Tetrahedron, 1964, Vol. 20, pp. 831 to 840. Pergamon Press Ltd. Printed in Northern Ireland

EQUILIBRATION STUDIES

THE DETERMINATION OF THE RELATIVE THERMODYNAMIC STABILITIES OF ONE SET OF ISOMERIC PYRONES

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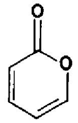
(*Received* 8 *November* 1963; *in revised form*, 26 *December* 1963)

Abstract—The bases of the order of stabilities and aromaticities usually assigned to the 2-pyrones and 4-pyrones are considered and found to be equivocal. Relative basicity and equilibration evidence is presented which indicates that the 2-pyrone, 4-methoxy-6-methyl-4-pyrone, is thermodynamically more stable than the 4-pyrone, 2-methoxy-6-methyl-4-pyrone. An estimation of the predictive power of the Hückel method for the relative stabilities of the pyrones is reported.

THE theoretical and experimental study of the molecular energetics of aromatic systems has been an area of fundamental chemical interest for over a century. Intensive interest in aromatic character following the precepts of the Hückel rule has led to a relatively sophisticated understanding of carbocyclic aromatic molecules. In the case of heteroaromatic molecules however the presence of the heteroatom introduces complexities such that the understanding of these systems has been less substantial. A resolution of these complications almost certainly will require further experimental information about heteroaromatic molecules.[1]

The determination of the relative stabilities of a set of isomeric 2- and 4-pyrones has been undertaken in order to obtain such information. The suitability of the pyrones for study is illustrated by the considerations that the parent heterocycles, 2-pyrone (I) and 4-pyrone (II), are π-isoelectronic with tropone (III)[2] and that isomeric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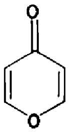
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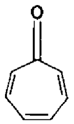
III

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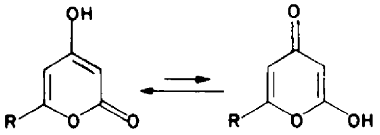
[1] Within the limits of the present discussion aromaticity is considered to be manifested by a molecular potential energy[3] which is lower than that of an appropriate classical model (one incorporating zero-point energies). M. E. Volpin, *Uspekhi Khim.* **29**, 298 (1960) has reviewed the concept of aromatic character. More recently comments on aromaticity have been made by J. A. Elvidge and L. M. Jackman, *J. Chem. Soc.* 859 (1961); A. T. Balaban and Z. Simon, *Tetrahedron* **18** 315 (1962); R. Breslow and E. Mohacsi, *J. Amer. Chem. Soc.* **85**, 431 (1963). D. Peters, *J. Chem. Soc.* 1274 (1960) has advocated a return to the "classical"criterion of reactivity for the aromaticity of hydrocarbons. In view of the uncertainties involved in comparing reactivities and in calculating reactivity indices, particularly for heteroaromatics, we prefer the above criterion.

[2a] H. J. Dauben and H. J. Ringold, *J. Amer. Chem. Soc.* **73**, 876 (1951); [b] W. von E. Doering and F. L. Detert, *Ibid.* For discussions of the aromatic character of tropone see, [c] P. L. Pauson, *Chem. Revs.* **55**, 9 (1955); [d] D. P. Craig, *Non-Benzenoid Aromatic Compounds* (Edited by D. Ginsburg) p. 29. Interscience, New York, N.Y. (1950). [e] T. Nozoe, *Ibid* p. 339.

pyrones may be compared to the same classical model. The latter consideration implies that the difference in the potential energy[3] of the isomeric pyrones will provide a measure of the difference in their aromatic character.

Traditionally, the lack of reactivity[4,5a,b] and the basicity[5b] of the 4-pyrones have been considered to indicate that these compounds are resonance hybrids which derive considerable stabilization in the ground state from significant contributions by dipolar resonance forms. On the other hand the reactivity[5a,b] and lack of basicity[5b] of the 2-pyrones have been interpreted to indicate that contributions of dipolar forms to the ground state of the 2-pyrones are slight. A spectral comparison of isomeric pyrones has been made in support of these assignments.[6] Essentially 4-pyrones have been considered to be aromatic compounds; whereas 2-pyrones have been considered to be non-aromatic.[5] However, Nakata *et al.*[7] have interpreted the alkylations of the pyronones on the basis of the greater thermodynamic stability of a 4-hydroxy-2-pyrone (IV) over a 2-hydroxy-4-pyrone (V). This order was apparently determined spectrally first by Chmielewska and Cieslak[8] and has since been reported by a number of other investigators.[9]



IV V

The purpose of the present paper is to examine the bases of the earlier assignment, to report the determination of the relative thermodynamic stabilities of one set of isomeric 2- and 4-pyrones and to interpret the relative stabilities of these pyrones with regard to present theories.

RESULTS AND DISCUSSION

Previous assignments. The assignments by Nakata *et al.*[7] and the results of the spectral investigations,[8,9] which indicate that the 2-pyrone(IV) is more stable than the 4-pyrone(V), afford an order of stability which is the reverse of the order of aromaticities deduced for the 2- and 4-pyrones from reactivity,[5a,b] spectral[6] and basicity[5b]

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[3] L. P. Hammett, *Physical Organic Chemistry* pp. 76–78. McGraw-Hill, New York, N.Y. (1940).

[4] [a] F. Arndt, E. Scholz and P. Nachtwey, *Ber. Dtsch. Chem. Ges.* **57**, 1903 (1924); [b] F. Arndt and L. Lorenz, *Ibid.* **63**, 3121 (1930).

[5] The general case has been cited by [a] A. R. Katritzky and J. M. Lagowski, *Heterocyclic Chemistry* pp. 52, 90. J. Wiley, New York, N.Y. (1960) and [b] R. H. Wiley, *Organic Chemistry* IV (Edited by H. Gilman) pp. 827–828. J. Wiley, New York, N.Y. (1953). A similar comparison of the parent heterocycles I and II has been made by [c] G. M. Badger, *The Chemistry of Heterocyclic Compounds* pp. 428–429. Academic Press, New York, N.Y. (1961).

[6] K. Nakanishi, *Infrared Absorption Spectroscopy* p. 204. Holden-Day, San Francisco, California (1952).

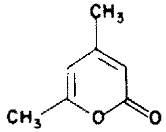
[7] [a] H. Nakata, S. Takahashi, K. Yamada and Y. Hirata, *Tetrahedron Letters* No. 16, 9 (1959); [b] H. Nakata, *Bull. Chem. Soc. Japan* **33**, 1688, 1693 (1960).

[8] I. Chmielewska and J. Cieslak, *Przemysl. Chem.* **8**, 196 (1952).

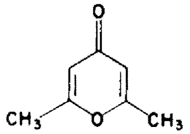
[9] [a] I. Chmielewska, J. Cieslak, K. Gorezynska, B. Kontnik and K. Pitakowska, *Tetrahedron* **4**, 36 (1958); [b] D. Herbst, W. B. Mors, O. R. Gottlieb and C. Djerassi, *J. Amer. Chem. Soc.* **81**, 2427 (1959); [c] J. D. Bu'Lock and H. G. Smith, *J. Chem. Soc.* 592 (1960); [d] K. Yamada, *Bull. Chem. Japan* **35**, 1323 (1962).

considerations. Although such a result is not inconceivable[10] an examination of the criteria previously used shows that these assignments are not convincing. In the earlier assignments[5a,b] chemical stability has been equated with aromatic character. However, if aromaticity is considered to be a ground state property manifested in the potential energy of a molecule,[1] reactivity criteria are not informative and may be quite misleading. The spectral and basicity criteria are discussed more fully in succeeding sections.

Infrared spectral correlation. A recent comparison of the IR spectra of 4,6-dimethyl-2-pyrone (VI) and 2,6-dimethyl-4-pyrone (VII) has led to the radionalization



VI



VII

that the lower carbonyl stretching frequency of VII, indicates a greater contribution by dipolar resonance forms to the ground state of 2,6-dimethyl-4-pyrone[11] than to 4,6-dimethyl-2-pyrone.[6] However, the assumption that the carbonyl stretching frequencies will be dominated by the same factors which determine the difference in potential energies of these isomers is not warranted. Rather it would seem that the differences in environment of the carbonyl groups precludes such a comparison.[12] Hence the IR spectral assignments do not provide any reliable information about the relative ground state energies or the aromaticities of the pyrones.

Relative basicities. In the years since the basicity of 2,6-dimethyl-4-pyrone was recognized by Collie and Tickle[13] a large amount of work has verified the basicity of the 4-pyrones and established the structures of the resulting pyrylium salts.[5,14] The lack of basicity of the 2-pyrones[5b] seems less well established. In fact, Wiley and Moyer[15] have reported that 2-pyrones are monoproponated in sulfuric acid and Janiszewska-Drabarek[16] has reported the formation of an adduct between 4-methoxy-6-methyl-2-pyrone and chloroplatinic acid. An experiment which might appear relevant to the relative basicities of the 2- and 4-pyrones is the formation of the hydrochloride of 2-methoxy-6-methyl-4-pyrone as a precipitate in the presence of 4-methoxy-6-methyl-2-pyrone.[9c,17] Unfortunately the precipitation introduces complications such that any conclusion about the relative basicities of the pyrones on the basis of this information would be unwarranted.

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[10] The relationship of stability and aromaticity is discussed more fully in a succeeding section.

[11] Other IR spectral assignments have been made for the 4-pyrone (VII) by A. R. Katritzky and R. A. Jones, *Spectrochim. Acta* **17**, 64 (1961) and D. Cook, *Canad. J. Chem.* **39**, 1184 (1961).

[12] M. J. S. Dewar, *Hyperconjugation* p. 103. Ronald Press Co., New York, N.Y. (1962), has noted similar cases.

[13] J. N. Collie and T. Tickle, *J. Chem. Soc.* 710 (1899).

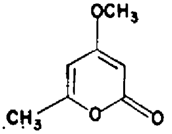
[14] [a] N. F. Hall and J. B. Conant, *J. Amer. Chem. Soc.* **49**, 4037 (1927); [b] D. Cook, *loc. cit.* and references cited therein.

[15] R. G. Wiley and A. N. Moyer, *J. Amer. Chem. Soc.* **76**, 5706 (1954).

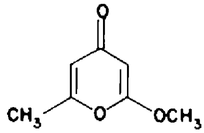
[16] S. Janiszewska-Drabarek, *Rocz. Chem.* **27**, 456 (1963).

[17] I. Chmielewska, J. Cieslak and T. Kraczklewicz, *Rocz. Chem.* **30**, 1009 (1965).

Before an interpretation could be made of the significance of the relative basicities of the 2- and 4-pyrones the correct order of basicities had to be established for these compounds. This was done by the non-aqueous titration of three sets of isomeric pyrones: 2-pyrone (I) and 4-pyrone (II); 4,6-dimethyl-2-pyrone (VI) and 2,6-dimethyl-4-pyrone (VII); and 4-methoxy-6-methyl-2-pyrone (VIII) and 2-methoxy-6-methyl-4-pyrone (IX). The titrations were carried out in acetic acid using perchloric acid as a titrant.[14a,18]



VIII



IX

Attempted titrations of the 2-pyrones (I, VI and VIII) led to titration curves which were essentially identical to that of the blank. On the other hand quantitatively correct titration curves were obtained for the titration of 2,6-dimethyl-4-pyrone (VII) and 2-methoxy-6-methyl-4-pyrone (IX). The titration curve obtained for 4-pyrone (II) in acetic acid did not allow an accurate quantitative analysis although the shape of the curve relative to that of a blank or of 2-pyrone (I) indicated that titration did occur. A quantitatively accurate end point was observed for the titration of 4-pyrone by the use of a solvent system of acetic anhydride-acetic acid.[18b] The pyrones (I, VI and VIII) were still not titratable in this medium. The titrations of the 4-pyrone isomers were reversible, no precipitation occurred during the titrations and the order of basicities for the 4-pyrones was that sensibly expected for the stabilization of the pyrylium salt by the substituents on the pyrone nucleus. Recovery experiments showed that the 2-pyrone (VIII) and the 4-pyrone (IX) could be recovered in high yield after neutralization of the acid. In every case then the 4-pyrone isomer was more basic than the corresponding 2-pyrone.

The interpretation usually given to this order of basicities, that it reflects the greater contribution of dipolar resonance forms to the ground state of the 4-pyrone,[5b] is not tenable. The only information directly obtainable from the relative basicities of the pyrones is that under the conditions of the titration the 4-pyrones and perchloric acid are of higher free energy than the corresponding 4-hydroxy-pyrylium perchlorates and that the 2-pyrones and perchloric acid are of lower free energy than the corresponding 2-hydroxy-pyrylium perchlorates. An interpretation of these facts with respect to the ground state energies of the isomeric pyrones may be made only insofar as it can be assumed that differences in solvation energies are small and insofar as valid assignments of relative free energies can be made to the isomeric pyrylium compounds. For example, if the assumption is made that 2-hydroxy-4-methoxy-6-methyl-pyrylium perchlorate (X) and 4-hydroxy-2-methoxy-6-methyl-pyrylium perchlorate (XI) have approximately the same free energy under the conditions of the titration, it follows directly from the relative basicities of 4-methoxy-6-methyl-2-pyrone (VIII) and 2-methoxy-6-methyl-4-pyrone (IX) that VIII is of lower free energy than IX under the titration conditions. These qualitative free energy arguments are illustrated in Fig. 1.

[18a] J. D. Fritz, *Analyt. Chem.* **22**, 1028 (1950); [b] J. S. Fritz and M. O. Fulda, *Ibid.* **25**, 1837 (1953).

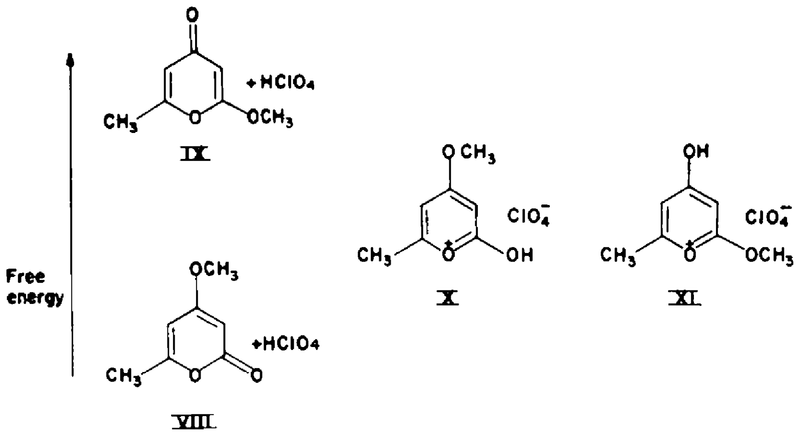
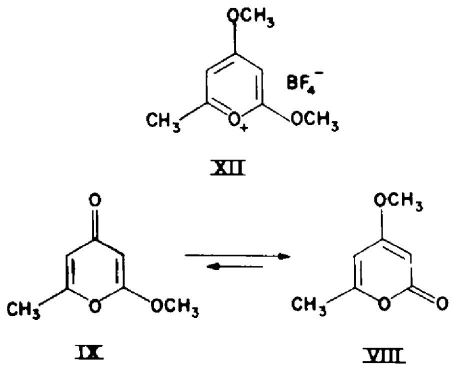


FIG. 1. Qualitative relative free energies of the reactants and products in the acid-base equilibria achieved during titration assuming approximately the same free energies for X and XI.

Consideration of the assumptions involved shows that these arguments cannot be considered to be rigorous nor can they be extended to the other sets of isomers.

Equilibration. The tautomeric equilibra which favor the 2-pyrones (IV) over the 4-pyrones (V)[8,9] provides examples of the greater thermodynamic stability of a 2-pyrone. However the known sensitivity of tautomeric equilibria to solvent effects[19] introduces ambiguities into the interpretation of the observed order of stabilities. Moreover the rapidity of proton transfers in such systems[19] precludes the detection of the minor isomer unless it can be observed spectrally.

These difficulties may be overcome by the equilibration of alkylated isomers formally derived from the tautomers by the catalytic function of their common alkylated derivative. In the present case conclusive information about the relative stabilities of one set of isomeric pyrones has been obtained from the equilibration of VIII with IX by the action of 2,4-dimethoxy-6-methyl-pyrylium fluoborate (XII) as a catalyst.[20] Heating the 4-pyrone (IX) with a catalytic amount of the pyrylium salt (XII) for three minutes at 140° or for forty minutes at 100° led to the 2-pyrone (VIII)



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[19] A. R. Katritzky and J. M. Lagowski, *Advances in Heterocyclic Chemistry* I (Edited by A. R. Katritzky), p. 318. Academic Press, New York, N.Y. (1963).

[20] A preliminary account of this reaction has appeared, P. Beak, *Tetrahedron Letters* 863 (1963). Extension of this equilibration to other systems is currently under investigation.

in 97% and 98% yields respectively.[21] Compound VIII was identified by IR and UV spectral criteria. From the latter it was established that the product of the reaction was at least 98% of the 2-pyrone, (VIII). Since the titrative analysis of a subsequent reaction product demonstrated that less than 0·5% of IX was present in the equilibrium mixture,[22] the equilibration product may be considered to be at least 99·5% VIII. The catalyst could be recovered in high yield. Although the amount of the 4-pyrone (IX), the isomer which was present in minor amounts at equilibrium, was not determined,[23] it follows directly from the principle of dynamic equilibrium that this process is an equilbration. Control experiments established that 2-methoxy-6-methyl-4-pyrone was stable in the absence of 2,4-dimethoxy-6-methyl-pyrylium fluoborate under the reaction conditions, that the minor isomer was not selectively lost in the product isolation, and that the reaction was not inhibited by the presence of galvinoxyl.[24] This result indicates that in the melt at 140° VIII is more stable than IX by a standard Helmholtz free energy of at least 4 kcal/mole.[25]

Relative aromaticities. Assignments of relative aromaticities[1] to the isomeric pyrones on the basis of their relative stabilities would be fundamentally incorrect since the observed difference in thermodynamic stability incorporates contributions from differences in kinetic and solvation energies as well as from differences in potential energy.[3] However it may be possible to determine the source of the stability difference for the 2-pyrone (VIII) and the 4-pyrone (IX) since the entropy difference between these isomers can in principle be obtained from determination of the equilibrium constant at different temperatures. Any extrapolation of the observed stability order to other sets of isomeric pyrones as well as any comment on the aromaticities of these molecules must be deferred until this entropy difference as well as other experimental information about related systems is obtained.

Molecular orbital calculations. Hückel molecular orbital treatment[26] was first applied to 4-pyrone by Brown[27] who concluded that 4-pyrone had appreciable contribution to its ground state by a dipolar structure. More recently Zahradnik *et al.*[28] have correlated the UV spectra of 2-pyrone (I), and 4-pyrone (II) with the results of Hückel calculations and have discussed the reactivity of 4-pyrone in the same frame of reference. The Czech workers used an inductive model for their calculations on 4-pyrone but did not employ this model for their calculations on 2-pyrone. As a result different parameters were used in the two calculations which arrived at the delocalization energies of 2-pyrone and 4-pyrone at $2{\cdot}896\beta$ and $2{\cdot}868\beta$, respectively.

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[21] S. Janiszewska-Draebarek[11] has reported the conversion of IX to VIII with methanolic HCl in unspecified yield.

[22] This experiment was carried out by Mr. James Bonham.

[23] Attempted titrate and vapor phase chromatographic analysis have not yet proven capable of detecting the minor isomer.

[24] P. D. Bartlett and T. Funahashi, *J. Amer. Chem. Soc.* **84**, 2596 (1962).

[25] Assuming that the melt is an ideal solution and that the pyrones do not differ appreciably in vapor pressure at 140°. The observed order of stability would be predicted by a naive consideration of the appropriate canonical forms according to the rules of resonance. J. Hine, *Physical Organic Chemistry* pp. 3–9. McGraw-Hill, New York, N.Y. (1962).

[26] A. Streitwieser, *Molecular Orbital Theory for Organic Chemist*, Chap. 3. Wiley, New York, N.Y. (1961).

[27] R. D. Brown, *J. Chem. Soc.* 2670 (1951).

[28] R. Zahradnik, C. Parkanyl and J. Koutecky, *Coll. Czech. Chem. Comm.* **27**, 1242 (1962).

Insofar as the energy difference in the ground states of 2-pyrone and 4-pyrone is dominated by the difference in π electronic energy of the two systems and insofar as such calculations have predictive, rather than correlative value it might be expected that the calculated delocalization energy would be greatest for the most stable isomer.[29] The results of molecular orbital calculations for 2-pyrone and 4-pyrone using the Hückel approximations and treating oxygen as a perturbation in the carbon skeleton with the assumption of the appropriate parameters are summarized in Table 1. The localized model used to obtain the delocalization energies was two isolated carbon-carbon double bands, a carbonyl group and an oxygen atom.

TABLE 1. CALCULATED DELOCALIZATION ENERGIES FOR 2-PYRONE AND 4-PYRONE

Parameters	2-Pyrone	4-Pyrone
$\alpha_O = \alpha + \beta^a$ $\beta_{CO} = 2\beta$	$2{\cdot}90\beta$	$2{\cdot}87\beta$
$\alpha_O = \alpha + 2\beta^b$ $\alpha_{C-O} = \alpha + {\cdot}2\beta$ $\beta_{CO} = 2\beta$	$3{\cdot}10\beta$	$3{\cdot}26\beta$
$\alpha_{\ddot{O}} = \alpha + 2\beta^c$ $\alpha_{\dot{O}} = \alpha + \beta$ $\beta_{C-O} = {\cdot}8\beta$ $\beta_{C=O} = \beta$	$2{\cdot}75\beta$	$2{\cdot}68\beta$

Parameters taken from: [a] footnote 28, [b] footnote 29, [c] footnote 26, p. 135.

Although it is interesting that appreciable delocalization energies are predicted for the pyrones the fact that the differences in delocalization energy obtained are neither consistently in one direction nor of sufficient magnitude to be used with any confidence discouraged further calculation. It would seem that the Hückel treatment does not have predictive power for the relative thermodynamic stabilities of the pyrones with the parameters customarily employed.

EXPERIMENTAL

The IR spectra were determined on a Perkin-Elmer infrachord spectrophotometer using chloroform solutions unless otherwise noted. The UV spectra were determined on a Carey model 14 m spectrophotometer using 95% ethanol solutions unless otherwise noted. The m.ps were determined on a Büchi–Tottoli oil bath apparatus and are uncorrected. The vapor phase chromatographs were carried out on an Aerograph A-90P. The titrations were carried out on a Polrad Automatic Recording Titrator model AT-2A using a calomel and a glass electrode. The PMR spectra were determined on a Varian A-60 spectrometer using 5% deuterochloroform solutions containing tetramethylsilane as an internal standard unless otherwise noted. The microanalyses was performed by Mr. Joseph Nemeth and associates. The MO calculations were done on an IBM 7090 computer.

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[29] A. Streitwieser, *Molecular Orbital Theory for Organic Chemists*, 248–249, Wiley, New York, N.Y. (1961).

Preparation of the isomeric 2- and 4-pyrones

The known pyrones were prepared by established procedures. 2-Pyrone (I) was prepared by the decarboxylation of 6-carboxy-2-pyrone according to the method of Fried and Elderfield.[30] The crude product was purified by vapor phase chromatography using a column of 20% carbowax 20 m supported on base-washed firebrick and contained in a 5 ft long ¼ in diameter copper tube at 180°, $n_D^{25^\circ}$ 1·5285 (reported 1·5272). The IR[31] and NMR spectral data were consistent with the established structure. 4-Pyrone (II) was prepared by the decarboxylation of cheledonic acid according to the method of Willstater and Pummerer.[32] The crude product was purified by vapor phase chromatography as for the case of 2-pyrone. The product had a m.p. 33–35° (reported 32·5°) and was characterized by the expected IR[31] and NMR spectra. 4,6-Dimethyl-2-pyrone (VI) was prepared by the by the method of Smith and Wiley,[33] m.p. 50–52° (reported[33] 50–51°). The IR[34] and NMR spectra were consistent with the established structure. 2,6-Dimethyl-4-pyrone (VII) was prepared by the method of Collie and Tickle,[13] m.p. 312–134° (reported[35] 132°). The established structural assignment was confirmed by the compound's IR[11] and NMR spectra. 4-Methoxy-6-methyl-2-pyrone (VIII) was prepared by the method of Bu'Lock and Smith,[9c] m.p. 88–90° (reported [9c] 87.5–88.5°). The IR[9b,9c,36], UV [9b,9c,36], (λ max 280 mμ, log ε 3·85) and NMR spectra were consistent with the established structure. 2-Methoxy-6-methyl-4-pyrone (IX) was prepared by the method of Bu'Lock and Smith,[9c] m.p. 94–96° (reported [9c] 92·5–94°). The IR[9b,9c,36], UV[9b,9c,36] (λ max 240 mμ, log ε 4·15) and NMR spectra were consistent with the established structure.

2,4-*Dimethyoxy-6-methyl-pyrylium Fluoborate* (XII).

(a) *From* 4-*methoxy-6-methyl-2-pyrone* (VII). To a solution of 58 mg (0·41 mm) of VIII in 0·2 ml redistilled 1,2-dichloroethane was added 0·3 ml (0·03 mm) 1·0 N silver fluoborate[37] in 1,2-dichloroethane followed by 0·144 ml (2·3 mm) methyl iodide.[38] The resulting mixture was allowed to stand 4·5 hr. The precipitated silver iodide and the resulting clear 1,2-dichloroethane solution were separated by centrifugation. The silver iodide was washed with 0·5 ml methanol and this wash was combined with the 1,2-dichloroethane solution. This clear solution upon dilution with 4 ml diethyl ether gave a white precipitate of XII which was separated from the ether solution by centrifugation and dried overnight in a vacuum desiccator, wt. 44 mg (61% yield based on silver fluoborate), m.p. 137–154°. Recrystallization of this material from 1,2-dichloroethane–carbon tetrachloride gave fine white needles, m.p. 152–154°; IR spectrum[39] (nujol mull) 3150 (m) 1670 (s), 1550 (s), 1225 (s), 1020–1100 (s), 945 (s), 910(s), 875 (s), 840 (m), 830 (m) cm^{-1}; UV spectrum (CH_2Cl_2), λ max 272 mμ (log. ε, 4·02), λ min 248 mm (log ε 3·44), NMR spectrum (CD_3COCD_3), the protons on the pyrylium ring resonate at 419 and 431 cs. downfield from the resonance of the internal standard tetramethylsilane with relative areas of 1·1 the protons of the methoxy groups resonate at 258 and 267 cs. downfield from the tetramethylsilane peak with relative areas of 2·9 and 3·0, the protons of the methyl group located on the pyrylium ring resonate at 161 cs. downfield from the tetramethylsilane peak with a relative area of 3·3. (Found; C, 39·78; H 4·56. $C_8H_{11}O_3BF_4$ requires; C, 39·74; H, 4,54%).

(b) *From* 2-*methoxy-6-methyl-4-pyrone*. The reaction of 10 mg of IX in 0·5 ml 1,2-dichloroethane with 10 mg silver fluoborate in 0·5 ml 1,2-dichloroethane and 0·03 ml methyl iodide in the manner described above gave 8·0 mg (58% yield based on silver fluoborate) of XII m.p. 140–149°. This material was determined to be identical to the compound obtained from the alternative synthesis (a) on the bases of m.p., mixed m.p. and IR spectral criteria.

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[30] J. Fried and R. C. Elderfield, *J. Org. Chem.* **6**, 566 (1941).

[31] R. N. Jones, C. L. Angell, T. Ito and R. J. D. Smith, *Canad. J. Chem.* **37**, 2010 (1959).

[32] R. Willstater and R. Pummerer, *Ber. Dtsch. Chem. Ges.* **37**, 3734 (1904).

[33] N. R. Smith and R. H. Wiley, *Organic Synthesis* **32**, 57 (1952).

[34] R. H. Wiley and J. E. Esterle, *J. Org. Chem.* **22**, 1257 (1957).

[35] J. N. Collie, *J. Chem. Soc.* **59**, 617 (1891).

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[38] The procedure is adapted from a synthesis of 4-ethoxy-2,6-dimethyl-pyrylium fluoborate reported by H. Meerwein, V. Henderich and K. Wunderlick, *Arch. Pharm.* **291**, 541 (1958).

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Titrations of the isomeric 2- *and* 4-*pyrones*. The acetic acid solvent and the perchloric acid–acetic acid titrant were dried with acetic anhydride until the water content was between 0·1 and ·01% as determined by a modified[40] Karl Fischer titration using a graduated 1·0 ml pipette to deliver the Karl Fischer reagent. The calomel and the glass electrodes were allowed to stand in the solvent for at least 12 hr before use. The perchloric acid titrant was made up to be approximately ·05 N and was standardized with anhydrous sodium acetate.

The titrations of known amounts of IX and VII gave an end-point within 3% of the expected value. The end-point break for the titration of 4-pyrone was not determinable from the curve obtained. The end-point of the 4-pyrone titration was more apparent when the titration was carried out in 30% acetic anhydride–acetic acid than when the titration was done in acetic acid. The solutions were clear during the titrations of the 4-pyrone isomers, and the curves obtained could be reversed by titration of the acidic solution with a sodium acetate solution. In the case of the attempted titrations of the 2-pyrone isomers I, VI and VIII the curves obtained were essentially identical to that of a blank.

Recovery of 4-*methoxy*-6-*methyl*-2-*pyrone from the titration conditions*. A solution of 15·1 mg (·108 mm) of VIII in glacial acetic acid was treated with 1·0 ml (·108 mm) of ·060 N perchloric acid in glacial acetic acid and the resulting solution was allowed to stand 5 min. The solution was then treated with 10 ml ·013 N sodium acetate and poured into 60 ml of an equivolume mixture of methylene chloride and water. The methylene chloride layer was washed (3 times with water, once with sat. $NaHC_3O$ aq.) and dried ($MgSO_4$). Evaporation of the methylene chloride gave 14·3 mg (95% recovery) of VIII which was identified by m.p. mixed m.p. and IR and UV spectra criteria.

Recovery of 2-*methoxy*-6-*methyl*-4-*pyrone from the titration conditions*. The treatment of a glacial acetic acid solution of 17·4 mg (1·24 mm) IX with 2·05 ml (·126 mm) ·06 N perchloric acid in glacial acetic acid followed by a work-up analogous to that described above gave 15·0 mg (86% recovery) of IX which was identified by m.p., mixed m.p. and IR and UV spectral criteria.

Conversion of 2-*methoxy*-6-*methyl*-4-*pyrone* IX *to* 4-*methoxy*-6-*methyl*-2-*pyrone* VIII *by the action of* 2,4-*dimethoxy*-6-*methyl-pyrylium fluoborate* XII *as an equilibration catalyst*

(a) *At* 100°. A mixture of 180 mg of IX and 17·4 mg 2,4-dimethoxy-pyrylium fluoborate was sealed in a glass tube and heated at 100° for 40 min. The tube was cooled, carefully broken open and the contents were leached 4 times with 10 ml portions of diethyl ether. The ether soluble and ether insoluble compounds were separated by filtration of the combined ether solutions.

The ether insoluble product was 17·1 mg impure XII as shown by m.p., 85–115°, and IR and UV spectral criteria.

The ether soluble product which was obtained by evaporation of the ether (red. press) amounted to 172 mg and was shown by m.p. 84–86°; mixed m.p. and IR and UV spectral criteria to be VIII.

Analysis of the UV spectra of mixtures of IX and VIII by the method described by Dewar and Urch[41] established that this procedure was capable of detecting 2% of the 4-pyrone IX in the presence of 98% of the 2-pyrone, VIII. The application of this method to the product from the equilibration mixture showed that this material was at least 98% VIII.

A series of separate runs using a mixture of 105 mg of IX and 11 mg 2,4-dimethoxy-pyrylium fluoborate with samples withdrawn after 55, 120 and 240 sec in conjunction with analysis of the UV spectra of the ether soluble product showed that the reaction has a first-order half-life of about 2·3 min at 100°.

(b) *At* 140°. A mixture of 182 mg of IX and 18 mg of XII when heated at 140° for 3 min gave 15 mg impure pyrylium salt (XII) as the ether insoluble product and 178 mg of VII as the ether soluble product produced by the same methods and criteria are discussed above. In a subsequent reaction at this temp it was shown by the titration of 148 mg of the reaction product, a method which was established to be capable of detecting at least 0·7 mg of VII under these conditions, that less than 0·5% of the 4-pyrone VII was present in the equilibration mixture.[22]

In a separate experiment it was shown that the reaction at 140° was not inhibited by galvanoxyl.[22,24]

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Control experiments

(a) 2-*Methoxl-6-methyl-4-pyrone* IX. Compound IX (3·5 mg) was heated in a sealed tube at 140° for 10 min. The product was shown by m.p., 90–92°, IR and UV spectral criteria to be unchanged 4-pyrone (IX).

(b) 4-*Methoxy-6-methyl-2-pyrone* (VIII). Compound VIII (8·3 mg) was heated in a sealed tube at 140° for 10 min. The product was shown by m.p. 85–88°, IR and UV spectral criteria to be unchanged VIII.

(c) 2,4-*Dimethoxy-pyrylium fluoborate* (XII). Compounds XII (5·3 mg) was heated in a sealed tube at 167° for 5 min. The product was shown by m.p., 146–150°, IR and UV spectral criteria to be unchanged pyrylium salt (XII).

Acknowledgement—The author is grateful to Dr. S. G. Smith for theoretical and practical discussion and for criticizing the manuscript and to Dr. W. H. Flygare for discussion of the molecular orbital calculations.