the tetrahydropyranylation of alcohols possessing acid-sensitive functional groups such as allylic hydroxyl, ketal, or epoxide (entry 3, 4, 8, and 9). PPTS would also be efficient for the methoxytetrahydropyranylation of alcohols.[6,10]

PPTS is efficient not only for the preparation of THP ethers but also for the deprotection of THP groups. The typical procedure is as follows.

A solution of geraniol THP ether (119 mg, 0.5 mmol) and PPTS (12.6 mg, 0.05 mmol) in ethanol (4 mL) was stirred at 55 °C (bath temperature) for 3 h. The solvent was evaporated in vacuo, and the residue was chromatographed on a silica gel column to afford pure geraniol (77 mg, 100%).

As shown by the results in Table I, the protecting group is quantitatively removed with this catalyst. Owing to its simplicity and mildness, the present procedure provides a highly efficient method for the preparation and deprotection of THP ethers.

Registry No.—PPTS, 24057-28-1; dihydropyran, 110-87-2; *p*-toluenesulfonic acid, 104-15-14; pyridine, 110-86-1.

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(8) PPTS is easily prepared as follows; *p*-toluenesulfonic acid monohydrate (5.70 g, 30 mmol) was added to pyridine (12.1 mL, 150 mmol) with stirring at room temperature (slightly exothermic). After stirring for 20 min, the excess of pyridine was removed with a rotary evaporator on a water bath at ca. 60 °C to afford a quantitative yield of PPTS as slightly hygroscopic colorless crystals. Recrystallization from acetone gave the pure salt (6.8 g, 90%), $C_{12}H_{13}NO_3S$, mp 120 °C.
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Reactivity of Photochemically Excited 3-Acylthiophenes, 3-Acylfurans, and the Formylthiophenes and Furans

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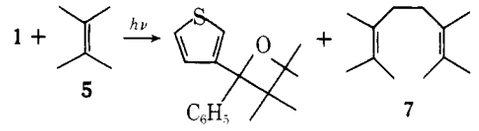
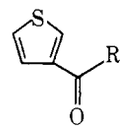
Recently I reported details of the photochemical reactions of 2-acetyl- and 2 benzoylthiophenes and furans with various alkenes.[1] The emission spectra of the four compounds indicated the lowest triplet to be of $\pi \rightarrow \pi^*$ character in each case. Consonant with this observation, the major photoprocess observed for the 2-acetyl derivatives was addition at ring positions, in a 4 + 2 fashion in the case of thiophene, and in the 2 + 2 manner for the furan. Surprisingly, the benzoyl compounds undergo oxetane formation to the complete exclusion of ring addition;[1,2] the reasons for this are not clear.

It has been observed by Arnold and Birtwell[3] that 3-benzoylthiophene and certain para-substituted derivatives thereof exhibit emission spectra indicative of $n \rightarrow \pi^*$ lowest triplet states, in contrast to the $\pi \rightarrow \pi^*$ assignment for the 2-benzoyl compounds. Consequently, a study of the photochemical reactions of 3-furyl and 3-thienyl ketones was deemed worthwhile. Although the behavior of the 3-substituted ketones proved to be relatively unexciting, we present our results here for comparison.

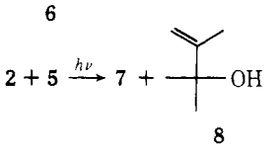
Irradiation of 3-benzoylthiophene (1) in the presence of excess 2,3-dimethyl-2-butene (**5**) gave, besides gum and recovered **1**, 28% of oxetane **6**. There was formed also 30% of a



5 **6** **7**



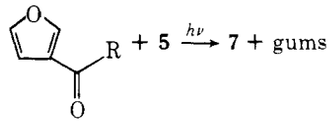
1, R = C_6H_5
2, R = CH_3



8

mixture of C_{12} hydrocarbons, mainly 2,3,6,7-tetramethylocta-2,6-diene (**7**), as was found in photochemical reactions of benzoic acid and its esters with the same alkene.[1,4,5]

Irradiation of 3-acetylthiophene (**2**) with alkene **5** afforded no oxetane or other cycloadducts, but instead afforded alcohol **8**, 2,3-dimethyl-1-buten-3-ol (17%), pinacol (12%), and 16% of the now familiar C_{12} hydrocarbon mixture. The pinacol most plausibly arises via 2 + 2 cycloreversion of the anticipated (but not observed) oxetane to acetone and an alkene analogous to **12** (vide infra). The acetone undergoes photoreduction of pinacol. The formation of **8** may be the result of either (a) dehydration of some of the pinacol produced, or (b) hydrogen abstraction of photoexcited **2**, followed by reaction of the dimethylbutenyl radical with traces of water in the solvent. Since the solvents employed were spectrograde, stored over molecular sieves, path (b) seems less likely. Since the publication of ref 4 and 5, alcohol **8** has been observed as a



3, R = C_6H_5
4, R = CH_3

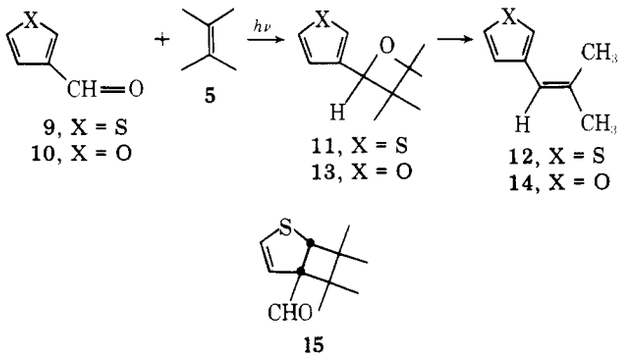
minor product sometimes present in the reaction mixtures from benzoic acid and methyl benzoate with **5**.[4,5]

Irradiation of 3-benzoylfuran (**3**), through uranium glass in the presence of an excess of alkene **5**, resulted only in slow decomposition to translucent gums; the only tractable product isolated was 14% of hydrocarbon **7**.

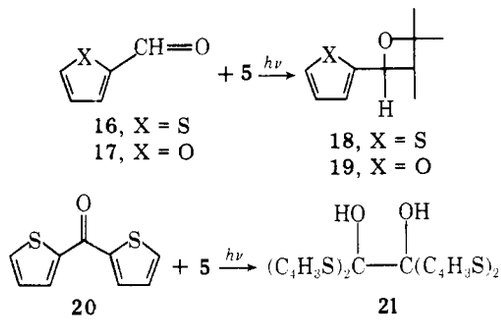
Irradiation through Pyrex of 3-acetylfuran (**4**) with either alkene **5** or furan for 18 h gave only 80% of recovered **4**, and in the experiments with **5**, 17% of hydrocarbon **7** and 11% of alcohol **9**.

The aldehydes 3-formylthiophene (**9**) and 3-formylfuran (**10**) proved to be considerably more reactive than the ketones **1–4**. Irradiation of **9** in the presence of excess 2,3-dimethyl-2-butene and separation of the products by GC afforded alkene 12 ($\Phi = 0.11$), the product of 2 + 2 cycloreversion of an initially formed oxetane, **11**, in the reverse sense to that via which it was formed, and also 2 + 2 ring adduct **15** (9%).

Irradiation of **10** under similar conditions, followed by GC purification, led to oxetane **13** as the sole product formed in 54% chemical yield (Φ = 0.12).



This facile addition across the carbonyl group of aldehydes **9** and **10** was in distinct contrast to the ketones **1–4**; consequently the 2-formyl compounds **16** (thiophene-2-aldehyde) and **17** (furfural) were examined. Both aldehydes underwent



clean oxetane formation with alkene **5** (even to the extent of the products being pure after a simple distillation, obviating the need for GC purification) in high efficiency. Spectral details are given in Table I.

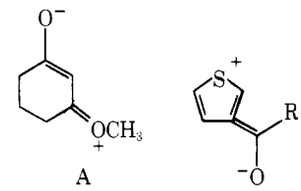
Finally, we include the results with di-2-thienyl ketone (**20**) and di-2-furyl ketone. The thienyl ketone **20** surprisingly gave neither oxetane nor cyclobutane, but instead the pinacol **21**, whereas **22** only decomposed to gums.

Thus the 3-acylthiophenes and 3-acylfurans examined (**1–4**) were found to be far more sluggish in their photochemical reactivity toward alkenes than the 2-acyl heterocycles which we had studied previously.[1] Furthermore, three of the four compounds yielded products derived only from radicals produced by hydrogen abstraction from the substrate alkene. This was surprising, especially for 3-benzoylthiophene, for that is the opposite of the behavior to be expected of an aryl ketone with the lowest lying n,π^* triplet excited state, to which category 1 had been assigned by Arnold and Birtwell.[3] One way of rationalizing the pronounced photochemical inertness of **1–4** may be in considering the similarity of their excited states to those of 2-cyclohexen-1-ones bearing in the 3 position groups capable of electron donation via resonance, such as methoxyl. These compounds, including 3-chloro- and 3-alkoxycyclohexenones, were previously found to be very slow in reacting with alkenes or with solvents containing abstractable hydrogen;[6] cycloadducts were minor products, when formed at all. This difference in behavior was attributed to the effect of the substituent on the electron distribution in the excited state. The nature of the ground state of such enones is perturbed as compared to that of simpler enones because of significant contribution from resonance structures of type A. It seems reasonable that the excited states of both the cyclohexenones and heterocycles **1–4** have considerably less 1,4-diradical character than those of the parent ketones. This

Table I

Oxetane	NMR signals		Mass spectra
13	2.6 (2 H, m) 3.7 (1 H, m, br) 4.7 (1 H, s)	8.56, 8.74, 8.83, 9.13 (3 H each, s)	*m/e* 181, 180 (CI) Base peak at 122 (EI)
18	2.6 (1 H, t, *J* = 2.4) 2.9 (1 H, t) 3.4 (1 H, m) 4.8 (1 H, s)	8.52, 8.71, 8.82, 9.10 (3 H each, s)	*m/e* 197, 196 (CI)
19	2.6 (2 H, t, *J* = 1.6 3.68 (1 H, d, *J* = 1.6) 4.86 (1 H, s)	8.57, 8.64, 8.85, 9.04 (3 H each, s)	*m/e* 181, 180 (CI)

effect should cause a reduced reactivity toward hydrogen abstraction or toward bonding to alkenes.



This, however, fails to account for the difference in reactivity of the heterocyclic ketones **1–4** and aldehydes **9–10**. All four of the aldehydes examined underwent efficient oxetane formation with **5** (for **9**, Φ = 0.3 at infinite substrate concentration), whereas the only ketone studied, either in the present report or in ref 1, to react with **5** with $\Phi > 0.02$ is 2-benzoylthiophene. In the carbocyclic series, benzaldehyde, acetophenone, and benzophenone undergo 2 + 2 cycloaddition to alkenes to afford oxetanes, all doing so with fairly high efficiency.[8] The reasons for the differences in the carbocyclic series and the heterocycles are evidently a blend of subtle electronic factors whose nature remains to be determined.

Experimental Section

Irradiations were conducted in an annular apparatus using light from a Hanovia 450-W medium-pressure mercury arc lamp, filtered through Corex (transmits >260 nm), Pyrex (>290 nm), or uranium glass (>330 nm), and cooled by ice water in an immersion well. All photochemical reaction solutions were flushed with argon for 1 h prior to irradiation. NMR spectra were obtained on Varian A-60 and XL-100 instruments. Mass spectra were obtained on a Hitachi Perkin-Elmer Model RMU-6E. Gas chromatography was performed on the following columns: column A, 2 ft × 0.25 in., 10% SE-30 on Chromosorb W; column B, 2 ft × 0.25 in., 15% Carbowax 20M on Chromosorb W; column C, 6 ft × 0.25 in., 10% SE-30; column D, 6 ft × 0.25 in., 15% Carbowax 20M; and column E, 6 ft × 0.375 in., 25% SE-30. Ketones **1–4** were prepared by reaction of the appropriate heterocyclic carboxylic acid with phenyl- or methyllithium.[9]

Photochemical Reaction of 3-Benzoylthiophene with 2,3-Dimethyl-2-butene. A solution of 3-benzoylthiophene (1.5 g) and 2,3-dimethyl-2-butene (20 g) in spectrograde hexane (100 mL) was irradiated in a Rayonet chamber equipped with 3500-Å lamps for 1.5 h. Distillation of the solvent and excess alkene gave a semicrystalline residue which was triturated with pentane at 0–5 °C and filtered. Recrystallization of the solid from ethyl acetate–hexane gave oxetane **6** as off-white prisms, mp 92 °C dec (0.60 g, 27%). Spectral data: IR (KBr) 1080–1005 cm^{-1}; NMR ($CDCl_3$) τ 2.3–2.9 (8 H, m), 8.64, 8.72, 8.89, and 9.02 (all 3 H each, s); *m/e* (chemiionization) 273 (P + 1), 214 (20), 189 (45), 105 (25), 84 (100). Anal. $C_{17}H_{20}OS$: (C, H).

From the mother liquors and triturate there was recovered unchanged **1** (0.38 g) plus a tarry residue.

Photochemical Reaction of 3-Acetylthiophene (2) with 2,3-Dimethyl-2-butene. A solution of 3-acetylthiophene (**2**, 1.0 g) and 2,3-dimethyl-2-butene (20 g) in spectrograde hexane (100 mL) was

irradiated through uranium glass for 30 h. Fractional distillation of the reaction mixture gave, besides 0.33 g of recovered **2**, an oil, bp 36–54 °C (0.8 mm), from which was isolated by GC on column B the following products: 0.070 g of 2,3,6,7-tetramethylocta-2,6-diene (**7**), identical with material isolated in other studies;[1,4] and 0.086 g (17%) of alcohol **8**, 2,3-dimethyl-1-buten-3-ol [IR (film) 3580 cm^{-1}; NMR (CCl_4) τ 5.2 (2 H, s, br), 8.02 (1 H, s, br), 8.3 (3 H, s, br), 8.56 (6 H, s); Anal. $C_6H_{12}O$ (C, H)].

Irradiation of 3-Benzoylfuran and 3-Acetylfuran with Alkene 5. Irradiation of hexane solutions of 3-benzoylfuran (**3**)[9] with excess alkene **5** through uranium glass filters for up to 40 h gave yellow solutions from which 10–20% of diene **7** could be isolated by vacuum distillation. Chromatography of the residue on silica gel gave only ~30% of recovered **3** and high molecular weight material.

From similar experiments with **4**, using a Pyrex filter, there was isolated ~70% of recovered ketone, together with 17% of **7**, 11% of **8**, and small amounts of tarry residue.

Photolysis of 3-Formylthiophene (9) with 2,3-Dimethyl-2-Butene. Irradiation of **9** (1.4 g, 0.012 mol) with alkene **5** (20 g) in spectrograde hexane through Pyrex for 2.5 h led to complete consumption of aldehyde. Workup as described above for **2** led to the isolation of (a) alkene **12** (retention time on column B at 110°, 5.8 min.) in 46% yield [IR (film) 1080 cm^{-1}; NMR τ 2.7–3.1 (3 H, m), 3.7 (1 H, m, br), 8.0 (6 H, s, br); mass spectrum (CI) *m/e* 138 (P, 100), 133 (72), 121 (67); Anal. $C_8H_{10}S$ (C, H)], and (b) 2 + 2 ring adduct **15** (retention time 16 min) [IR (film) 1720 cm^{-1}; NMR τ 3.7 (1 H, m), 3.9 (2 H, m, br), 6.8 (1 H, s), 8.45, 8.69, 8.80, and 8.82 (3 H each, s); mass spectrum *m/e* 196 (P, 7), 181 (19), 112 (47), 84 (100); Anal. $C_{11}H_{16}OS$ (C, H)].

The photochemical reactions of aldehydes **10**, **16**, and **17** with **5** were conducted in the same manner. Spectral data on the products are given in Table I.

Photochemical Reaction of Di-2-thienyl Ketone with 2,3-Dimethyl-2-butene. A solution of ketone **20** (1.0 g) and alkene **5** (20 g) in spectrograde hexane was irradiated through a uranium glass filter for 6 h. Evaporation of solvent and excess alkene gave a yellow residue which, on trituration with 3:1 hexane–benzene, partially crystallized. Recrystallization of the solid from benzene–hexane gave 0.56 g of white prisms: mp 127–128 °C; IR (KBr) 3500 cm^{-1}; NMR ($CDCl_3$) τ 2.6–3.2 (12 H, m), 6.49 (2 H, s, br); mass spectrum *m/e* 310 (P, CI). Anal. $C_{18}H_{14}O_2S_4$ (C, H).

Acknowledgments. The author is grateful to William Landis of the National Institutes of Health for the mass spectra of the new compounds reported herein, and to the referees for suggestions.

Registry No.—**1**, 6453-99-2; **2**, 1468-83-3; **3**, 6453-98-1; **4**, 14313-09-8; **5**, 563-79-1; **6**, 63466-41-1; **7**, 18495-18-6; **8**, 10473-13-9; **9**, 498-62-4; **10**, 498-60-2; **12**, 63466-42-2; **13**, 63466-43-3; **15**, 63466-44-4; **16**, 98-03-3; **17**, 98-01-1; **18**, 63466-45-5; **19**, 63466-46-6; **20**, 704-38-1; **21**, 51248-22-7.

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Deuterium or Tritium Labeling by Ionic Hydrogenation. A Convenient Route to Specifically Labeled Dethiobiotin

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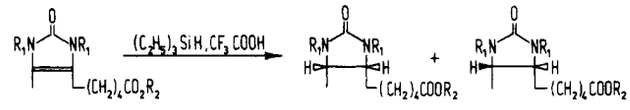
In connection with our investigation of the biosynthetic conversion of dethiobiotin to biotin, we had to synthesize specifically C-3 and/or C-4 deuterated and tritiated *cis*-dethiobiotin.[1] One convenient route was the reduction of the unsaturated precursor 4-methyl-5-(ω-carboethoxyamyl)-2-imidazolone (**1a**).[2] After a thorough investigation we found that ionic hydrogenation was the only efficient noncatalytic method to reduce the carbon–carbon double bond of the imidazolone ring.[3]

Scheme I



1a, R_1=H; R_2=C_2H_5
1b, R_1=Ac; R_2=C_2H_5

2a, R_1=H; R_2=C_2H_5
2b, R_1=Ac; R_2=C_2H_5
2c, R_1=H; R_2=H

3a, R_1=H; R_2=C_2H_5
3b, R_1=Ac; R_2=C_2H_5
3c, R_1=H; R_2=H

This paper reports our study of the scope of this reduction and observations regarding the stereoselectivity of the reaction and regioselectivity of the labeling with deuterated silanes.

We also explore the possibility of using the different combinations of hydrogenating pairs CF_3COOH, CF_3COOD, R_3SiH, and R_3SiD to invert the labeling regioselectivity or to prepare dideuterated compounds. The corresponding tritiated compound has been obtained with Et_3Si^3H. Reductions with Et_3Si^3H which have not yet been performed appear of general interest for specific tritiation of organic molecules.

Results and Discussion

Stereoselectivity. Since our goal was to obtain *cis*-dethiobiotin, we investigated the factors which might influence the course of hydrogenation and lead to the desired isomer (Table I).

1a treated with 1 equiv of Et_3SiH or Et_3SiD in CF_3COOH at 50 °C afforded in 70% yield a 1/1 mixture of *cis*- and *trans*-(*dl*) dethiobiotin ethyl ester (**2a** and **3a**) (run 1, see also Scheme I).

These isomers have been separated by TLC as *N*-diacetyl derivatives **2b** and **3b**. The cis isomer **2b** has been identified after treatment with sodium hydroxide by comparison with an authentic sample of dethiobiotin obtained by Raney nickel desulfuration of biotin.[4] The structure of the trans isomer **3b** was based on NMR and mass spectral data (see Experimental Section).[5] We also carried out, with the same hydrogenating pair, the reduction of the *N,N'*-diacetyl derivative **1b** (run 2), the double bond of which is more reactive because of the dearomatization of the imidazolone ring.[6] In this case, we observed an important variation of the stereoselectivity with a high predominance of the cis isomer (cis/trans: 95/5). The same variation in isomer ratio is observed for reductions of 3,4-dimethyl-2-imidazolone (**4a**) and its *N,N'*-diacetyl derivative **4b** (runs 6, 7).

On the other hand, the variation of steric bulk of the different hydride donors tested, Et_3SiD, Ph_3SiD, Ph_2SiD_2, and Ph_3GeD, does not lead to significant variations (runs 2–5).

Since examination of molecular models shows that the acetyl groups in **1b** and **4b** do not increase significantly, with respect to **1a** and **4a**, the steric discrimination between the two faces of the imidazolone ring, our results clearly show that steric interaction between the intermediate carbenium ion and hydride donor is not the major factor governing the stereochemistry of ionic hydrogenation as previously claimed.[7a,8]

Regioselectivity. In order to select the best conditions for specific incorporation of deuterium at C-3 and/or C-4, we carried out reduction of **1a** and **1b** using hydride donors of different donating ability and steric bulk.[7a,9]

Some results are listed in Table II. In runs 1–4 the isolated dethiobiotin has incorporated, as expected, only one deuterium atom (mass spectrometry determination). There is al-