflect the presence of rotational isomers, but indicate that the splitting arises from a Fermi resonance effect.

There does not appear to be any single criterion for deciding whether rotational isomerism or Fermi resonance causes a carbonyl compound to show a doublet C=O absorption. The distinction requires spectroscopic evidence from (i) a comparison of the fundamental and overtone regions [10], (ii) a change of solvent dielectric constant [14], and (iii) a study of closely related compounds. Deuterated analogues are especially important in the third approach because the position of a putative rotameric equilibrium would not be affected appreciably by deuterating the substrate; further, replacement of protium by deuterium would produce only a small change in C=O frequency, by a mass effect, and would not introduce complications by altering the polar effects operating in the system. A series of deuterated furan carbaldehydes have thus been prepared [15, 16], and a detailed investigation into the origin of the carbonyl doublet of furan-2-carbaldehyde has been undertaken [17]. The results are summarized in Table 1.

Evidence from approaches (i) and (ii) is not found to be conclusive. Thus, with rotamers of different dipole moments the equilibrium constant could be influenced by solvent polarity, and with the aldehyde (1) the observed effects of changing the solvent could be

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TABLE 1[a] [17]. Deuterated Aldehydes

Aldehyde	R^1	R^2	R^3	R^4	ν_{CO}, cm^{-1}		
					fundamental region		overtone region CCl_4
					CCl_4	MeCN	
1	H	H	H	H	1700 (1), 1681 (0,34)	1692 (0,85), 1676 (1)	3371 (1), 3355 (0,58)
2	H	D	H	H	1697[b]	1690 (1), 1672 (0,33)	3375 (1), 3346 (0,36)
3	H	H	D	H	1700 (0,89), 1691 (1)	1690 (1), 1682 (0,98)	3367
4	H	H	H	D	1694	1683	3370
5	H	D	D	H	1696 (1), 1690 (1)	1690 (0,43), 1682 (1)	—[c]
6	H	D	H	D	1697	1684	3372
7	H	H	D	D	1695	1685	3370
8	H	D	D	D	1694	1682	3370
9	D	H	H	H	1682 (1), 1672 (0,69)	1668	—[c]
10	D	H	H	D	1675	1665	—[c]

[a] The results in Tables 1-4, 7, 9-12, and 16 were obtained by examining solutions at 303 K (unless otherwise stated) at a spectral slit width of 1.5 cm^{-1} on a spectrometer purged continuously with dry air. Solutes and solvents were dried immediately before use, solutions were made up in a dry box, and cells of path lengths 1 cm and 1 mm (for CCl_4, fundamental region), 5 cm (CCl_4, overtone region), and 1 mm and 0.1 mm (for MeCN, fundamental region) were used. Band positions are in cm^{-1}; where more than one band is shown, the experimental trace was resolved into symmetrical components, using an analogue computer, and the component positions are followed, in parentheses, by their relative absorbances.

[b] Broad band.

[c] Not investigated.

rationalized by assuming that the lower wave number form has the higher dipole moment. Likewise, the variation in the relative absorbances of the doublets' components found on examining the overtone region might result from the rotamers' C=O absorptions having different anharmonicities. These results emphasize also that it is necessary to examine a range of analogues. Thus, three of the deuterated aldehydes — (3), (5), and (9) — resemble the protioaldehyde in showing doublets; this could be construed as favoring rotational isomerism if it were not for the markedly different values of the components' relative absorbances in compounds (3) and (5). The crucial observation is that all the aldehydes deuterated at position 5 show singlets in both carbon tetrachloride and acetonitrile at slightly lower wave numbers than the higher wave number band of furan-2-carbaldehyde. The C=O doublet of furan-2-carbaldehyde therefore arises from Fermi resonance between a "true" C=O stretching band (at ∿1694 cm^{-1} in CCl_4, from the 5-D analogue) and a nearby interacting absorption; the latter originates in a vibration involving the C(5)—H bond.

This result together with the evidence from the other investigations [1-12] requires that the C=O stretching bands of the syn- and anti-forms of furan-2-carbaldehydes have almost exactly equal wavenumbers.

A series of halogenated aldehydes [15, 18] is shown in Table 2. Only two exhibit C=O doublets in carbon tetrachloride, and the singlets obtained after deuteration of these compounds at positions 5 establish the occurrence and the origin of Fermi resonance. In all cases examined there is the expected change in position (a decrease of ∿10 cm^{-1}) on passing to the more polar solvent. Comparison of corresponding 3- and 5-halogenated compounds in the senses of isomeric pairs, e.g., aldehydes (11) and (18), and of different halogens, e.g., aldehydes (17)-(19), indicates that any halogen at either of these positions lowers the position of the C=O absorption by ∿10 cm^{-1} as a result of overall electron donation to the carbonyl group. A halogen substituent at position 4, where mesomerism is inhibited, shows the reverse effect. It appears reasonable that the syn-forms of the 3-halogenated aldehydes and both rotamers of the 5-halogenated isomers should absorb at similar positions. However, in the anti-forms of the 3-halogenated compounds the field effect arising from almost parallel C—Hal and C=O dipoles would be expected to move the bands to higher wave numbers by ∿20 cm^{-1} (cf. α-halogenated ketones [19]). The observation of single bands at normal positions sug-

TABLE 2 [17]. Halogenated Aldehydes (experimental datails given in Table 1)

Aldehyde	R^1	R^2	R^3	R^4	ν_{CO}, cm^{-1}	
					CCl_4	MeCN
11	H	Br	H	H	1691[a]	1681
12	H	I	H	H	1690	1680
13	H	H	Br	H	1705,5 (1), 1690,5 (0,74)	1701[a] (0,49), 1686 (1)
14	H	H	Br	D	1697	1689
15	H	H	I	H	1705 (1), 1689 (0,70)	1699 (0,36), 1684 (1)
16	H	H	I	D	1698	1688
17	H	H	H	Cl	1690,5	1683
18	H	H	H	Br	1689	1682
19	H	H	H	I	1691	1682
20	H	H	Br	Cl	1693	1685
21	H	H	Br	Br	1694	1687

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[a] Band broadened to high cm^{-1}.

TABLE 3 [17]. Alkyl- and Aryl-Substituted Aldehydes and 2-Furyl Ketones[a] (experimental details given in Table 1)

Compound	R^1	R^2	R^3	R^4	ν_{CO}, cm^{-1}, CCl_4
22	H	Me	H	H	1688
23	H	*i*-Pr	H	H	1686
24	H	H	*i*-Pr	H	1687
25	H	H	H	Me	1686
26	H	H	H	*i*-Pr	1686
27	H	H	*i*-Pr	*i*-Pr	1685
28	H	H	H	Ph	1683,5
29	H	H	H	*p*-ClC_6H_4	1685
30	H	H	H	*p*-BrC_6H_4	1684
31	H	H	H	1-$C_{10}H_7$	1683
32	H	H	H	2-$C_{10}H_7$	1681
33	Me	H	H	H	1683,5
34	Et	H	H	H	1685
35	Me	Me	H	H	1677
36	Et	Me	H	H	1678,5
37	Ph	H	H	H	1656 (1), 1650 (1)
38	Ph	H	H	Br	1656 (0,94), 1647,5 (1)
39	Ph	H	H	I	1654,5 (0,71), 1652,5 (0,21), 1646,5 (1)
40	*p*-$MeOC_6H_4$	H	H	H	1649 (0,78), 1641,5 (1)
41	*p*-$MeOC_6H_4$	H	H	Br	1643[b]
42	2,4-$Me_2C_6H_3$	H	H	H	1656[c]
43	2,4,6-$Me_3C_6H_2$	H	H	H	1663

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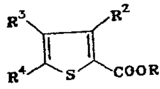
[a] References 15 and 18.
[b] Band broadened to high cm^{-1}.
[c] Band broadened to low cm^{-1}.

gests that the 3-halogenated aldehydes resemble 4-bromofuran-2-carbaldehyde (13) [20] in having a marked preference for the syn-conformation.

The positions of the CO bands in the aldehydes and ketones reported in Table 3 are as expected, the lowest values being found with the p-anisoyl compounds (40) and (41). Single bands do not imply marked or exclusive preference for one rotameric form: For example, a solution of 2-furyl methyl ketone (33) has one C=O band, but almost certainly contains appreciable amounts of both rotational isomers [21, 4] under the conditions used. The origin of the doublets shown by the aryl 2-furyl ketones (37)-(40) has not been established. Although the doublet of the benzoyl compound (37) is retained in its 5-deuterated analogue, ^1H NMR examination does not give clear evidence for the existence of rotameric forms [22].

NMR Studies. The many investigations by ^1H NMR techniques into the rotational isomerism of furan-2-carbaldehyde indicate that the compound has K ([syn]/[anti]) $\simeq$ 6 at 183 K and K $\simeq$ 1 at 303 K [3, 4, 5, 23].

TABLE 4 [27]. Series of Alkyl Furan-2-Carboxylates  [experimental details given in Table 1.

Enthalpy differences (ΔH°, J·mole^{-1}, statistical error ±300 J·mole^{-1}) between forms giving doublet absorptions are for direction: form with the higher cm^{-1} → form with lower cm^{-1}]

Ester	R¹	R²	R³	R⁴	ν_{CO}·cm^{-1}			ΔH^0
					fundamental region		overtone region, CCl$_4$	
					CCl$_4$	MeCN		
44a	Me	H	H	H	1740 (1), 1725 (0,94)	1733 (1), 1725 (0,77)	3469 (1), 3437 (1), 3424 (0,91)	−900
45a	Me	H	H	D	1740 (1), 1725 (0,91)			
46a	Me	H	D	H	1742 (1), 1727 (0,98)	1733 (1), 1723 (0,71)	3467 (0,81), 3438 (1)	
47a	Me	D	H	H	1741 (1), 1727 (0,93)	1732 (1), 1722 (0,70)	3468 (0,83), 3436 (1)	
48a	Me	H	D	D	1743 (1), 1728 (0,95)	1733 (1), 1724 (0,73)	3468 (0,81), 3440 (1)	
49a	Me	D	D	H	1738 (1), 1725 (0,97)	1731 (1), 1722 (0,69)	3468 (0,82), 3435 (1)	
50a	Me	D	H	D	1741 (1), 1726 (0,94)	1732 (1), 1723 (0,72)	3468 (0,82), 3438 (1)	
51a	Me	D	D	D	1742 (1), 1727 (1)	1735 (1), 1724 (0,77)	3468 (0,80), 3438 (1)	
*44*b	Et	H	H	H	1734 (0,90), 1718 (1)	1726 (1), 1717 (0,83)	3453 (0,83), 3422 (1)	−1900
*45*b	Et	H	H	D	1734 (0,90), 1718 (1)			
*46*b	Et	H	D	H	1737 (0,83), 1721 (1)	1729 (1), 1717 (0,84)	3452 (0,82), 3420 (1)	
*47*b	Et	D	H	H	1734 (0,85), 1720 (1)	1727 (1), 1715 (0,83)	3448 (0,85), 3422 (1)	
*48*b	Et	H	D	D	1738 (0,85), 1722 (1)	1729 (1), 1717 (0,82)	3454 (0,83), 3424 (1)	
*49*b	Et	D	D	H	1735 (0,89), 1718 (1)	1726 (1), 1715 (0,81)	3448 (0,84), 3420 (1)	
*50*b	Et	D	H	D	1737 (0,86), 1721 (1)	1728 (1), 1717 (0,83)	3452 (0,85), 3421 (1)	
*51*b	Et	D	D	D	1736 (0,89), 1720 (1)	1728 (1), 1716 (0,90)	3454 (0,86), 3422 (1)	
*44*c	*t*-Bu	H	H	H	1729 (1), 1711 (1)	1719 (1), 1710 (0,83)	3440 (0,87), 3408 (1)	−2500
*45*c	*t*-Bu	H	H	D	1729 (1), 1711 (1)			
*46*c	*t*-Bu	H	D	H	1731 (1), 1714 (0,95)	1722 (1), 1709 (0,87)	3438 (0,87), 3406 (1)	
*47*c	*t*-Bu	D	H	H	1730 (1), 1712 (1)	1721 (1), 1708 (0,77)	3436 (0,90), 3408 (1)	
*48*c	*t*-Bu	H	D	D	1732 (1), 1715 (0,97)	1722 (1), 1709 (0,81)	3442 (0,90), 3407 (1)	
*49*c	*t*-Bu	D	D	H	1729 (1), 1712 (0,94)	1720 (1), 1707 (0,79)	3436 (0,88), 3404 (1)	
*50*c	*t*-Bu	D	H	D	1731 (1), 1714 (0,98)	1720 (1), 1707 (0,82)	3438 (0,87), 3406 (1)	
*51*c	*t*-Bu	D	D	D	1729 (1), 1712 (0,98)	1719 (1), 1707 (0,84)	3438 (0,95), 3405 (1)	
52a	Me	H	H	Br	1748 (0,59), 1738 (0,94) 1731 (1), 1720 (0,88)[a]	1731 (1), 1719 (0,67)	3466 (0,71), 3431 (1)	
53a	Me	D	D	Br	1743 (0,77), 1729 (1)	1731[b]		

54a	Me	H	H	Cl	1745 (0,69), 1728 (1)	1736 (1), 1725 (0,98)	3468 (0,65), 3436 (1)	−2500
55a	Me	H	H	I	1743 (0,76), 1727 (1)	1736 (1), 1725 (1)	3466 (0,77), 3432 (1)	−1500
56a	Me	H	H	NO_2	1756 (0,46), 1737 (1)	1744 (1), 1735 (0,98)	3490 (0,50), 3454 (1)	−1100
57a	Me	H	Br	H	1746 (1), 1728 (1)	1738 (0,83), 1727 (1)		−1200
58a	Me	H	Br	D	1747 (1), 1729 (0,88)	1739 (1), 1726 (0,72)	3470 (1), 3442 (0,89)	
59a	Me	H	Br	Br	1745 (0,89), 1730 (1)	1737 (1), 1726 (0,60)	3476 (0,90), 3444 (1)	−1600
60a	Me	H	Br	Cl	1746 (1), 1729 (0,90)	1739 (1), 1726 (0,68)	3474 (1), 3438 (1)	−1500
61a	Me	H	I	H	1746 (1), 1728 (0,84)	1737 (1), 1725 (0,69)	3472 (1), 3440 (0,92)	−1500
62a	Me	H	I	D	1744 (1), 1727 (0,85)	1735 (1), 1724 (0,71)	3472 (1), 3440 (0,88)	
63a	Me	Br	H	H	1733[b]	1727[b]		
64a	Me	Br	H	Br	1732[b]	1726[b]		
65a	Me	I	H	H	1731[b]	1726[b]		
*52*b	Et	H	H	Br	1735 (0,67), 1719 (1)	1726 (1), 1716 (0,83)	3455 (0,68), 3423 (1)	−700
*53*b	Et	D	D	Br	1736 (0,63), 1719 (1)	1727 (1), 1716 (0,83)		
*54*b	Et	H	H	Cl	1741 (0,76), 1722 (1)	1729 (1), 1717 (0,86)	3454 (0,75), 3422 (1)	−2000
*55*b	Et	H	H	I	1737 (0,65), 1720 (1)	1727 (0,95), 1715 (1)	3450 (0,71), 3420 (1)	−2600
*56*b	Et	H	H	NO_2	1747 (0,45), 1728 (1)	1738 (1), 1726 (0,83)	3478 (0,47), 3440 (1)	−1600
*57*b	Et	H	Br	H	1739 (0,91), 1724 (1)	1730 (1), 1722 (0,83)		−400
*58*b	Et	H	Br	D	1740 (1), 1725 (0,93)	1732 (1), 1721 (0,74)	3458 (1), 3430 (0,95)	
*59*b	Et	H	Br	Br	1741 (0,92), 1725 (1)	1733 (1), 1723 (0,84)	3464 (0,94), 3428 (1)	−1500
*60*b	Et	H	Br	Cl	1741 (0,82), 1723 (1)	1734 (1), 1721 (0,89)	3464 (0,79), 3430 (1)	−1600
*61*b	Et	H	I	H	1740 (1), 1724 (0,98)	1732 (1), 1719 (0,76)	3458 (1), 3430 (1)	−1600
*62*b	Et	H	I	D	1740 (1), 1724 (0,95)	1731 (1), 1719 (0,72)	3458 (1), 3430 (0,98)	
*63*b	Et	Br	H	H	1727[b]	1721[b]		
*64*b	Et	Br	H	Br	1727[b]	1721[b]		
*65*b	Et	I	H	H	1726[b]	1719[b]		
*52*c	*t*-Bu	H	H	Br	1729 (0,91), 1711 (1)	1719 (1), 1710 (0,83)	3446 (0,59), 3409 (1)	−1900
*53*c	*t*-Bu	D	D	Br	1731 (0,67), 1712 (1)	1721 (1), 1711 (1)		
*54*c	*t*-Bu	H	H	Cl	1733 (0,80), 1712 (1)	1724 (1), 1709 (0,93)	3442 (0,81), 3408 (1)	−2000
*55*c	*t*-Bu	H	H	I	1728 (0,64), 1710 (1)	1720 (1), 1708 (0,88)	3440 (0,64), 3404 (1)	−1500
*56*c	*t*-Bu	H	H	NO_2	1742 (0,49), 1722 (1)	1731 (1), 1718 (0,88)	3465 (0,52), 3425 (1)	−2600
*57*c	*t*-Bu	H	Br	H	1734 (1), 1718 (0,91)	1724 (1), 1717 (0,77)		−1500
*58*c	*t*-Bu	H	Br	D	1732 (1), 1717 (0,96)	1724 (1), 1714 (0,57)	3442 (1), 3415 (0,98)	
*59*c	*t*-Bu	H	Br	Br	1735 (0,86), 1715 (1)	1729 (0,93), 1714 (1)	3450 (0,92), 3414 (1)	−2500
*60*c	*t*-Bu	H	Br	Cl	1733 (0,81), 1717 (1)	1728 (0,95), 1717 (1)	3444 (0,90), 3414 (1)	−1300
*61*c	*t*-Bu	H	I	H	1733 (1), 1717 (0,88)	1724 (1), 1712 (0,66)	3444 (1), 3416 (0,88)	−700
*62*c	*t*-Bu	H	I	D	1733 (1), 1717 (0,90)	1724 (1), 1714 (0,63)	3444 (1), 3416 (1)	
*63*c	*t*-Bu	Br	H	H	1723[b]	1715[b]		
*64*c	*t*-Bu	Br	H	Br	1722[b]	1717[b]		
*65*c	*t*-Bu	I	H	H	1726 (1), 1718 (1)[a]	1713	3436	

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[a] Fermi resonance (see text).

[b] Unsymmetrical band.

The ^{13}C NMR spectrum below 213 K in CH_2Cl_2/CD_2Cl_2 shows two C-3 resonances [intensity ratio (higher to lower field signals) 1:10 at 203 K, separation about 9 ppm] and two C=O resonances (10:1, about 3 ppm) [6]. The intensity ratio may not reflect exactly the ratio of the rotamers because of the possible differences in relative Overhauser enhancements: The use of a solution in $CDCl_3$ containing $Cr(acac)_3$, which minimizes this difference, but which may also alter the equilibrium position by a dielectric effect [5], leads to a ratio of 5:1. Shielding considerations [24, 3] suggest, in agreement with but independently of the PMR work, that the syn-form predominates.

Study of the solvent dependence of the furan-2-carbaldehyde conformational equilibrium has been complicated by the fact that solvents of dielectric constant $< \sim 5$ are incapable of holding sufficient material in solution at low temperature for a satisfactory continuous-wave NMR spectrum to be run. A combination of different experimental procedures — ^1H NMR (on solutions in Me_2O and Me_2CO at low temperatures), dipole moment measurements (CCl_4 and PhH solutions), and room-temperature measurements of NMR long-range coupling constants (in CCl_2F_2, Me_2O, Me_2CO, and Me_2SO solutions) — indicates that the difference in free energy between the syn- and anti-forms of the aldehyde are strongly dependent on the nature of the solvent, the anti-form being more stable than the syn- in media of dielectric constant $> \sim 5$ [5]. Direct evidence from pulsed Fourier transform ^1H NMR studies of very dilute solutions of furan-2-carbaldehyde in nonpolar solvents [25] and evidence from ^1H [5, 1] and ^{13}C [25] studies of a concentrated solution in a more polar solvent at 183 K show that the NMR signals due to the formyl and 3-H hydrogen atoms, and to the ring and carbonyl ^{13}C atoms, are split because of the conformational heterogeneity. Whereas in the solution of high dielectric constant the anti-isomer is only $\sim 9\%$ abundant (determined from the ^1H and ^{13}C integrals and previously published signal assignments [1, 26]), it is found, in agreement with the earlier study [5], that this form becomes markedly more favored relative to the syn-form in media of low dielectric constant.

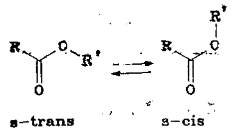
2. 2-Carboxylic Esters

Infrared Studies. The IR carbonyl absorptions in CCl_4 solution of 66 furan-2-carboxylic esters (Me, Et, and t-Bu) containing deutero-, halogeno-, and nitro-substituents are given in Table 4. Of the esters examined [27], one shows four bands, eight show single bands, and 57 show well-separated doublets. Distinction between the causes of the multiplet absorptions is made by the approaches discussed under furan-2-carbaldehyde and establishes rotational isomerism as being generally responsible for the gross features of the band structure.

Dramatic solvent dependence of the absorptions is observed for only two compounds, ester (52a), which has the four-component absorption in CCl_4, and ester (65c); replacement of protium by deuterium at 3-, 4-, and 5-positions of the ring causes little change in the form of the absorptions except for ester (52a) where the four-component absorption collapses to a doublet in the 3,4-dideutero-derivative (53a).

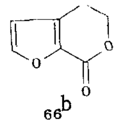
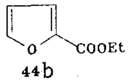
Support for the attribution of the ester multiple absorptions is provided by studying the lactone (66) [28], which is considered to be a "fixed conformational ester." The doublet absorption of this ester (Table 5) could not arise from rotational isomerism, and detailed examination suggests that Fermi resonance is responsible for the band doubling; the spectrometric behavior of this compound is markedly different from that of a typical ester, and ethyl furan-2-carboxylate is shown for comparison in Table 5.

Simple esters usually adopt an s-trans configuration: the rare s-cis form is only observed when R is small and R' bulky (e.g., t-butyl formate [29, 30]. The methyl and ethyl esters in Table 4 do not have any of the special structural features which would be expected



to destabilize the s-trans-form, and even with the t-butyl esters, this form is expected to be markedly preferred (cf. t-butyl formate and acetate [29b]). Thus, of the four planar conformations (Scheme 1), the syn-s-trans- and anti-s-trans-forms are taken to be responsible for the doublets. The positions of the higher wave number components of the doublets are more sensitive than those of the lower wave number components towards solvent polarity, and as the dielectric constant of the solvent is increased the higher wave number components be-

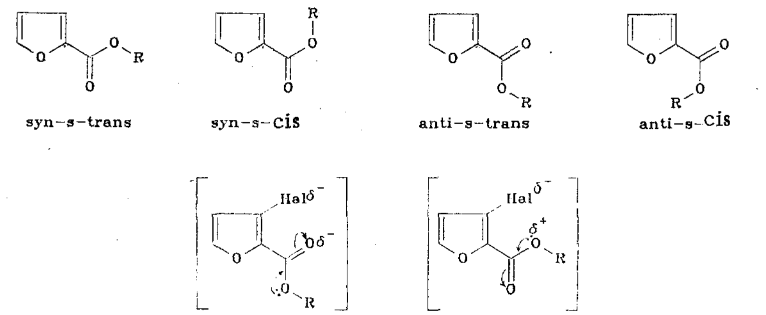
TABLE 5 [27]. Comparison of the Lactone (66) with Ethyl Furan-2-Carboxylate (44b)[a]

Compound	T, K	ν_{CO}, cm^{-1}		
		fundamental region		overtone region, CCl_4
		CCl_4	MeCN	
 66^b	258 303 348	1755 [80,0], 1737 [20,0] 1756 [76,5], 1737 [13,5] 1758 [73,0], 1737 [5,5]	1748 (0,58), 1733 (1)	3486
 44b	258 303 348	1733 [55,0], 1717 [45,0] 1734 [53,5], 1718 [39,0] 1735 [52,5], 1719 [34,0]	1726 (1), 1717 (0,83)	3453 (0,87), 3422 (1)

[a]The figures in square brackets are the areas of component bands expressed as percentages of the total area of the doublet at 258 K [31]; the figures in parentheses are relative absorbances, as in Table 1.

[b]Reference 28.

Scheme 1



come relatively more intense: Both observations show that the rotamers responsible for the higher wave number bands have higher dipole moments than those associated with the lower wave number bands.

Introduction of halogen substituents at position 4 of the heterocyclic ring increases the wavenumbers of the C=O bands, while halogens at position 5 have little effect: Bearing in mind the lower electron-withdrawing tendency of an ester group compared with that of a formyl group, these results are interpreted as discussed previously for furan-2-carbaldehydes [17]. However, apart from one ester, the 3-halogenated compounds have single C=O bands. [The results in Table 4 demonstrate that Fermi resonance operates with the exceptional ester, t-butyl 3-iodofuran-2-carboxylate (65c).] The field effect arising from almost parallel C–Hal and C=O dipoles in an anti-s-trans-form of a 3-halogeno-ester (Scheme 1) is expected to increase the wave number of its absorption by 20 cm^{-1} (cf. α-halogenated ketones [19]) relative to that of an anti-s-trans-5-halogenated isomer band. In contrast, with the syn-s-trans-rotamers the 3-halogenated ester is expected to have the lower wave number since the field effect here ought to enhance the +M effect of the alkoxy group. (Esters of certain 3-alkylfuran-2-carboxylic acids exhibit well-defined carbonyl doublets [28] and show that the appearance of only single bands with the 3-halogeno-esters is not simply a result of steric hindrance.) Thus, the positions of the 3-halogeno-ester absorptions suggest that the bands arise from syn-s-trans-conformations and correspond to the higher wave number components of the 4- and 5-halogeno-ester doublets; the correspondence is supported by the solvent effects, the behavior of the single bands resembling that of the higher wave number components of the doublets.

Table 4 also provides many comparisons between 5-halogenated esters and their nonhalogenated analogues, in which the situation is not complicated by Fermi resonance [e.g., the pairs (44a)-(54a), (44b)-(52b), and (44c)-(52c)]. In view of the close similarity between the spectra of corresponding esters it is logical to extend to the nonhalogenated esters the correlations developed for the halogenated compounds. Independent consideration of the nonhalogenated esters leads to the same correlations. Thus, vector treatment indicates that the dipole moment of the syn-s-trans-form should be bigger than that of the anti-s-trans-rotamer: As the dielectric constant of the solvent is increased, the syn-s-trans-form becomes relatively more important and, from the observed effects, it is then to be associated with the higher wave number component of a doublet. The higher wave number of the syn-s-trans-form probably has its origin in the electrostatic repulsion that would arise from proximity of the ring oxygen and the negatively charged oxygen of dipolar canonicals, i.e., electrostatic inhibition of mesomerism reducing the single bond character of the formal C=O group.

The accumulated evidence leads to the general conclusion that where esters of furan-2-carboxylic acids show carbonyl doublets arising from rotational isomerism, the high wave number band arises from the syn-s-trans-form and the lower wave number band from the anti-s-trans-form.

Determination of Thermodynamic Parameters from Infrared Data. The determination of the energy differences between the rotameric forms of furan esters in carbon tetrachloride solution by variable-temperature IR measurements is complicated by (i) the possible "natural decrease" of the band intensities with increasing temperature, and (ii) uncertainties in assessing the integrated absorption coefficients of the rotameric bands [31]. The origin of natural decrease [32] is obscure, but its effect may be nullified or reduced in a rotameric system by using the relative band areas of the isomer absorptions [31]; this allows reliable enthalpy differences to be obtained without knowing, and irrespective of the values of, the band absorption coefficients.

The approach generally used for obtaining quantitative thermodynamic data from variable-temperature IR spectrometry is as follows [33]. Suppose an IR cell (path length p) contains a solution [concentration c (g/liter)] at temperature T (K) of a compound which exists as a mixture of two stable rotational isomers each having a characteristic carbonyl band suitable for intensity measurement. For the equilibrium h (form with higher C=O frequency) $\rightleftarrows$ l (form with lower C=O frequency) let A_h be the area of the band of rotamer h (i.e., a quantity proportional to the intensity of the band), α_h the integrated absorption coefficient of rotamer h, c_h the concentration (g/liter) of rotamer h, K the equilibrium constant (c_l/c_h), and ΔH° and ΔS° the enthalpy and entropy changes, respectively, for the conversion h $\rightleftarrows$ l. If the barrier to rotation is small compared with thermal energy, then

$$K = A_l\alpha_h / A_h\alpha_l \tag{1}$$

$$\log (A_l/A_h) = (-\Delta H^0/2.303RT) + (\Delta S^0/2.303R) + 1 \log (\alpha_l/\alpha_h) \tag{2}$$

$$A_l = -(\alpha_l/\alpha_h)A_h + \alpha_l pc \tag{3}$$

Application of Eq. (2) to the results of variable-temperature runs affords ΔH° if ΔS° and the ratio α_l/α_h are independent of temperature. To find K, from Eq. (1), this ratio must be known. If the α values are assumed to be independent of temperature, the ratio can be found from Eq. (3) by a plot of A_l versus A_h at different temperatures. The value of K gives ΔG°, the free energy change for h $\rightleftarrows$ l, and ΔS° follows since ΔH° is known.

In order to circumvent the difficulties arising from the effect of natural decrease, plots of log (A_l/A_h) versus 1/T are used to derive the ΔH° values given in Table 4 [27]. The results reveal that the thermochemically more stable forms are those containing an anti-s-trans-conformation of the ester groups.

Attempts to evaluate free energy and entropy differences have been unsuccessful [34]. As explained earlier, to evaluate K, and hence ΔS°, values of the α_l/α_h ratio for a particular compound must be assumed to be independent of temperature. Such a procedure, however, gives essentially meaningless results and suggests that the assumption, inherent in the approach of Eq. (3), that α_l (or α_h) is independent of temperature is false.

Values of ΔH° are known to be unreliable when obtained from the temperature variation of NMR coupling constants in a solvent whose dielectric constant (usually high) has a large temperature coefficient [35]. Thus, dielectric constant change per se would influence the equilibrium proportions of rotational isomers with different dipole moments. Although this factor would be expected to be small with carbon tetrachloride solutions, investigations have been carried out with the object of separating the effect of a change in the dielectric constant (ε) of the solvent from that of changes in both dielectric constant and temperature [31].

TABLE 6 [31]. Correction for Dielectric Constant Variation

Exponent	Ester	44a	44b	44c
Regression of $\log(A_l/A_h)$ vs. ε	Slope ε $(\Delta H^0)_\varepsilon$	$-0{,}02$ $-0{,}985$ -959	$-0{,}07$ $-0{,}942$ -2140	$-0{,}07$ $-0{,}997$ -2710

The effect of dielectric constant change with temperature may be simulated by using appropriate solvent mixtures at constant temperature; carbon tetrachloride and acetonitrile are usually chosen, since the dielectric constants of these solvents, and mixtures of them, at various temperatures have been measured accurately [36]; further, acetonitrile is not expected to favor one rotamer by preferential solvation. For three esters (44a-c) values of A_l/A_h have been measured at a fixed temperature in carbon tetrachloride—acetonitrile mixtures whose dielectric constants are found by graphical interpolation from Kalliorinne's data [36]. Treatment of the results involves the following stages. The variation of the ε values of carbon tetrachloride with temperature [36] are expressed mathematically [Eq. (4)].

$$\varepsilon = 175.27(1/T) + 1.64 \tag{4}$$

$$\log(A_l/A_h) = m\varepsilon + m'(1/T) + \text{constant} \tag{5}$$

$$\log(A_l/A_h) = (175.27m + m')(1/T) + \text{constant} \tag{6}$$

$$-\Delta H^0/2{,}303R = m' = \{\text{observed slope } [\log(A_l/A_h) \text{ vs } 1/T]\} - 175.27\,m \tag{7}$$

Equation (5) is adopted as a simple way of representing two factors (ε and T) influencing the relative band areas of the rotamers. Combination of Eqs. (4) and (5) gives Eq. (6); comparison of Eqs. (5) and (2) leads to Eq. (7). Plots of $\log_1 (A_l/A_h)$ versus ε afford m values for the esters. The figures for (175.27m + m') are available from examinations at a fixed initial concentration over a range of temperatures; hence m' and corrected enthalpy values, symbolized by $(\Delta H^\circ)_\varepsilon$ in Table 6, are evaluated. Comparison of these with the ΔH° values (Table 4) for esters (44a-c) shows that the dielectric variation effect is negligible for carbon tetrachloride solutions in the temperature range of the variable-temperature studies, and the effect is not investigated with the other esters.

NMR Studies. Variable-temperature ^1H NMR measurements of furan esters have not been informative [27]; evidence for rotational isomerism, however, has been obtained from the ^{13}C NMR spectrum of t-butyl furan-2-carboxylate in CH_2Cl_2/CD_2Cl_2 which shows broadening of resonances with decrease in temperature [6]. The broadening does not pass its maximum at 183 K and is presumed to be due to a very low rotational energy barrier.

3. 2-Carbonyl Halides

Data from the IR and NMR spectra of furan- and thiophen-2-carbonyl chlorides and fluorides (and one bromide) at about room temperature are presented in Table 7 [37], and the results of examining selected compounds over a temperature range are collected in Table 8 [37].

^{19}F NMR Studies. The ^{19}NMR signals of the furan carbonyl fluorides (94) and (97) (Table 8) provide the clearest evidence for the occurrence of rotational isomerism. As the temperature is lowered the signals broaden gradually and, at certain temperatures, become so broad that they are no longer visible. A further decrease in temperature results in the appearance of two ^{19}F signals. [These effects were not revealed in an earlier examination of furan-2-carbonyl fluoride [38] (at 32°) where evidence for the occurrence of rotational isomerism was adduced from comparisons of the observed coupling constants with those calculated for the separate isomers]. The energy barrier to rotation in the fluorides must be low, and success in detecting the individual forms stems from the large differences (up to ∿10 ppm) between their ^{19}F chemical shifts (cf. the CHO difference of ∿0.18 ppm for the syn- and anti-

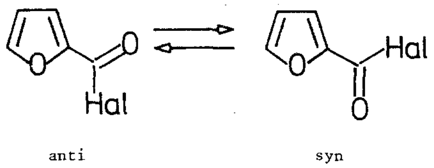
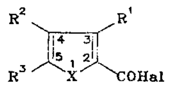


TABLE 7 [37]. IR and NMR Spectra of Furan- and Thiophene-2-Carbonyl Halides[a]



Compound					IR bands (303°K), fundamental region, cm⁻¹		¹H NMR signals (308°K, CCl_4)			
	X	Hal	R¹	R²	R³	CCl_4	MeCN	δ τ	form	J, Hz	assignment
1	2	3	4	5	6	7	8	9	10	11	12
67	O	Cl	H	H	H	1797 (0,40), 1780 (0,84), 1756 (0,57), 1744 (1)	1778 (0,33), 1749 (1)	2.26 2.55 3.38	4 4 4	1,7; 0,9 3,6; 0,9 3,6; 1,7	5-H 3-H 4-H
			(overtones)			3524 (0,92), 3501 (1), 3476 (0,70)					
68	O	Br	H	H	H	1780 (1), 1769 (0,68), 1746 (0,23)		2.16 2.51 3.39	4 4 4	1,8; 0,8 3,1; 0,8 3,1; 1,8	5-H 3-H 4-H
69	O	Cl	D	H	H	1787 (0,44), 1755 (1)	1781 (0,28), 1746 (1)	2.29 3.40	d d	1,8 1,8	5-H 4-H
			(overtones)			3522 (0,84), 3495 (1)					
70	O	Cl	H	D	H	1794 (0,25), 1766 (1), 1749 (0,58)	1759 (1), 1749 (0,83)	2.29 2.59	d d	0,8 0,8	5-H 3-H
			(overtones)			3513 (1), 3480 (0,83)					
71	O	Cl	H	H	D	1768 (1), 1753 (0,60)	1760 (1), 1753 (0,72)	2.59 3.41	d d	3,8 3,8	3-H 4-H
			(overtones)			3513 (1), 3470 (0,44)					
72	O	Cl	D	D	H	1795 (0,17), 1765 (1), 1748 (0,62)	1759 (1), 1746 (0,92)	2.29	s		5-H
73	O	Cl	D	H	D	1792 (0,12), 1768 (1), 1752 (0,60)	1759 (1), 1748 (0,86)	3.42	s		4-H
74	O	Cl	H	D	D	1792 (0,12), 1770 (1), 1755 (0,59)	1759 (1), 1749 (0,84)	2.60	s		3-H
			(overtones)			3518 (1), 3488 (0,78)					
75	O	Cl	D	D	D	1767 (1), 1753 (0,63)	1759 (1), 1749 (0,90)				
			(overtones)			3510 (1), 3475 (0,68)					
76	O	Cl	Br	H	H	1755	1749	2.36 3.28	d d	1,9 1,9	5-H 4-H
			(overtones)			3495 (1), 3473 (0,71)					
77	O	Cl	I	H	H	1750	1745	2.37 3.17	d d	1,8 1,8	5-H 4-H
78	O	Cl	H	Br	H	1795 (0,26), 1764 (1), 1747 (0,50)	1793 (0,14), 1756 (1), 1746 (0,31)	2.25	d	0,9	5-H
			(overtones)			3516 (1), 3478 (0,67)		2.54	d	0,9	3-H
79	O	Cl	H	Br	D	1812 (0,13), 1795 (0,19), 1768 (1), 1755 (0,43)	1761 (1), 1748 (0,19)	2.57	s		3-H
			(overtones)			3518 (1), 3480 (0,48)					
80	O	Cl	H	I	H	1794 (0,30), 1765 (1), 1748 (0,52)	1793 (0,20), 1755 (1), 1745 (0,34)	2.28	d	0,8	5-H

			(overtones)			3520 (1), 3484 (0,56)		2.50	d	0,8	3-H
81	O	Cl	H (overtones)	I	D	1768 (1), 1755 (0,57), 1738 (0,12) 3519 (1), 3482 (0,56)	1761 (1), 1747 (0,12)	2.51	s		3-H
82	O	Cl	H (overtones)	H	Cl	1807 (0,13), 1762 (1), 1745 (0,62) 3506 (1), 3474 (0,52)	1752	2.50 3.59	d d	3,6 3,6	3-H 4-H
83	O	Cl	H (overtones)	H	Br	1804 (0,16), 1762 (1), 1752 (0,20), 1744 (0,55) 3555 (0,26), 3505 (1), 3475 (0,56)	1801 (0,09), 1759 (0,38), 1748 (1)	2.66 3.46	d d	3,8 3,8	3-H 4-H
84	O	Cl	D (overtones)	D	Br	1776 (0,39), 1761 (1), 1746 (0,73) 3530 (0,94), 3509 (1), 3475 (0,59)	1758 (0,70), 1748 (1)				
85	O	Cl	H (overtones)	H	I	1802 (0,22), 1762 (1), 1745 (0,78) 3510 (1), 3476 (0,77)	1800 (0,11), 1754 (1), 1744 (0,85)	2.75 3.26	d d	3,5 3,5	3-H 4-H
86	O	Cl	H (overtones)	H	NO_2	1768 (1), 1750 (0,66) 3521 (1), 3486 (0,74)	1752 (1), 1742 (0,65)	2.41 2.59	d d	3,8 3,8	3-H 4-H
87	O	Cl	Br (overtones)	H	Br	1750 3482	1746	3.35	s		4-H
88	O	Cl	H (overtones)	Br	Br	1766 (1), 1747 (0,60) 3512 (1), 3476 (0,58)	1758 (1), 1746 (0,61)	2.57	s		3-H
89	O	Cl	H (overtones)	Br	Cl	1767 (1), 1748 (0,64) 3512 (1), 3478 (0,61)	1758 (1), 1748 (0,66)	2.54	s		3-H
90	S	Cl	H (overtones)	H	H	1759 (0,45), 1750 (1) 3511 (0,42), 3483 (1), 3450 (0,23)	1757 (0,51), 1743 (1)	2.07 2.17 2.82	4 4 4	4,0; 1,5 5,0; 1,5 5,0; 4,0	3-H 5-H 4-H
91	S	Cl	H	Br	H	1764 (0,22), 1751 (1)	1762 (0,28), 1749 (1)	2.08 2.27	d d	1,6 1,6	5-H 3-H
92	S	Cl	H	H	Br	1760 (0,56), 1746 (1)	1757 (0,54), 1744 (1)	2.37 2.90	d d	4,0 4,0	3-H 4-H
93	S	Cl	Br	H	Br	1768 (1), 1750 (0,29)	1766 (1), 1748 (0,67)	2.77	s		4-H
94[b]	O	F	H (overtones)	H	H	1828 (1), 1816 (0,54), 1807 (0,12) 3630 (1), 3610 (0,82)	1821 (1), 1812 (0,77)	2.26 2.62 3.39	8 8 8	2,5; 1,6; 0,8 3,6; 0,8; 0,6 3,6; 1,6; 0,8	5-H 3-H 4-H
95	O	F	H (overtones)	H	D	1828 (1), 1816 (0,64) 3637 (1), 3614 (0,70)	1818 (1), 1812 (–)[c]	2.65 3.41	4 4	3,8; 0,6 3,8; 0,9	3-H 4-H
96	O	F	D (overtones)	D	D	1830 (1), 1822 (0,71), 1814 (0,72) 3633 (1), 3609 (0,72)	1824 (–), 1815 (1)[c]				
97	O	F	H	H	Br	1828 (1), 1813 (0,61)	1819 (1), 1811 (0,63)	2.67[d] 3.46[d]	d 4	3,7 3,7; 0,8	3-H 4-H
98[b]	S	F	H	H	H	1813 (0,39), 1807 (1)	1808 (0,43), 1799 (1)	2.10 2.23 2.72	m m 8	 4,8; 3,9; 2,1	? 5-H ? 3-H 4-H

TABLE 7 (continued)

1	2	3	4	5	6	7	8	9	10	11	12
99[b]	S	F	H	Br	H	1818 (–), 1810 (1)[c]	1813 (–), 1803 (1)[c]	2.12 2.25	d 4	1,7 2,3; 1,7	3-H 5-H
100[b]	S	F	H	H	Br	1814 (0,48), 1805 (1)	1809 (0,75), 1797 (1)	2.25 2.74	d 4	4,1 4,1; 2,0	3-H 4-H
101[b]	S	F	Br	H	Br	1817 (1), 1793 (0,53)	1810 (1), 1788 (0,40)	2.75	d	3,0	4-H

[a] IR experimental details are given in Table 1. Very weak IR bands (<5% of the total absorption in a particular region) are not listed. For NMR signals other than singlets (s), doublets (d), triplets (t), and multiplets (m), the number of lines is indicated, and where appropriate the descriptions are followed by J values (Hz) or apparent J values.

[b] Positions (Φ* values, see Table 8) and form of ^{19}F signals (CCl_4 solutions at 308 K): (94), –15.2, broad d, J 2.2; (98), –23.5, distorted t, J 2.9 and 2.8; (99), –23.3, d, J 2.0; (100), –22.4, d, J 2.15; and (101), –32.0, d, J 3.0.

[c] Closeness of components prevents accurate curve resolution.

[d] In $CDCl_3$.

forms of furan-2-carbaldehyde [1]). Thus, it is not surprising that the ring proton signals of fluorides are not observed to coalesce. (The ^{1}H NMR data for furan-2-carbonyl fluoride is included in Table 8 to illustrate this point.) The ^{19}F results establish that solutions of the fluorides in trichloroflurومethane at 293 K contain appreciable amounts of each rotamer.

Infrared Studies. Carbon tetrachloride solutions of the fluorides show multiple IR absorptions (mostly doublets) in the carbonyl region (Table 7) [37]. Shifts (usually of 5-10 cm^{-1}) of the bands to lower wave numbers occur with all the fluorides when the solvent is

TABLE 8 [37]. Examinations over a Range of Temperatures [NMR signals. The positions (Φ^* values) of ^{19}F signals are shifts in ppm relative to CCl_3F. The coupling constants (J) and half-intensity widths ($\omega_{1/2}$) are in Hz. The form of resolved signals is shown (in parentheses) after the Φ^* values; the multiplicity of the other signals (broad and/or weak) is uncertain.]

Compound (94) in $MeCHCl_2$

^{1}H NMR spectra							^{19}F spectra^a			
T, K	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{3,F}$	$J_{4,F}$	$J_{5,F}$	T, K	Φ^*	J	$\omega_{1/2}$
308	3,62	0,78	1,74	0,47	0,75	2,39	303	−14,7 (d)	2,18	4,3
273	3,62	0,78	1,76	0,47	0,60	2,47	243	−14,5^c		16,0
243	3,62	0,78	1,76	0,46	0,49	2,62	218			
223	3,63	0,80	1,76	—^{b}	0,30	2,90$_b$	203	−13,3		18,0
188	3,64	^{b}	1,77	—^{b}	<0,2	—	183	−13,2 (d)^d	3,4	6,3
								−17,5		6,6

Compound (94), ^{19}F spectra (pulsed Fourier transform)

in CD_2Cl_2				in CCl_3F			
T, K	Φ^*	J	$\omega_{1/2}$	T, K	Φ^*	J	$\omega_{1/2}$
298	−14,6 (d)	2,05	4,4	297	−14,7 (d)	2,91	4,5
258	−14,4		12,4	193	−13,4		9,8
					−17,9		25,0
203	−13,3		10,2	183	−13,4 (d)^d	3,32	6,9
	−17,8		28,6		−17,9		6,9
183	−13,2 (d)^d	3,42	5,5				
	−17,8 (d)	3,08	5,5				

Compounds (97)-(101), ^{19}F spectra^a

Compound	T, K	Φ^*	$\omega_{1/2}$	Compound	T, K	Φ^*	$\omega_{1/2}$
97 in $MeCHCl_2$	293	−13,5	2,8	98 in CCl_3F	283	−23,8	4,5
	253	−13,0	30			(t., J∼2,7)	
	233c				273	−23,8	7
	193	−11,1^d	5		223	−23,9	45
		−17,7	17		193^c		
	183	−11,1^d	2,3		173	−20,5^d	13,5
		−17,7	8			−28,2	18
99 in CCl_3F	293	−23,0	3	100 in CCl_3F	293	−22,3	4,5
		(d, J=2,0)			243	−22,2	27
	223	−22,9	13		193^c		
	193^c						
	173	−21,0^d	30		∼168	−18,0^d	7
		−25,8	45			−28,5	9
	∼168	−21,0^d	15				
		−25,8	20				
101 in CCl_3F	293	−32,3	3,5				
		(d, J=2,4)					
	253	−32,6	7				
		(d, J=2,3)					
	223	−33,0	9				
	203	−33,2	18				
	173^c						

TABLE 8 (Continued)

IR C=O bands. The areas of the higher and lower wave number bands ($A_h + A_l$) = 100% at the lowest temperature shown for each solution [31].[a]

Solvent	T, K	91		92		93		95		98		99[e]		100		101	
		A_h	A_l	A_h	A_l	A_h	A_l	A_h	A_l	A_h	A_l	A_h	A_l	A_h	A_l	A_h	A_l
CCl_4	258	15	85	34	66	72	28	73	27	40	60	~40	~60	32	68	69	31
	303	16	78	35	63	69	21	65	26	44	53	~35	~55	30	62	59	31
	348	18	71	35	61	66	14	54	29	46	47	~33	~50	33	52	55	31
CCl_3F	173							80	20	41	59	~40	~60	35	65	77	23
	258[f]							70	25	42	55	~35	~55	32	55	60	25
	303							58	24	46	49	~33	~50	30	45	55	26

Percentages of Rotamers. ν_h is the form with the higher wave number C=O band (IR results), and Φ_h* that with the higher field ^{19}F signal (NMR results).

Compound	Solvent	T, K	ν_h	ν_l	Φ_h*	Φ_l*
(94) and (95) see text	CCl_3F	183	78	22	72	28
	CD_2Cl_2	183			84	16
	$MeCHCl_2$	183			80	20
98	CCl_3F	173	41	59	57	43
99	CCl_3F	173	~40	~60	63	37
100	CCl_3F	173	35	65	61	59

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[a] Continuous wave spectra (see text).

[b] Line broadening prevented measurement of J (but no coalescence implied).

[c] Signal too broad to be located

[d] The stronger of the two signals at this temperature.

[e] The closeness of the components prevents accurate curve resolution [39].

[f] Wave numbers of components: (95), 1829, 1817; (98), 1814, 1808; (99), 1819, 1812; (100), 1816, 1807; and (101), 1818, 1795.

changed from carbon tetrachloride to the more polar acetonitrile. Examination of three fluorides in the overtone region reveals doublets with the expected wave number separations. Further, the intensity values found in the variable-temperature IR study with fluoride (95) in carbon tetrachloride and in trichlorofluoromethane (Table 8) are consistent with the occurrence of an equilibrium between forms having only a small enthalpy difference. Nevertheless, Fermi resonance is not entirely dormant; it is manifest, for example, in the presence of a third band (at 1807 cm^{-1}) in the spectrum of furan-2-carbonyl fluoride (94), and presumably influences the intensity of the 1816 cm^{-1} band [cf. the 5-deutero-analogue (95)].

Although the occurrence of rotational isomerism has been established [6] with the furan compound (67), neither rotational isomerism nor Fermi resonance alone provides a satisfactory basis for interpreting the IR spectra of all the chlorides in Table 7. The simplest explanation of the four bands shown by furan-2-carbonyl chloride (67) is that rotamers are present and give separate bands which are each split by the resonance effect. Deuteration, notably at position 5 [17], is expected to inhibit or remove the resonance, and the doublets of compounds (69) and (71) may then be ascribed to rotamers. However, certain features are not easily rationalized by this interpretation; 4-bromo-5-deuterofuran-2-carbonyl chloride (79) has four bands, the positions of the higher wave number bands of the deutero-compounds (69)-(75) are surprisingly different, and while 3,5-dibromothiophen-2-carbonyl chloride (93) shows a doublet the corresponding furan compound (87) has only one band. (It may also be noted [19] that benzoyl chloride and all three monobromo derivatives give doublets, at least some of which must be the result of Fermi resonance.) With most of the chlorides, changing the solvent from carbon tetrachloride to acetonitrile causes a decrease in the relative intensities of the lower wave number bands which, assuming rotational isomerism, may be attributed to the rotamers having the lower dipole moments; there are, however, several chlorides which show the opposite behavior.

Despite the complications caused by the unpredictable incursion of Fermi resonance, certain trends emerge: Corresponding pairs of chlorides and fluorides (both within one heterocyclic series, and from the two series) show fairly consistent differences in band positions; the wave numbers shifts caused by changing the solvent are general, and substitution of halogen atoms at different ring positions produces changes in band positions similar to those observed (and discussed) previously with furan-2-carbaldehyde.

Correlation of NMR and IR Results. Interpretation of the spectra may be illustrated by the key compound, furan-2-carbonyl fluoride (94), which has been examined in most details.

No coalescence phenomenon is observed in the ^{1}H (in $MeCHCl_2$, Table 8) or ^{13}C (in CD_2Cl_2) NMR spectra [40] of furan-2-carbonyl fluoride at temperatures down to $\sim$190 K; however, the critical changes which do occur as temperatures decrease are the gradual decrease of the 4-H—F coupling and the gradual increase of the 5-H—F coupling, and the gradual appearance of a long-range 2-C—F coupling which is absent in the room-temperature spectra. The carbon-13 result is explained by assuming that the syn- and anti-forms have $J_{2,C-F}$'s of opposite sign which are fortuitously balanced to about zero at room temperature in CD_2Cl_2. Thus, the equilibrium shifts in favor of the rotamer in which the main fluorine coupling is to 5-H. That this isomer is already predominant at room temperature is established by comparing the J_{H-F} values at 308 K with those of the individual rotamers at low temperature (the latter being obtained from the ^{19}F spectra since, as noted earlier, there is no coalescence in the ^{1}H NMR spectra). The variable-temperature ^{19}F spectra (also in $MeCHCl_2$) then show that this predominant rotamer is the one having the higher field (stronger) ^{19}F signal; at room temperature the chemical shift of the weighted average signal is close to that of this isomer. Although the main ^{19}F signal of the low-temperature spectra is a doublet, examination by the continuous wave NMR method does not reveal the form of the weaker signal. The compound has thus been studied using pulsed Fourier-transform NMR (which gives a more favorable signal-to-noise ratio), and in one solvent (dichlorodideuteromethane) both ^{19}F signals appear as doublets. (For further development of the interpretation it is important to note that the three nonpolar solvents used for the NMR work lead to similar values for the rotamer proportions at low temperature as shown in Table 8. In dideuterodichloromethane the F—H coupling observed as a weighted average in the room-temperature ^{19}F spectrum is significantly lower than either of the individual rotamers' F—H couplings determined at low temperature. It may be that this situation arises from the intrinsic temperature dependence of coupling constants; alternatively, the individual J_{F-H} values may be of opposite sign.) If, as has been suggested [41], the W rule established for H—H couplings in heterocyclic systems [2, 3] also applies to H—F couplings, the predominant isomer (with the 5-H—F coupling) must be the syn-rotamer. The lower J value of the minor (anti-) zigzag-coupled 4-H—F rotamer shows the transmission through the W system to be less effective when the heteroatom is not involved. These correlations do not necessarily hold with the other acid fluorides in Table 8 (examined by continuous-wave NMR only, and consequently with uncertain multiplicities for their low-temperature ^{19}F signals), but the overall resemblance in NMR behavior between these compounds and the key fluoride (94) suggests a common pattern of rotational isomerism.

Since Fermi resonance renders furan-2-carbonyl fluoride (94) unsuitable for detailed IR work, the 5-deutero-analogue (95), which has a well-resolved doublet, has been used for variable-temperature work. (There can be little, if any, difference between the conformational preferences of these two compounds.) The variation in the relative intensities of the components shows that the rotamer with the higher wave number C=O band is the one which [in compound (94)] has the higher field ^{19}F signal. However, this does not apply generally; with three fluorides in Table 8 the higher wave number C=O rotamer has the lower-field ^{19}F signal.

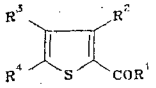
The gratifying agreement in the proportions of rotamers as determined for several fluorides by ^{19}F NMR and IR techniques (shown in the last section of Table 8) may be fortuitous in view of the experimental difficulties and the assumption made in the IR calculations that pairs of rotamers have equal integrated absorption coefficients [31].

THIOPHENES

1. 2-Aldehydes

Thiophene-2-carbaldehyde has been examined by several physical methods in attempts to define its conformation under various conditions [42]. The observation of twin carbonyl bands in the Raman spectrum of the neat liquid was ascribed to intermolecular association [43], whereas the results of ultrasonic studies were interpreted in terms of an equilibrium between rotational isomers [44]. Dipole moment measurements of a solution in benzene suggested the presence of only one form, the syn-rotamer [45, 46], but microwave examination of the aldehyde in the vapor phase indicated an exclusive preference for the anti-conformation [7, 47]. (The apparent conflict between these claims may be illusory, as explained in a similar case [5].) The gradual accumulation of results from ^{1}H NMR studies [4, 20, 23, 48, 49] has proved conclusively that solutions in solvents such as acetone and deuterochloroform contain exclusively, or very predominantly, the syn-form of the aldehyde. While the anti-

TABLE 9 [42]. Series of Thiophene-2-Aldehydes[a]



Aldehyde	R¹	R²	R³	R⁴	Solvent	T, K	Band A	Band B	Band C	Band other
1	2	3	4	5	6	7	8	9	10	11
Fundamental region										
102	H	H	H	H	CCl_4	258	1687 (49,5)	1676 (35)	1659 (7)	1707 (2,5), 1683 (6)
					CCl_4	303	1688 (62)	1677 (29)	1659 (5,5)	1708 (2,5), 1683 (1)
					MeCN	303	1688 (23,5)	1676 (50)	1663 (26,5)	
103	H	D	H	H	CCl_4	258	1685 (80)		1669 (20)	
					CCl_4	303	1687,5 (80)	1679 (6)	1669,5 (14)	
					MeCN	303	1682 (37,5)	1677 (3,5)	1670 (59)	
104	H	H	D	H	CCl_4	258	1687 (64)	1680 (13)	1670 (23)	
					CCl_4	303	1689 (74)	1681 (7,5)	1670,5 (19,5)	
					MeCN	303	1684 (42)	1677 (8,5)	1668 (49,5)	
105	H	H	H	D	CCl_4	258	1683,5 (86)	1670 (8)	1659,5 (6)	
					CCl_4	303	1685,5 (88)	1671,5 (6,5)	1657,5 (8,5)	
					MeCN	303		1678 (70,5)	1660,5 (29,5)	
106	D	H	H	H	CCl_4	258	1687,5 (20)	1672,5 (42)	1659,5 (22)	1653,5 (16)
					CCl_4	303	1687 (21)	1673 (52)	1659 (16)	1653,5 (11)
					MeCN	303		1673,5 (22)	1657,5 (36)	1645,5 (36)
107	H	Br	H	H	CCl_4	258	1690 (24,5)	1672,5 (75,5)		
					CCl_4	303	1690,5 (31)	1673 (69)		
					$CHCl_3$	303	1690 (15)	1667,5 (85)		
108	H	Br	H	D	CCl_4	258	1688,5 (26)	1671 (74)		
					CCl_4	303	1687 (37)	1672 (63)		
					MeCN	303	1688 (16)	1666 (84)		
109	D	Br	H	H	CCl_4	258		1654 (100)		
					CCl_4	303		1655 (100)		
					MeCN	303		1649,5 (100)		
110	H	I	H	H	CCl_4	258	1685 (39)	1669,5 (61)		
					CCl_4	303	1685 (52,5)	1670,5 (47,5)		
					MeCN	303	1685,5 (18)	1665 (82)		
111	H	H	Br	H	CCl_4	258	1689 (73)	1673 (27)		
					CCl_4	303	1690 (80)	1673,5 (20)		
					MeCN	303	1686 (47)	1673 (44,5)		1712 (8,5)
112	H	H	Br	D	CCl_4	258	1690 (100)			
					CCl_4	303	1691,5 (100)			
					MeCN	303	1681 (100)			
113	H	H	I	H	CCl_4	258	1687 (82)	1671 (18)		
					CCl_4	303	1689 (87)	1671,5 (13)		
					MeCN	303	1682,5 (60)	1670 (40)		
114	H	H	H	Br	CCl_4	258		1678 (100)		
					CCl_4	303	1687 (13)	1680,5 (87)		
					$CHCl_3$	303	1677,5 (4)	1670,5 (96)		
115	H	D	H	Br	CCl_4	258	1689,5 (3)	1678 (82,5)		1699,5 (14,5)
					CCl_4	303	1690,5 (5,5)	1680 (77)		1698,5 (17,5)
					MeCN	303		1671 (100)		
116	D	H	H	Br	CCl_4	258	1682 (18)	1662 (82)		
					CCl_4	303	1682,5 (21)	1663 (79)		
					MeCN	303		1655 (100)		
117	H	H	H	I	CCl_4	258	1684,5 (26)	1676 (74)		
					CCl_4	303	1685,5 (39)	1677,5 (61)		
					$CHCl_3$	303		1670 (100)		
118	H	Br	H	Br	CCl_4	258		1673 (100)		
					CCl_4	303		1674 (100)		
					MeCN	303		1668 (100)		
119	D	Br	H	Br	CCl_4	258	1686 (11)	1670 (10)	1650 (79)	
					CCl_4	303	1686 (12)	1670 (9)	1651,5 (79)	
					MeCN	303	1685 (9)	1669 (6)	1648 (85)	

TABLE 9 (continued)

1	2	3	4	5	6	7	8	9	10	11
120	H	H	Br	Br	CCl_4	258		1684 (100)		
					CCl_4	303		1685 (100)		
					MeCN	303		1676 (100)		
121	H	Br	Br	Br	CCl_4	258		1675 (100)		
					CCl_4	303		1676,5 (100)		
					MeCN	303		1670,5 (100)		
Overtone region										
102	H	H	H	H	CCl_4	303		3355 (0,87), 3343 (1)		
106	D	H	H	H	CCl_4	303		3320 (1), 3305 (0,88)		
109	D	Br	H	H	CCl_4	303		3294		
116	D	H	H	Br	CCl_4	303		3333 (0,50), 3310 (1)		
119	D	Br	H	Br	CCl_4	303		3319 (0,45), 3289 (1)		
121	H	Br	Br	Br	CCl_4	303		3336		

[a] IR experimental details are given in Table 1. The groupings of bands under the headings A, B, and C are made on the basis of their wave numbers and are not intended to imply common vibrational origins.

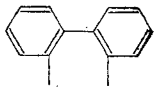
form could not be detected in the ^1H NMR work, the occurrence of an equilibrium between rotamers has been established by ^{13}C NMR spectrometry (the C-3 resonance of thiophene-2-carbaldehyde in nonpolar solvent broadens with decrease in temperature to a maximal value of 198 K and then sharpens to resume its original height at ∿283 K [6]).

Solutions of thiophene-2-carbaldehyde show multiple absorptions in the IR carbonyl region [8, 9, 50, 51]. Initial work [8] excluded intermolecular association and the occurrence of a "hot transition" as the cause of the band splitting [52]. At that time, before definitive NMR investigations, it seemed reasonable to correlate the components of the doublet with two rotameric forms, although the supposed enthalpy difference between these (7400 J mole^{-1}) was surprisingly high. Soon afterwards, Andrieu et al. [50] concluded, from examinations of the derived 2-^{2}H- and ^{18}O-aldehydes, that the doublet arose from the operation of Fermi resonance, and acceptable resonance parameters were calculated on this basis [51]. However, there were some disturbing aspects (e.g., the doublet nature of the ^{18}O-aldehyde's absorption [50]) and it seemed desirable to obtain conclusive evidence for the Fermi resonance explanation.

The basic features of our investigation, as in the similar work on furan-2-carbaldehyde [17], are the examination of a series of deuterated and halogenated analogues prepared for this purpose [15, 16, 18]. The IR background discussed earlier under furan-2-carbaldehyde [17] is assumed.

Although rigorous analysis of the absorption of thiophene-2-carbaldehyde (102) in carbon tetrachloride reveals five bands in the C=O fundamental region, two (listed under "other bands" in Table 9) are very weak and in essence the spectrum comprises three bands, A, B, and C; of these the more intense components, A and B, constitute the "doublet" described in the literature [8, 9, 50, 51]. The spectra of the 3-, 4-, and 5-deutero-compounds [aldehydes (103)-(105)] are much simpler, since each has a main absorption (band A) with lower wave number components whose intensities decrease markedly as the temperature is raised. Increasing the dielectric constant of the solvent has a dramatic effect with aldehydes (102)-(106); the main absorptions are at lower wave numbers (bands B or C), and the spectra of the deutero-compounds become more complex. These results by themselves establish that the multiplet of the parent aldehyde (102) originates in Fermi resonance. Further, since deuteration in the thiophene ring will not have an appreciable effect on the position of an aldehyde's C=O stretching vibration [17], the "true" C=O band of thiophene-2-carbaldehyde in carbon tetrachloride solutions is at ∿1687 cm^{-1}. Inspection of the deutero-compounds' spectra shows that the resonance is most effectively inhibited by deuteration at position 5, though the differences between the effects of deuteration at different ring positions are less marked than is the case with furan-2-carbaldehydes [17]. The overtone region of thiophene-2-carbaldehyde (102) shows two bands (cf. the reported single band [50]), of which only the higher wave num-

TABLE 10 [57]. C=O Absorptions of Alkyl Thiophene-2-Carboxylates

Ester	R^{1}	R^{2}	R^{3}	R^{4}	ν_{CO}, cm^{-1}						
					fundamental region				overtone region		
					CCl$_4$	CCl$_4$	MeCN	MeCN	CCl$_4$	CCl$_4$	ΔH° (CCl$_4$)
122a	Me	H	H	H	1721		1711		3422		
*122*b	Et	H	H	H	1717		1708				
*122*c	*t*-Bu	H	H	H	1710		1700		3422		
123a	Me	H	H	D	1721		1711		3444		
*123*c	*t*-Bu	H	H	D	1708		1699				
124a	Me	Me	Me	H	1714		1708 (62)^{a}	1697 (38)^{a}	3421		
*124*b	Et	Me	Me	H	1710		1703 (57)^{a}	1690 (43)^{a}			
*124*c	*t*-Bu	Me	Me	H	1705 (77)	1693 (23)	1698 (52)^{a}	1683 (48)^{a}			
125a	Me	Ph	Ph	H	1728 (60)	1702 (40)	1723 (60)^{a}	1697 (40)^{a}			2700
*125*b	Et	Ph	Ph	H	1723 (53)	1698 (47)	1717 (55)^{a}	1690 (45)^{a}	3436 (62)	3382 (38)	3100
*125*c	*t*-Bu	Ph	Ph	H	1719 (39)	1694 (61)	1712 (35)^{a}	1683 (65)^{a}			1200
126a	Me	Ar^{b}	Ar^{b}	H	1728 (62)	1700 (38)	1718 (70)^{a}	1692 (30)^{a}			1200
*126*b	Et	Ar^{b}	Ar^{b}	H	1722 (58)	1696 (42)	1715 (60)^{a}	1686 (40)^{a}	3435 (60)	3379 (40)	3800
*126*c	*t*-Bu	Ar^{b}	Ar^{b}	H	1716 (44)	1691 (56)	1711 (42)^{a}	1681 (58)^{a}			2100
127a	Me			H	1719		1710				800
128a	Me	Br	H	H	1734 (58)	1709 (42)	1725 (73)	1703 (27)	3447 (54)	3398 (46)	300
*128*b	Et	Br	H	H	1727 (56)	1703 (44)	1720 (70)	1697 (30)			1500

*128*c	*t*-Bu	Br	H	H	1720 (37) 1726 (19)[c]	1698 (44)	1712 (50) 1723 (12)[c]	1691 (38)	3418 (45)	3376 (55)	
129a	Me	H	Br	H	1724		1719				
*129*b	Et	H	Br	H	1719		1713				
*129*c	*t*-Bu	H	Br	H	1711		1705				
130a	Me	H	H	Br	**1724** (68)	**1716** (32)	**1721** (43)	**1711** (57)	**3428** (75)	**3411** (25)	3700
*130*c	*t*-Bu	H	H	Br	**1713** (64)	**1704** (36)	**1708** (60)	**1696** (46)			2400
131a	Me	Br	H	Br	1735 (64)	1707 (36)	1728 (75)	1702 (25)	3449 (65)	3396 (35)	3400
*131*b	Et	Br	H	Br	1730 (63)	1702 (37)	1724 (75)	1698 (25)	3440 (60)	3384 (40)	2500
*131*c	*t*-Bu	Br	H	Br	1726 (48)	1697 (52)	1718 (66)	1693 (34)	3431 (51)	3376 (49)	2300
132a	Me	H	Br	Br	**1728** (62)	**1720** (38)	**1726** (42)	**1715** (58)			
*132*b	Et	H	Br	Br	**1723** (66)	**1712** (34)	**1720** (58)	**1707** (42)	**3430** (70)	**3408** (30)	
*132*c	*t*-Bu	H	Br	Br	**1719** (60)	**1705** (40)	**1714** (54)	**1700** (46)	**3418** (50)	**3398** (50)	3400
133a	Me	Br	Br	Br	1738 (63)	1708 (37)	1732 (75)	1705 (25)	3460 (60)	3400 (40)	2700
*133*b	Et	Br	Br	Br	1733 (63)	1704 (37)	1729 (70)	1700 (30)	3451 (56)	3386 (44)	1500
*133*c	*t*-Bu	Br	Br	Br	1729 (54)	1700 (46)	1724 (70)	1695 (30)	3442 (51)	3377 (49)	1100
134a	Me	H	H	NO_2	**1732** (83)	**1724** (17)	**1731** (59)	**1720** (41)	3451 (80)	3430 (20)	
*134*b	Et	H	H	NO_2	**1728** (85)	**1718** (15)	**1726** (62)	**1713** (38)	3440 (85)	3422 (15)	
*134*c	*t*-Bu	H	H	NO_2	**1721** (73)	**1712** (27)	**1718** (65)	**1706** (35)	3426 (81)	3412 (29)	
135a	Me	H	NO_2	Br	1735 (55)	1723 (45)	1732 (54)	1719 (46)	3459 (50)	3433 (50)	−800
*135*b	Et	H	NO_2	Br	1732 (54)	1719 (44)	1728 (53)	1713 (47)	3446 (55)	3422 (45)	−800
*135*c	*t*-Bu	H	NO_2	Br	1725 (52)	1710 (48)	1719 (64)	1705 (36)	3432 (51)	3408 (49)	−1500

[a] $CHCl_3$ (not MeCN) as solvent. [b] Ar = p-MeO·C_6H_4. [c] Fermi resonance (see text).

TABLE 11 [57]. Comparison [70] of the Ethyl Esters (122b) and (131b) with the Lactone (136)

Compound	T, K	ν_{CO}, cm^{-1}					
		fundamental region				overtone region	
		CCl$_4$	CCl$_4$	MeCN	MeCN	CCl$_4$	CCl$_4$
*122*b	258	1715 (100)		1708 (100)		3413 (100)	
	303	1717 (91)					
	348	1718 (84)					
*131*b	258	1728 (66)	1700 (34)	1724 (75)	1698 (25)	3440 (60)	3384 (40)
	303	1730 (54)	1702 (31)				
	348	1731 (49)	1704 (30)				
136 [71]	258	1733 (71)	1719 (29)	1729 (33)	1712 (67)	3444 (100)	
	303	1735 (68)	1719 (19)				
	348	1736 (65)	1719 (9)				

ber band (3355 cm^{-1}) can be related to the fundamental (1688 cm^{-1}) if an acceptable anharmonicity constant (0.0061) is to be obtained.

Although deuteration of a compound exhibiting Fermi resonance often simplifies the spectrum, the IR C=O absorption of the 2-[^{2}H]aldehyde (106) is compounded of four bands. Deuteration in the aldehyde group is expected to lower the "true" C=O stretching frequency by ~15 cm^{-1}: this has the effect of bringing the C=O band into a potition suitable for more extensive resonance involving at least two other modes. Correlation of the fundamental (~1673 cm^{-1} in carbon tetrachloride) with the higher wave number overtone (3320 cm^{-1}) gives an anharmonicity constant of 0.0076.

Since five of the halogenated aldehydes in Table 9 [(107), (110), (111), (113), and (114)] are known from ^{1}H NMR work [20, 23] to have a marked preference for the syn-conformation under a range of conditions, the observed multiple absorptions cannot be ascribed to rotational isomerism. Comparisons within the various structural types provide independent evidence against such an interpretation and establish that Fermi resonance is again the cause. Thus, for example, the 5-bromoaldehyde (114) has two C=O bands at 303 K (A and B, Table 9), the 5-bromo-2-[^{2}H]aldehyde (116) has two bands whose intensities do not exactly parallel those observed in the protio-compound, and the 5-bromo-3-deuteraldehyde (115) has three bands. Also, although the 4-bromoaldehyde (111) has two C=O bands, the 5-deuterated analogue (112) has only a single band.

The notion that deuteration does not necessarily simplify a spectrum is further illustrated by comparing, for example, the 3,5-dibromoaldehyde (118) with its 2-deuterated companion (119). Indeed, with thiophene-2-carbaldehydes bromination is sometimes more effective than deuteration for spectrum simplification. When two or three bromine substituents are present, Fermi resonance is no longer rampant; the C=O vibrations are seen clearly and their positions may be interpreted along the usual lines. The results, together with those of the monobrominated compounds, show that the position (in cm^{-1}) of the C=O stretch is appreciably decreased, slightly decreased, and slightly increased by a bromine substituent at positions 3, 5, and 4 respectively. These trends are in agreement with the expected variations in the inductive and mesomeric effects of bromine at different sites: there is also the implication that, at least in the 3-bromoaldehydes, there is no significant proportion of the anti-forms since this would lead to higher carbonyl wave numbers by a dipolar field effect [19].

2. 2-Carboxylic Esters

Several series of thiophene-2-carboxylic esters (methyl, ethyl, and t-butyl) containing a variety of nuclear substituents (deutero, alkyl, aryl, bromo, and nitro) have been prepared [53-55, 18, 28] and analyzed [56] for the presence of rotational isomerism by IR spectrometry (the only work previous to this reported a single carbonyl band in the IR spectrum of ethyl thiophene-2-carboxylate [57]). The results are presented in Tables 10 and 11.

Most of the esters show doublets in the carbonyl region which do not arise from intermolecular association or hot transitions. Fermi resonance occurs in one ester (128c) which has three bands, but this effect is also excluded as the general cause of band doubling. [The lactone [28] (136), which serves as a "fixed conformation ester," provides a clear example of band doubling due to Fermi resonance; its spectrometric characteristics (see Table

11) are in marked contrast to those of typical thiophene esters.] The results in Table 11 (comparison of fundamental and overtone regions, the effect of changing solvent dielectric, and the temperature variation of the relative areas of the doublets' components as reflected in the enthalpy differences) establish that the doublets are a consequence of rotational isomerism between, very probably, the syn-s-trans- and anti-s-trans-forms (see Scheme 2).

Scheme 2

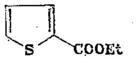
anti-s-trans syn-s-trans

Esters (a-c) *128, 130—135* and (less certainly) *125, 126* — doublets, anti-s-trans (higher wave number), syn-s-trans (lower wave number)

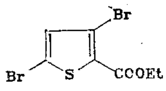
Ester 129a: single band, syn-s-trans
Ester 127a: single band, anti-s-trans

Correlation of the doublet components with particular forms can be approached in several ways, but the bromo-esters appear to be the most amenable to interpretation.

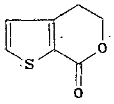
As bromine substituents are introduced into the thiophene nucleus there is a general, usually small, increase in the carbonyl wave number. However, superimposed on this are distinct effects which are characteristic of the position of substitution. The differences are exemplified by comparing the monobromo methyl esters (128a, 129a, and 130a): The 5-bromo-ester (130a) shows a doublet with a separation between components of 8 cm^{-1}, the 4-bromo-ester (129a) a singlet, and the 3-bromo-ester (128a) a doublet with a big separation (25 cm^{-1}) arising from displacement of the components to unusually high and low wave number. It seems most likely that a direct field effect is responsible for the displacement of the 3-bromo-ester (128a) and suggests, as in the furan case, that the higher wave number component arises from the anti-form where the C—Br and C=O dipoles are almost parallel (see Scheme 1). This assignment is also applied to the less well-separated components of the 5-bromo-ester (130a) since a reversed correlation would necessitate an unacceptably large shift by the field effect in the 3-bromo-isomer. Common assignments for the bands of the 3- and 5-bromo-esters are confirmed by the solvent effects. As expected, the anti-form (higher wave number) is the more polar (and, therefore, more favored in acetonitrile) with the 3-bromo-compound (128a), but the less polar (less favored) with the 5-bromo-isomer (130a). Although the single bands of the 4-bromo-esters (129a-c) could be the superimposed absorptions of the rotamers, the probability of such a coincidence appears to be reduced by the presence of a halogen substituent in the 2-oxo-furan system [17, 27]. On passing from a particular form of a 5-bromo-ester (—I, +M effects of Br) to the corresponding form of a 4-bromo-compound (—I effect only) an increase of wave number is to be expected. The observed results (Table 10) suggest that the 4-bromo-esters exist predominantly in one form, and that this is the syn rotamer.



122b



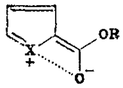
131b



136

The carbonyl absorptions of the tribromo-esters (compounds 130a-133c) and the nitro- and bromo-nitro-esters (134a-135c) are in consonance with the forgoing analysis (bearing in mind the different mesomeric properties of Br and NO_2 groups).

The higher wave number components of the 3,4-diaryl-esters (125a-126c) are correlated, as with the bromo-esters, to the anti-forms. [Ester (127a), which shows a single band attributed to the anti-form, differs from the other 3,4-diaryl compounds in that strain cannot be relieved by out-of-plane twisting of the substituents: Destabilization of the syn-form of this ester would probably result from the close proximity of the methoxy group to the ortho position of the aromatic ring at position 3.] Ironically, the results of the simplest esters (122a-124c), none of which show well-resolved doublets, are the most difficult to interpret. The single bands could encompass absorptions of two forms; even if only one form is present the positions of the bands do not reveal its identity.



A comparison of thiophene and furan esters shows that the structural features leading to band doubling differ in the two series: the higher wave number components of thiophene esters' doublets arise from the anti-forms, whereas those of furan compounds are associated with syn-rotamers. Although it does not seem possible to distinguish clearly between the many factors which may underlie this difference, a rationalization emerges from consideration of the consequences of mesomerism in the syn-forms. This effect brings the negatively charged acyl oxygen into the vicinity of the positively charged hetero-atom. It has been suggested [58, 59] that the development of positive charge (in the ground state) on the hetero-atom is more favorable with thiophene than with furan; consequently, in the syn-form of a thiophene ester the extent of mesomerism would be enhanced by the favorable $S^+...O^-$ interaction, and the C=O wave number would be lowered. However, the magnitude of this interaction does not appear to be large enough to have a marked effect on the relative stabilities of the forms; with the exception of the bromo-nitro-thiophene esters (135a-c) the anti-forms are the thermodynamically more stable rotamers in the two series.

3. 2-Carbonyl Halides

The discussion of IR and NMR spectra data of thiophene-2-carbonyl halides follows similar lines to that given under furan halides. The variable temperature ^{19}F NMR results [37] (Table 8) provide strong evidence for the presence of rotational isomerism [cooling the solutions results in signal broadening and, in three of the four fluorides, compounds (98)-(100), the appearance of two ^{19}F NMR signals; with the fourth, compound (101), the disappearance occurs at only the lowest obtainable temperature], while the IR carbonyl spectral doublets [37] (Table 7) are correlated, by the arguments given in the furan case, with individual rotamers.

N-PROTIO- AND N-ALKYLPYRROLES

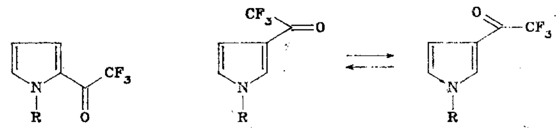
1. 2-Aldehydes and 2-Ketones

Pyrrole-2-carbaldehyde has twin carbonyl peaks in the IR spectrum (1664 and 1654 cm^{-1}, carbon tetrachloride solution) which arise from a monomer—dimer equilibrium [60-62]. Thermodynamic parameters are calculated by the IR method [8] to be ΔH° —295 $kJ\cdot mole^{-1}$ and ΔS° —64 $J\cdot K^{-1}\cdot mole^{-1}$.

N-Methylpyrrole-2-carbaldehyde has been shown by ^1H NMR techniques to have K ([syn]/[anti]) = 22 at 213 K and K = 9 at 303 K [21, 2]. The ^{13}C NMR spectrum of this compound in nonpolar solvent shows broadening, but no splitting of the signals, with decrease in temperature: The C-3 resonance (cf. thiophene-2-carbaldehyde) broadens to a maximal value at 253 K and then sharpens to resume its original height at 223 K [6]. Thus, although the N-methyl-2-carbaldehyde exists very largely in the syn-conformation (from the ^1H NMR results) over the whole temperature range, the ^{13}C results still demonstrate the occurrence of rotational isomerism.

The conformational preferences of eleven trifluoroacetylpyrroles have been investigated by IR and NMR (^1H and ^{19}F) techniques [63] and the results collected in Table 12. A solution in carbon tetrachloride of the simplest compound [(137), R = H] shows two bands in the CO region, and the most obvious interpretation is that the lower wave number band (at 1671 cm^{-1}) arises from intramolecular N—H...O=C bonding. However, variable concentration experiments (second section of Table 12) exclude this possibility: Association does occur at certain concentrations, but it is intermolecular in nature (CO band at 1647 cm^{-1}) and the 1671 cm^{-1} band probably arises from the incursion of Fermi resonance. The result that all the other trifluoroacetyl compounds (in carbon tetrachloride) give only single CO bands does not require them to exist in one preferred conformation. Similarly, the absence of a temperature effect on the ^1H NMR spectra (Table 13) does not exclude the possibility of there being appreciable amounts of easily converted rotamers with very similar ^1H signals. However, the ^{19}F NMR results (Tables 13 and 14) do give clear evidence about the conformational situations: The 2-trifluoroacetyl compounds adopt one conformation, either predominantly or exclusively, whereas the 3-isomers exist as mixtures of two forms. (These forms, which appear to differ little in enthalpy, are present in a ratio of ∿3:1, but it is not known whether the major component has the syn- or the anti-N,O arrangement. Since neither involve close proximity of the carbonyl oxygen and ring nitrogen atoms it is not surprising that their C=O bands are at about the same position.) The preferred conformation of 1-methyl-2-trifluoroacetylpyrrole [(137), R = Me] is established by the nuclear Overhauser enhancement experiment (Table 15) to be the syn-form, and since there is strong similarity between the spectra

TABLE 12 [63]. Spectra and Conformations of Trifluoroacetylpyrroles[a]



137 syn 138 syn 138 anti

Compound	IR spectra, ν_{CO}, cm^{-1}		^{19}F NMR, ppm, in $CDCl_3$
	CCl_4	MeCN	
137, R=H	1683 (60) 1671 (40)	1670	−3,1, d, *J*=2,2 Hz
137, R=Me	1680	1673	−4,0, d, *J*=2,1 Hz
137, R=Et	1680	1669	−4,4, d, *J*=2,1 Hz
137, R=*n*-Pr	1681	1672	−4,2, d, *J*=2,0 Hz
137, R=*i*-Pr	1678	1669	−4,5, d, *J*=2,2 Hz
137, R=Ph	1688	1686 (20); 1677 (80)	−4,0, d, *J*=2,0 Hz
137, R=*p*-$MeOC_6H_4$	1689	1681	−4,0, d, *J*=2,2
137, R=*p*-$NO_2C_6H_4$	1697	1682	−3,8, d, *J*=1,9
138, R=*i*-Pr	1690	1682	−2,1, 3 lines, *J*=1,0 and 0,9 Hz
138, R=*t*-Bu	1698	1686	−2,1, 3 lines, *J*=1,0 and 0,9 Hz
138, R=1- Adamantyl	1696	1686	−2,5, 3 lines, *J*=1,1 and 0,9 Hz
137, R=H in CCl_4	ν_{NH}		ν_{CO}
15 mg/ml	3448 (35), 3318 (65)		1683 (32), 1671 (20), 1647 (48)
1,5 mg/ml	3448 (65), 3318 (35)		1683 (34), 1671 (30), 1647 (26)
0,10 mg/ml	3448		1683 (60), 1671 (40)

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[a] IR experimental details are given in Table 1. ^{19}F NMR spectra were recorded at an irradiation frequency of 84.6 MHz; the positions of signals are ppm from external trifluoroacetic acid, coupling constants (J) are in Hz, and, unless stated otherwise, solutions in $CDCl_3$ were examined at 303 K with trifluoroacetic acid as external standard.

TABLE 13 [63]. Effect of Temperature Variation (303 K → 195 K) on NMR Signals of Solutions in $(CD_3)_2CO$

Compound	^1H Signals	^{19}F Signals
137, R=H	No change	No change
137, R=Me	" "	" "
138, R=*t*-Bu	" "	Signal at −2,2 — two signals at −2,0 and −3,1
138, R=1-Adamantyl	" "	Signal at −2,5 — two signals at −2,3 and −3,2

TABLE 14 [63]. ^{19}F Signals (of Solutions in CD_3OD) Decoupled by Irradiation of 2-H and 4-H

Compound	*T*, K	No. of signals	Signal areas (%) at 195°K		Coalescence temp., K
			low field	high field	
138, R=*t*-Bu	203	2	72	28	208
	210	1			
138, R=1-Adamantyl	208	2	73	27	212
	216	1			

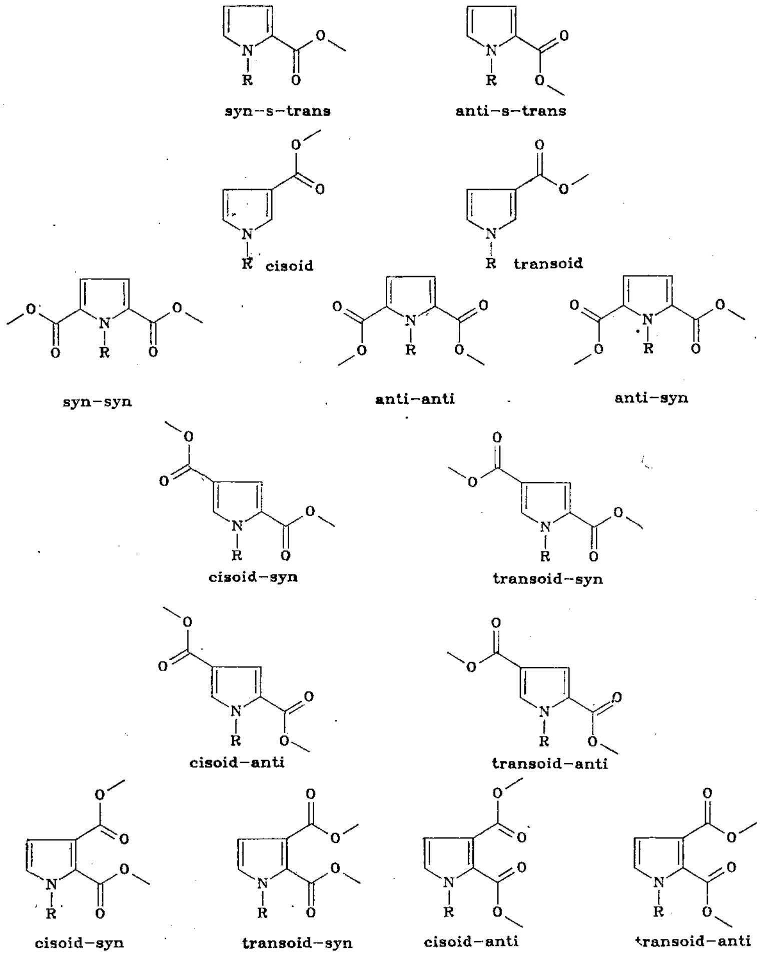
of the series of 2-isomers it is reasonable to assume that they all adopt this arrangement. Comparison with the literature shows that trifluoroacetyl- and acetylpyrroles are alike in their conformational propensities: The 2-acetyl compounds, whether N-substituted or not, have a strong preference for the syn-form [64], and 1-t-butyl-3-acetylpyrrole exists as a 3:1 mixture (in which the main form is known to be the anti rotamer) [65].

TABLE 15 [63]. Effect of H-Irradiation on ^{19}F Signal of (137), R = Me in $CDCl_3$ Containing C_6F_6 at 303 K

H-irradiated	Ratio of ^{19}F signal areas
—	1,50
3-H	1,78 (gated)
	1,84 (not gated)
N—CH_3	1,50 (gated)
	1,55 (not gated)

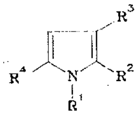
2. 2-Carboxylic Esters

Infrared Studies. The positions of the IR carbonyl fundamental and overtone absorptions for 19 N-alkylpyrrole 2- and 3-mono-, and 2,3-, 2,4-, and 2,5-diesters are presented in Table 16 [66], while their possible conformations are shown below:



2-Methoxycarbonyl-N-alkylpyrroles (139)-(143) display essentially singlet carbonyl bands in the fundamental region. The band asymmetry in esters (141)-(143) may be a consequence of Fermi resonance, since change of solvent from carbon tetrachloride to acetonitrile removes the asymmetry. By contrast, the 2-alkoxycarbonyl-furans discussed previously display well-separated IR carbonyl doublets [27] (separation ∿30 cm^{-1}) arising from rotational isomerism between syn-s-trans and anti-s-trans forms: The relative intensities of the doublet component bands are only slightly affected by change of solvent dielectric constant. It seems unlikely, therefore, that syn and anti conformers in the N-alkylpyrrole analogues would have essentially the same carbonyl absorption frequencies, and it follows that 2-mono-esters of N-alkylpyrroles exist in solution in only one form, probably syn-s-trans, syn being the preferred conformation of N-alkylpyrrole-2-carbaldehydes and of certain -2-ketones [63].

TABLE 16 [66]. N-Alkylpyrrole Esters (experimental details in Table 1)



Compound	R^1	R^2	R^3	R^4	$\nu_{CO}\cdot cm^{-1}$					
					fundamental region				overtone region CCl_4	
					CCl_4		MeCN			
139	CH_3	CO_2CH_3	H	H	1713		1709		3409	
140	C_2H_5	CO_2CH_3	H	H	1712		1707		3414	
141	n-C_4H_9	CO_2CH_3	H	H	1709[a]		1707		3404	
142	i-C_3H_7	CO_2CH_3	H	H	1704[a]		1702		3391	
143	t-C_4H_9	CO_2CH_3	H	H	1713[a]		1710		3410	
144	t-C_4H_9	H	CO_2CH_3	H	1717[a]		1709[a]		—[d]	
145	CH_3	CO_2CH_3	H	CO_2CH_3	1735	1712	1731	1709	3458	3412
146	C_2H_5	CO_2CH_3	H	CO_2CH_3	1733	1710	1730	1707	3458	3404
147	n-C_4H_9	CO_2CH_3	H	CO_2CH_3	1733	1709	1726	1706	3455	3405
148	i-C_3H_7	CO_2CH_3	H	CO_2CH_3	1734	1710	1730	1708	3459	3408
149	t-C_4H_9	CO_2CH_3	H	CO_2CH_3	1731	1715	1725	1713	3457	3422
150	$C_{10}H_{15}$[c]	CO_2CH_3	H	CO_2CH_3	1735	1716	1723	1712	3451	3416
151	CH_3	H	CO_2CH_3	CO_2CH_3	1726[b]	1715	1721[b]	1713	3418[a]	
152	C_2H_5	H	CO_2CH_3	CO_2CH_3	1728[b]	1712	1722[b]	1711	3417[a]	
153	n-C_4H_9	H	CO_2CH_3	CO_2CH_3	1725[b]	1712	1720[b]	1710	3416[a]	
154	i-C_3H_7	H	CO_2CH_3	CO_2CH_3	1726[b]	1711	1718[b]	1709	3409[a]	
155	t-C_4H_9	H	CO_2CH_3	CO_2CH_3	1724[b]	1715	1722[b]	1711	3423[a]	
156	$C_{10}H_{15}$[c]	H	CO_2CH_3	CO_2CH_3	1726[b]	1713	1722[b]	1711	3418[a]	
157	t-C_4H_9	CO_2CH_3	CO_2CH_3	H	1737	1722	1735	1713	—[d]	

---

[a] Broadening to high wave number side of the band.
[b] Estimated shoulder position.
[c] $C_{10}H_{15}$ = 1-adamantyl.
[d] Insufficient sample for analysis.

The greater stability on the syn over the anti rotamer for pyrrole-2-aldehydes and -ketones in low-polarity solvents [25, 63] is due to its lower dipole moment: The moments of the pyrrole ring and the oxo-group are mutually opposed. Similar considerations may obtain for the -2-esters in which the syn-s-trans rotamer is expected to have a much lower dipole moment than the anti rotamer. Steric effects appear to be of little consequence, there being no systematic change in either band structure or absorption frequency on variation in the bulk of the N-alkyl group.

The asymmetric singlet IR band observed in the carbonyl region of 3-methoxycarbonyl-N-t-butylpyrrole (144) is open to two interpretations: The molecule exists either in one rotameric form (with the band asymmetry perhaps arising from Fermi resonance) or as a mixture of rotamers with approximately equal carbonyl absorption frequencies. From NMR evidence, an equilibrium between cisoid and transoid forms is known to exist in 3-keto-N-alkylpyrroles [63] (although this does not lead to IR carbonyl band doubling). It seems likely, therefore, that both conformers are in equilibrium in the ester case, but that the field effects experienced by the ester functions in the two conformations are not sufficiently different for doubling of IR carbonyl bands to occur.

All the 2,5-dimethoxycarbonyl-N-alkylpyrroles (145)-(150) display well-separated IR carbonyl doublets (∿20 cm^{-1} apart) in which the lower wave number components are at roughly the same positions as the carbonyl absorptions of the corresponding 2-mono-esters.

If, as a first approximation, the two ester groups are considered independently of one another, then the observed doubled carbonyl bands may be attributed to mixtures of conformers containing syn- and anti-ester functions, in which the lower wave number bands arise from the syn function (in agreement with the previous 2-mono-ester assignment) and the higher wave number bands from the anti function. The emergence of this anti conformation (unobserved for 2-mono-esters) may be rationalized by consideration of the relative magnitudes of ester group and pyrrole dipole moments. The anti-syn conformer is expected to have a lower dipole moment than the syn-syn conformer with the anti-anti conformer having the highest moment. On this basis, the higher wave number absorption of a 2,5-di-ester carbonyl doublet results from the anti-ester component of the anti-syn form, and the lower wave number absorption from the syn-ester components of both the syn-syn and anti-syn forms. In agreement with this assignment, the intensity of the carbonyl band at lower wave number increases relative to that of the band at higher wave number for all the compounds studied here as the dielectric constant of the solution is increased, either by change of solvent from carbon tetrachloride to acetonitrile or by increase in substrate concentration, necessary for the overtone studies. This is rationalized as being a consequence of the increased stabilization of the more polar syn-syn form over the less-polar anti-syn form, and hence decrease in the percentage of anti-conformation present.

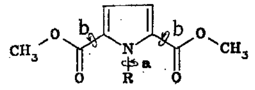
A study of the temperature dependence of the areas of the doublet components in an attempt to derive thermodynamic parameters gives inconclusive results, since three bands are required to achieve acceptable fits to the observed band contours. The validity of the assumption that the ester groups are essentially independent may thus be in doubt, since if there were an electronic interaction through the ring between the ester groups, then the energy of a syn-ester carbonyl vibration in the anti-syn-conformer might not be the same as that of a syn-ester carbonyl vibration in the syn-syn-conformer. Furthermore, the possibility of anhydride-like vibrational coupling between the carbonyl groups may not be excluded, even though the degree of such coupling is known to fall off rapidly as group separation increases (the carbonyl band separation in anhydrides is ∿60 cm^{-1} whereas that in peroxides is only ∿25 cm^{-1} [67]). Both these effects would tend to complicate the observed band profiles in an unpredictable manner.

The 2,4-dimethoxycarbonyl-N-alkylpyrroles' [(151)-(156)] carbonyl absorptions display only single maxima, but the bands have distinct shoulders to the high wave number side. The position of the major component of each absorption is close to that of the corresponding 2-mono-ester. This, together with the absence of well-separated carbonyl bands, implies that the 2-ester group is conformationally fixed in the syn-form: The 4-ester group may then be cisoid or transoid. There are thus two possible conformations for the 2,4-di-esters: syn-cisoid and syn-transoid. The origin of the IR band asymmetry can then be ascribed either to (a) slightly different carbonyl absorption frequencies of the 4-ester group in the transoid and cisoid forms, arising either from a slight intrinsic difference in field effects experienced by the ester group in the two conformations (as discussed for the 3-mono-ester case) or from an electronic interaction between the 2- and 4-ester groups along the lines discussed in the 2,5-di-ester case, or to (b) anhydride-like coupling.

2,3-Dimethoxycarbonyl-N-t-butylpyrrole (157) displays well-separated IR carbonyl doublets in carbon tetrachloride and acetonitrile.

On the basis of the previous discussion, the position of the higher wave number component may imply the presence of the 2-ester group in an anti-conformation. Change of solvent from carbon tetrachloride to acetonitrile causes a shift to low wave number for both component bands, as expected. The magnitude of the shift for the lower-frequency component is larger than that observed for the 2-ester group in the 2-mono-, 2,4-di-, and 2,5-di-esters studied here (2-4 cm^{-1}) and is comparable to the shift in 3-methoxycarbonyl-N-t-butylpyrrole (8 cm^{-1}). It appears, therefore, that the lower wave number component may owe its origin to the 3-ester group. The possible conformations are then anti-cisoid and anti-transoid. It should, however, be borne in mind that steric interactions are likely to be especially significant in a 1,2,3-trisubstituted pyrrole. Resulting out-of-planarity of ester groups and the pyrrole ring could lead to anomalous IR carbonyl band positions and solvent-induced shifts, thereby exacerbating the band-assignment problem.

NMR Studies. Two esters, 2,5-dimethoxycarbonyl-N-t-butyl- (149) and -N-adamantyl-(150) pyrrole have been examined by variable-temperature proton and carbon-13 NMR spectrometry for evidence of rotational isomerism due to restricted rotation about either (a) the N-alkyl group bond or (b) the ring-carbonyl group bonds:



R=t-C_4H_9,$C_{10}H_{15}$

The carbon-13 NMR spectra of (149) and (150) show little change on cooling of the deuterodichloromethane solutions to −70°C: the proton spectra, however, show significant broadening of the ester-methyl and N-alkyl signals (although not of the aromatic signals) at this temperature. Although the results are inconclusive, the absence of appreciable broadening of the aromatic protons at −70°C seems to suggest that hindrance to rotation mode (a) is responsible for the observed changes. This implies a very low energy barrier for rotation mode (b) (certainly lower than those barriers measured for N-alkylpyrrole-2-carbaldehydes, $E_a \sim 45$ kJ·mole^{-1} [68] and pyrrole-2,5-dicarbaldehyde, $E_a \sim 39$ kJ·mole^{-1} [69], and is compatible with results obtained for furan-2-esters in which no coalescence phenomenon in either carbon-13 or proton NMR spectra is observed even at 183 K [6, 27]. This could be a consequence of reduced π-electron donation for the heteroaromatic ring into the carbonyl bond when the carbonyl carbon atom bears an additional group capable of π-donation.

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