Table IV. Calculated Deuterium Exchange Rate Constant (min^{-1}) of Indole Ring Hydrogens of Tryptamine Derivatives[a]

Ring substitution	H-2	H-4	H-5	H-6	H-7
5-OH	9.4×10^{-4}	6.5×10^{-2}		2.5×10^{-3}	
5-CH_3	5.4×10^{-4}	3.6×10^{-4}		2.0×10^{-4}	
6-OH	1.9×10^{-2}		1.5×10^{-2}		3.5×10^{-2}
H	6.4×10^{-4}	6.6×10^{-6}	1.8×10^{-4}	3.4×10^{-5}	2.6×10^{-5}

[a] In 1.0 N DCl at 25 °C.

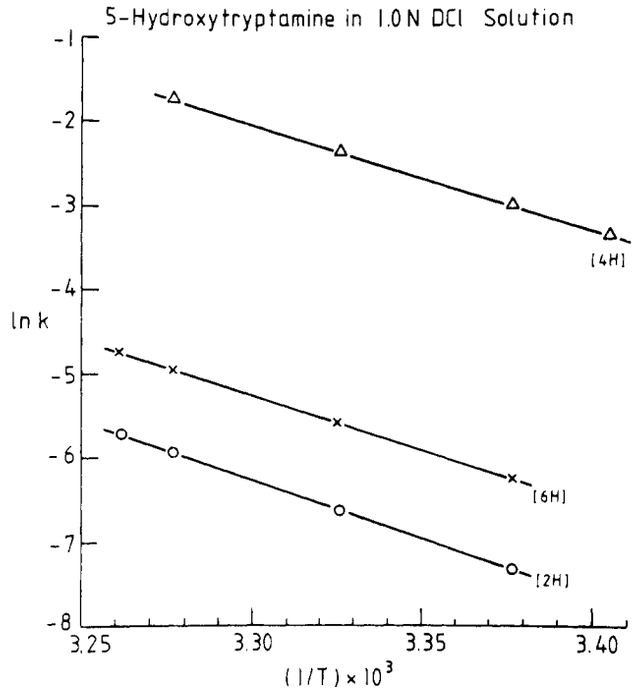

Figure 6. Arrhenius plot of the first-order rate constants of deuterium exchange of 5-hydroxytryptamine.

$Ae^{-\Delta E^{\ddagger}/RT}$ (Table II). It has been observed in these experiments that the first-order rate constants exponentially increase with increasing negative acidity function, $-H_0$,[9-12] of deuterium chloride, yielding the relationship, $k = k_0 e^{-H_0 x}$, where χ is a slope giving the value 2.45, and k_0 is the rate constant at the zero acidity function (Figure 5). It has been shown in these experiments that χ is independent of both ring proton species and temperature. The Arrhenius activation energy, $\Delta E^{\ddagger}$, for the deuterium exchange of the indole ring protons also shows a constant value of about 26 kcal/mol (Figure 6 and Table III). The constant values of these two parameters ($\chi = 2.45$ and $\Delta E^{\ddagger} = 26$ kcal/mol) for all species investigated ensure the validity of the temperature-independent Brønsted catalysis law ($\ln k = \alpha + \beta \ln K$),[13-15] where k and K represent the rate constant and equilibrium constant, respectively. Under these two conditions the logarithm of the rate constants then should be proportional to the stability of the ring-protonated aromatic conjugate acids.

Structural analysis shows that the deuterium exchange rate constants correlate with the stability of the resonance structure of the indole ring protonated conjugate acid (Table IV). These observations provide a basis for the validity of the Brønsted catalysis law in the protonation of the indole ring.

Experimental Section

5-Hydroxytryptamine creatine sulfate, 5-hydroxytryptamine bioxalate, 6-hydroxytryptamine creatine sulfate, 5-methyltryptamine, and tryptamine hydrochloride were purchased from Sigma Chemical Co., and used without further purification. Deuterium oxide and deuterium chloride were obtained from ICN Isotope and Nuclear Division. Throughout the experiments, 0.05 M solutions were prepared by dissolving the sample in DCl/D_2O solution of a known concentration, transferred quickly to the NMR tube, and equilibrated for few minutes in thermostated sample holder. When the temperature of measurement is significantly different from the room temperature, the samples were prepared in a water bath of desired temperature.

The 220-MHz NMR spectra were obtained in Fourier transform mode using a Varian HR 220 spectrometer equipped with a variable temperature unit and Nicolet Technology Corp. (NTC) pulse and Fourier transform accessories. A single 90° pulse was used to obtain each spectrum (2500 Hz sweep width and 8192 computer data points). There was sufficient time between successive spectral acquisitions to allow for proton relaxation. Chemical shifts are reported in parts per million (ppm) relative to internal TSP [3-(trimethylsilyl-2,2,3,3,-d_4)propionic acid sodium salt), and peak integrations were determined with the aid of the NTC NMR program. The collected data were analyzed using a simple regressional analysis method.

Acknowledgment. This research was supported by a Grant (MH-17489) from the National Institute of Mental Health. The 220-MHz NMR facilities at the Rockefeller University operated by a consortium are supported by a National Science Foundation Grant (BMS 74-12247).

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Pyridinium *p*-Toluenesulfonate. A Mild and Efficient Catalyst for the Tetrahydropyranylation of Alcohols

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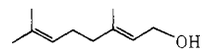
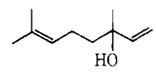
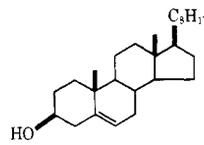
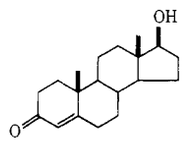
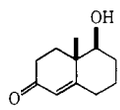
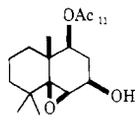
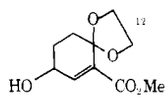
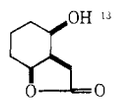
Tetrahydropyranylation of hydroxyl groups has been recognized as the useful and representative method for the protection of alcohols.[2] In addition, it has recently been shown that 2-tetrahydropyranyl (THP) ethers are important pre-

Table I. Tetrahydropyranylation of Alcohols and Hydrolysis of Tetrahydropyranyl Ethers with Pyridinium *p*-Toluenesulfonate

			Tetrahydropyranylation[a]			Hydrolysis of THP ethers[a]	
Registry no.	Entry	Alcohol	Reaction time, h	Isolated yield,[b] %	Registry no.	Reaction time, h	Isolated yield,[b] %
112-53-8	1	$CH_3(CH_2)_{11}OH$	3.5	96	63588-79-4	3	99
108-93-0	2		5.5	97	709-83-1	3.5	96
106-24-1	3		4	99[c]	59632-99-4	3	100
78-70-6	4		5	94	38844-76-7	1.5	99
57-88-5	5		5	97	6252-45-5	4	99
58-22-0	6		5.5	100[d]	516-63-2	3.5	98
878-47-7	7		4.5	99[d]	6252-45-5	3.5	95
52612-30-3	8		3	100[d]	516-63-2	3.5	98
63588-78-3	9		3	97	63588-80-7		
54911-63-6	10					3	100

[a] All of products showed satisfactory microanalytical values and spectral data. [b] Purified by silica gel chromatography unless otherwise stated. [c] Purifield by distillation. [d] Two equivalents of dihydropyran and 0.2 equiv of PPTS were used.

cursors for the synthesis of primary[3] and allylic alcohols,[4] and alkyl halides.[5]

For the tetrahydropyranylation of alcohols, *p*-toluenesulfonic acid is the most common catalyst and seems to be superior to other catalysts[6] such as hydrochloric acid,[2] phosphoryl chloride,[2] and boron trifluoride etherate.[7] Owing to its strong acidity, however, *p*-toluenesulfonic acid is still undesirable for highly acid-sensitive alcohols. We wish to report a much more efficient preparation of THP ethers from alcohols by the use of a new catalyst, pyridinium *p*-toluenesulfonate (PPTS).

Crystalline PPTS can easily be prepared from pyridine and *p*-toluenesulfonic acid monohydrate.[8] It is soluble in methylene chloride, chloroform, ethanol, and acetone, and slightly soluble in benzene but insoluble in ether. The procedure for the tetrahydropyranylation is remarkably simple and mild. The following is illustrative.

A solution of geraniol (154 mg, 1.0 mmol) and dihydropyran (126 mg, 1.5 mmol) in dry methylene chloride (7 mL) containing PPTS (25 mg, 0.1 mmol) is stirred for 4 h at room temperature. Then the solution is diluted with ether and washed once with half-saturated brine to remove the catalyst. After evaporation of the solvent, distillation [bp 140 °C (bath temperature)/10 mmHg] gives an essentially quantitative yield of geraniol THP ether (236 mg, 99%).

The results are summarized in Table I. The excellent yields realized in the present procedure demonstrate this catalyst to be superior to other catalysts. For example, testryl THP ether (entry 6) which was recently prepared in moderate yields using boron trifluoride etherate (67%)[7] or *p*-toluenesulfonic acid (71%)[6] is obtained quantitatively with our catalyst. Furthermore, THP ether of 4aβ-methyl-4,4a,5,6,7,8-hexahydronaphth-5β-ol-2(3*H*)-one (entry 7), which has frequently been used as the useful synthetic intermediate, was previously prepared in the reaction of long duration (2 days) in only 48% yield using hydrochloric acid as the catalyst,[9] while the present procedure affords it in 99% isolated yield after only 4.5 h.

It is noteworthy that PPTS is a weaker acid (pH 3.0 in 1.0 M aqueous solution) than acetic acid (pH 2.4 in 1.0 M aqueous solution). Consequently, our catalyst is mild enough to be used on complex systems containing sensitive polyfunctional groups. Thus, we have encountered no serious difficulty for

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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(13) For the THP ether of this alcohol, see P. A. Grieco, N. Marinovic, and M. Miyashita, *J. Org. Chem.*, **40**, 1670 (1975).

Reactivity of Photochemically Excited 3-Acylthiophenes, 3-Acylfurans, and the Formylthiophenes and Furans

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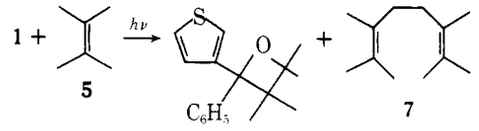
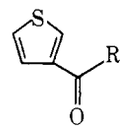
Recently I reported details of the photochemical reactions of 2-acetyl- and 2 benzoylthiophenes and furans with various alkenes.[1] The emission spectra of the four compounds indicated the lowest triplet to be of $\pi \rightarrow \pi^*$ character in each case. Consonant with this observation, the major 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.

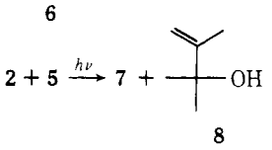
Irradiation of 3-benzoylthiophene (1) in the presence of excess 2,3-dimethyl-2-butene (**5**) gave, besides gum and recovered **1**, 28% of oxetane **6**. There was formed also 30% of a



5 **6** **7**



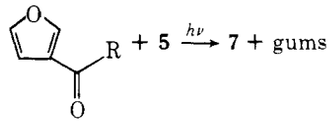
1, R = C_6H_5
2, R = CH_3



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%).