tions in this medium always showed a sharp end-point break of from 30–60 mv. for pseudo-phenols and phenols to 150–190 mv. for "hyperacid" dihydroxydiphenylmethanes and carboxylic acids. Some judgment of the relative acidities of different compounds could also be made on the basis of the bucking potential needed to obtain the same millivolt reading at half-neutralization. In general, however, the antimony electrodes did not give potentials reproducible from one day to the next, being apparently too much influenced by the surface condition of the metal, etc. Also, despite sharp and unmistakable end-points, the initial portion of a titration curve was generally irregular. Titration curves for this medium are therefore not given here.

Titrations in benzene–isopropyl alcohol were carried out as described by Lykken[4] and as set forth in A.S.T.M. methods D 663-46T. Isopropyl alcohol (Eimer and Amend, No. A-416) and benzene (Mallinckrodt, thiophene-free) were used as received. A Beckman No. 4990 glass electrode was found suitable for these titrations, though the electrode tends to a lower and lower peak *p*H for any given substance over the course of several months and must finally be replaced. To get the entire course of all titrations within the scale of the Macbeth *p*H meter, the instrument was adjusted to read *p*H 2.0 in a *p*H 4.0 buffer. All readings of "apparent *p*H" read on the scale during titration were then adjusted accordingly by adding two *p*H units. The highest reading possible thus becomes "apparent" *p*H 16. The curves obtained by this method, as shown in Figs. 1 and 2, are typical of a class unless stated to be specifically of one compound. Thus the curve given as that of a dihydroxydibenzyl ether is actually one obtained using bis-(2-hydroxy-3-methyl-5-*t*-butylbenzyl) ether, but the titration curves of all the compounds of this class investigated resemble each other so closely that it was deemed useless to give the curves of more than one.

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The Absorption Spectra of the 2-Furyl and 2-Thienyl Analogs of Chalcone[1]

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In a previous publication[2] dealing with the absorption spectra of α,β-unsaturated ketones A—CH=CH—CO—B it was noted that the replacement of the phenyl by the 2-furyl group in position A gave a consistent bathochromic effect of 33–34 mμ regardless of whether the B group consisted of a phenyl or a 2-thienyl group and, furthermore, that the replacement of the phenyl by the 2-thienyl group in position B gave a smaller but rather constant bathochromic effect regardless of whether the A group was the phenyl or the 2-furyl group. In a later publication[3] it was possible to express the effects of substituents on the absorption spectra of chalcones in terms of several generalizations relating the degree of batho- and hypsochromic effects to the electronic nature and the location of the substituents. Since the replacement of the phenyl groups in the chalcone molecule by resonating heterocyclic nuclei can be regarded as a way of forming substituted chalcones, and in view of the above mentioned regularities, it became desirable to examine the whole series of eight chalcone analogs in which one or both phenyl groups are replaced by the 2-thienyl and/or the 2-furyl group.

The spectral results obtained in this study are listed in Table I. (1) The replacement of the phenyl by either the 2-furyl or the 2-thienyl group causes an approximately threefold greater bathochromic effect when the replacement occurs in position A. (2) There is a small but consistent difference between the effects caused by the 2-furyl and the 2-thienyl groups. The 2-thienyl group causes a slightly greater bathochromic effect when the replacement occurs in position A while the opposite is true when the replacement occurs in position B.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF A—CH=CH—CO—B

No.	A	B	Absorption maxima λ, mμ	$\epsilon \times 10^{-4}$	λ', mμ	$\epsilon' \times 10^{-4}$
1	Phenyl	Phenyl	312[a]	2.67[a]	230[a]	0.89[a]
2	2-Thienyl	Phenyl	345	1.92	275	1.01
3	2-Furyl	Phenyl	344[b]	2.68[b]	260[b]	0.85[b]
4	Phenyl	2-Thienyl	320[b]	1.93[b]	..	..
5	Phenyl	2-Furyl	324	1.07	228	0.85
6	2-Thienyl	2-Thienyl	354	3.70	285	.85
7	2-Furyl	2-Thienyl	353[b]	2.43[b]	243[b]	.56[b]
8	2-Furyl	2-Furyl	354	6.08	256	.43
9	2-Thienyl	2-Furyl	355	4.82	(298)	(.99)

[a] Reported in ref. 3. [b] Reported in ref. 2.

The first of the above conclusions is in excellent agreement with generalization no. 1 which was deduced from the examination of the spectra of a great number of substituted chalcones.[3] This implies that the two heterocyclic nuclei have a greater electron-donating character than the phenyl group, and this conclusion agrees with the observations of Braude and co-workers[4] dealing with the spectra of vinyl derivatives of the three ring systems. Also the decrease in rates of the acid-catalyzed semicarbazone formation when benzaldehyde is compared to 2-furancarboxaldehyde and 2-thienaldehyde[5] can be attributed to the greater electron-releasing effects of the heterocyclic nuclei which effect would thus stabilize the protonated aldehyde intermediate toward the attack of the semicarbazide molecule.

The slightly greater electron-releasing effect of the 2-thienyl group as compared to the 2-furyl group (deduced from their relative bathochromic effects in position A) is confirmed by the results of Braude.[4] The results of the same group of investigators[6] dealing with the rates of the acid-catalyzed rearrangements of substituted 1-crotyl alcohols, however, seem to indicate a greater electron release in the case of the 2-furyl group and these investigators attribute the difference to the greater "electromeric polarizability" of the 2-furyl group as compared to that of the 2-thienyl group.

The slightly greater bathochromic effect noted when the 2-furyl group replaces the 2-thienyl group in the position B implies that under these circumstances the first group is more electron-attracting.[7] The fact that the 2-furyl group can be more electron-attracting than either the phenyl or the 2-thienyl group is brought out by the comparison of

(1) From the M.Sc. thesis of Henry J. Planinsek, Duquesne University, Aug., 1951.

(2) H. H. Szmant and A. J. Basso, THIS JOURNAL, **73**, 4521(1951).

(3) H. H. Szmant and A. J. Basso, *ibid.*, **74**, 4397 (1952).

(4) E. A. Braude, *et al.*, *J. Chem. Soc.*, 4155 (1952).

(5) K. C. Schreiber and F. J. Vancheri, Meeting-in-Miniature, Pittsburgh, Pa., June 11, 1953.

(6) E. A. Braude and J. S. Fawcett, *J. Chem. Soc.*, 4158 (1952).

(7) The bathochromic effect of electron-attracting groups at B in the case of substituted chalcones was summarized as generalization no. 3 in ref. 3.

the acidities of the respective carboxylic acids,[8] and probably also by the comparison of the rates of the alkaline hydrolysis of the carboxylic esters.[9]

It is noteworthy that the principal absorption bands of the four chalcone analogs, in which the 2-thienyl and 2-furyl groups replace both of the phenyl groups, are located within a very narrow range. This would seem to imply the absence of any special resonance contributions by the 2-thienyl group in which the sulfur atom has an expanded valence shell.

Experimental

All of the heterocyclic chalcone analogs were prepared according to the directions of Weygand and Strobelt.[10] The absorption spectra were determined in 95% ethanol using a Beckman DU spectrophotometer. The spectral characteristics of the compounds discussed here are summarized in Table I, and the absorption curves of all of the compounds are reproduced in Figs. 1 and 2.

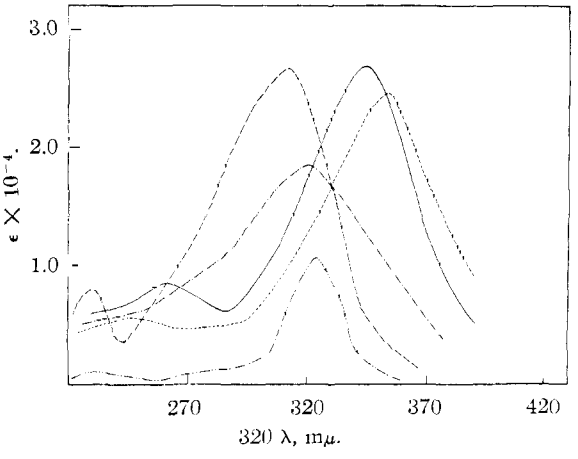

Fig. 1.—Ultraviolet absorption spectra of compounds listed in Table I: — —, no. 1; ———, no. 3; —·—·, no. 4; —·—·—·, no. 5; ------, no. 7.

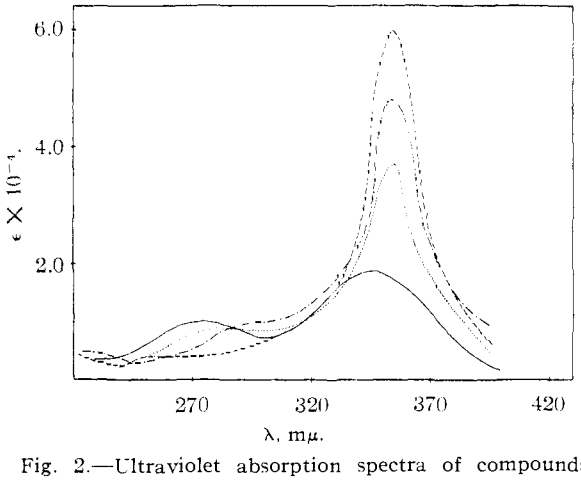

Fig. 2.—Ultraviolet absorption spectra of compounds listed in Table I: ——, no. 2; . . . . . , no. 6; — — —, no. 8; —·—·—, no. 9.

(8) W. Catlin [*Iowa State Coll. J. Sci.*, **10**, 65 (1935)] reports the ionization constants of 2-furoic and 2-thiophenecarboxylic acids as 75×10^{-5} and 34×10^{-5}, respectively. Both of these acids are thus considerably stronger than benzoic acid (6.3×10^{-5}).

(9) See ref. 6 for the discussion of these results.

(10) C. Weygand and F. Strobelt, *Ber.*, **68B**, 1839 (1935).

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A Preparation of Progesterone-4-C^{14}

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This investigation was undertaken to fulfill the need for substantial quantities of ring-labeled progesterone-C^{14} required as a starting material for biological and chemical conversion to radioactive corticosteroids.[1] By including radiocarbon in the 4-position of the steroid nucleus, it was hoped that the label would persist in the metabolic fragments as indicated by studies conducted with cholesterol-4-C^{14}.[2]

Three procedures have been published concerning the inclusion of radiocarbon in the α,β-unsaturated 3-ketone grouping of several steroids, the phenyl acetate method,[3-5] the Reformatsky reaction[3,6] and the Grignard reaction.[7-9] In view of the reported superior yields and adaptability to larger scale synthesis, the latter procedure was used to prepare methyl 3-keto-Δ^4-etienate (Ia). Experience in these laboratories has shown that this substance is converted in excellent yield to desoxycorticosterone acetate and progesterone by modifications of published procedures.[6,10]

When methyl 3-keto-Δ^4-etienate (Ia) was ozonized[3] in 3-g. lots, at least 90% was transformed to acidic material from which a 70–75% theoretical yield of keto acid IIa[11] was obtained. Periodate oxidation[3] of the neutral residue gave small additional amounts of IIa. The separation of neutrals from acidics was readily effected using sodium carbonate. Dilute sodium hydroxide caused concurrent saponification of the labile 17-carbomethoxy group of IIa.[12] In contradistinction, methyl ester

(1) Progesterone-4-C^{14} was the key intermediate in the recently completed partial synthesis of cortisone-4-C^{14} acetate—a project arranged under contract with the Endocrinology Study Section of the National Institutes of Health, U. S. Public Health Service. The project was directed by a committee of the Study Section consisting of Dr. C. Huggins, chairman, Dr. S. R. Hall, executive secretary, and Drs. T. F. Gallagher, Sloan-Kettering Institute, M. Tishler of Merck & Co., Inc., and G. Pincus of the Worcester Foundation, and by Dr. A. D. Odell, formerly of Frosst & Co. but now with Syntex, S. A. Progesterone-4-C^{14} was converted to pregnane-3,11,20-trione-4-C^{14} by Drs. H. G. Kolloff and R. H. Levin of the Upjohn Co., Kalamazoo, Mich., and returned to us for completion of the synthesis of cortisone acetate by known methods; *cf.* T. H. Kritchevsky, D. L. Garmaise and T. F. Gallagher, THIS JOURNAL, **74**, 483 (1952).

(2) I. L. Chaikoff, M. D. Siperstein, W. G. Dauben, H. L. Bradlow, J. F. Eastham, G. M. Tomkins, J. R. Meier, R. W. Chen, S. Hotta and P. A. Srere, *J. Biol. Chem.*, **194**, 413 (1952).

(3) R. B. Turner, THIS JOURNAL, **72**, 579 (1950).

(4) J. Ashmore, W. H. Elliott, E. A. Doisy, Jr., and E. A. Doisy, *J. Biol. Chem.*, **200**, 661 (1953).

(5) M. Gut, *Helv. Chim. Acta*, **36**, 906 (1953).

(6) R. D. H. Heard and P. Ziegler, THIS JOURNAL, **72**, 4328 (1950).

(7) B. Belleau, Thesis, McGill University, 1950.

(8) (a) G. I. Fujimoto, THIS JOURNAL, **73**, 1856 (1951); (b) G. I. Fujimoto and J. Prager, *ibid.*, **75**, 3259 (1953).

(9) R. D. H. Heard and P. Ziegler, *ibid.*, **73**, 4036 (1951).

(10) A. L. Wilds and C. H. Shunk, *ibid.*, **70**, 2427 (1948).

(11) T. Reichstein and H. G. Fuchs, *Helv. Chim. Acta*, **23**, 676 (1940).

(12) J. R. Jamieson, unpublished data from these laboratories.