Benzotriazole-Mediated Conversions of *para*-H-Substituted Pyrylium, Benzo[*b*]pyrylium, and Xanthylium Salts into *para*-Position Functionalized Derivatives (An Indirect Electrophilic Substitution of Electron-Deficient Heteroaromatics)

Alan R. Katritzky,[*,§] Peter Czerney,[‡] and Julian R. Levell[§]

Center for Heterocyclic Compounds, Department of Chemistry, University of Florida,
Gainesville, Florida 32611-7200, and Institut für Physikalische Chemie,
Friedrich Schiller-Universität Jena, Lessingstrasse 10, D 07743 Jena, Germany

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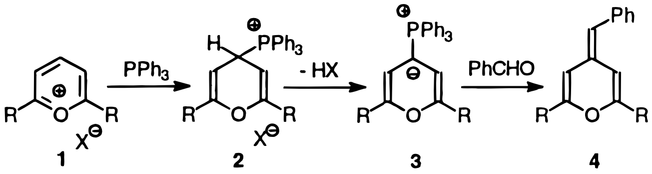
4*H*-Substituted pyrylium **9**, benzo[*b*]pyrylium **15**, and xanthylium salts **22** react with benzotriazole to give the corresponding 4*H*-(benzotriazol-1-yl)pyrans **10**, benzo[*b*]pyrans **16**, or xanthenes **23**. Novel anion precursors **10**, **16**, and **23** undergo smooth lithiations at the positions α to the benzotriazol-1-yl function, *i.e.*, at the *para*-position of the *O*-heterocycle. Subsequent trapping with different alkyl halides gives intermediates **14**, **21**, and **25**, which are converted by mineral acid into *para*-functionalized pyrylium **11**−**13**, benzo[*b*]pyrylium **17**−**20**, and the xanthylium **24** salts in good to excellent yields.

Introduction

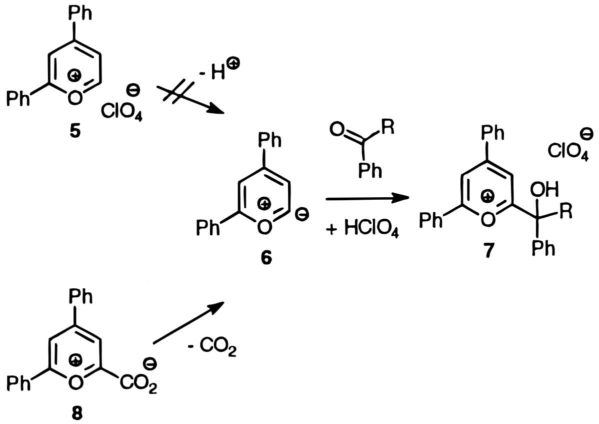
Positively charged *O*-heterocycles such as pyrylium,[1] benzo[*b*]pyrylium,[2] and xanthylium salts[3] are good electrophiles that readily undergo reactions with nucleophiles but resist electrophilic attack. Various attempts to generate six-membered rings carrying eight π-electrons, which have inverse reactivity (Umpolung) and should be capable of substitution by electrophiles, have been reported, but such systems are rarely stable for steric and electronic reasons. Thus, Krivun and co-workers investigated the reactions of various 4*H*-substituted pyrylium and benzo[*b*]pyrylium salts with triphenylphosphine as well as with di- and triethyl phosphite.[4] The first step of all these reactions, see, *e.g.*, **1** → **2** (Scheme 1), is the addition of the phosphorus nucleophile at the 4-position, resulting in a *P*-substituted 4*H*-pyran. On treatment with a strong base, **2** can be deprotonated at the 4-position to form an eight π-electron system, *cf.* **3**, *in situ*. These compounds form bipyranylidenes *via* intermolecular condensation and elimination of the *P*-substituent. Aryl aldehydes were also used as electrophiles in Wittig-type reactions to form 4-alkylidenepyrans, *cf.* **4**.[5]

4*H*-Pyrans, whether unsubstituted or substituted in the 4-position with aryl groups, have a low tendency to be transformed into systems formally containing eight π-electrons. Reaction of BuLi/THF with 4*H*-pyrans at −80 to −120 °C produces blue-violet solutions, containing only small amounts of the pyranyl anions, as measured by deuteration.[6] Nor is direct deprotonation of pyrylium salts (**5** → **6**) known, although 2-(hydroxymethyl)-substituted pyrylium salts **7** have been reported by reactions of 2-carboxypyrylium salts **8** with aldehydes *via* a decarboxylated intermediate **6** (Scheme 2).[7] 4-Alkyl-substituted pyrylium species have been synthesized by photoinduced radical reactions of pyrylium salts with alkylstannanes.[8]

Scheme 1



Scheme 2



We now report that the easily prepared pyrylium **9**, benzo[*b*]pyrylium **15a**−**d**, and xanthylium **22** salts undergo facile nucleophilic addition of benzotriazole in the 4-position. Subsequent deprotonation, reaction with an electrophile, and final loss of benzotriazole anion, as outlined in Schemes 3−5, provides a convenient alternative to the sequences of Schemes 1 and 2. Benzotriazole

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[§] University of Florida.

[‡] Friedrich Schiller-Universität Jena.

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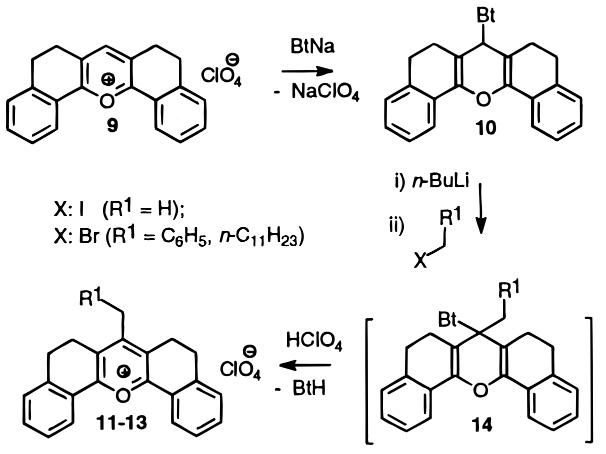
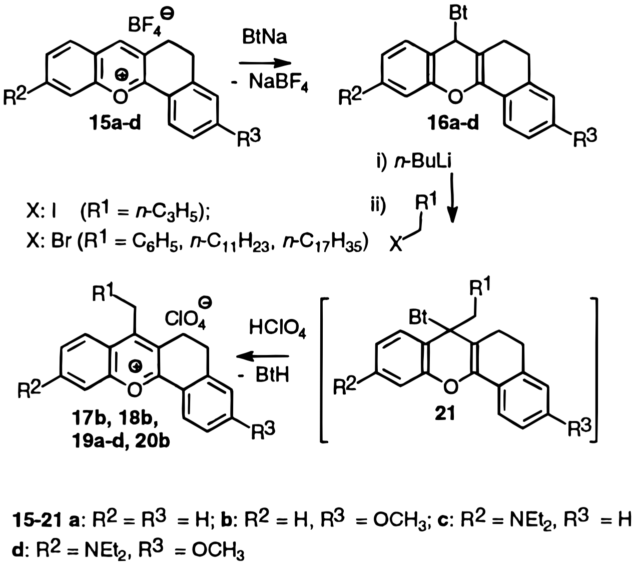
Scheme 3



11: R^1 = H; **12**: R^1 = C$_6$H$_5$;
13: R^1 = n-C$_{11}$H$_{23}$

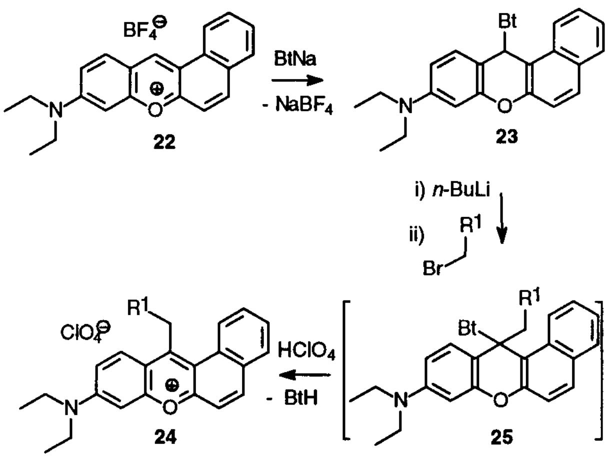
Scheme 4



15-21 a: R^2 = R^3 = H; **b**: R^2 = H, R^3 = OCH$_3$; **c**: R^2 = NEt$_2$, R^3 = H; **d**: R^2 = NEt$_2$, R^3 = OCH$_3$

17: R^1 = C$_6$H$_5$; **18**: R^1 = n-C$_3$H$_5$; **19**: R^1 = n-C$_{11}$H$_{23}$; **20**: R^1 = n-C$_{17}$H$_3$

Scheme 5



24 : R^1 = n-C$_{11}$H$_{23}$

is well-known to act as both a good anion-stabilizing group and a good leaving group.[9] Herein, we utilize both of these opportunities of benzotriazole chemistry to realize a general method for electrophilic substitution at the *para*-position to the oxygen of pyrylium, benzo[*b*]pyrylium, and xanthylium salts.

The syntheses of the 4*H*-(1*H*-benzotriazol-1-yl)-1-pyrans **10**, benzo[*b*]pyrans **16a**–**d**, and xanthenes **23** proceed under mild conditions at room temperature, giving as products only the benzotriazol-1-yl isomers. Nearly quantitative yields were obtained by using THF as solvent and NaH as base. Compounds **10**, **16a**–**d**, and **23** are colorless, crystalline, and stable to neutral and basic conditions but easily eliminate benzotriazole to regenerate the colored, highly fluorescent salts **9**, **15**, and **22**, respectively, upon treatment with even weak acids. The full absorption and fluorescence spectral characterization of compounds **9** and **15** has been published.[10]

All attempts at one-pot, three-component reactions using 2-hydroxyaryl aldehyde, aryl methylene ketone, and benzotriazole gave, at best, very low yields of **16** (isolated after column chromatography), even though there was some literature precedent for analogous condensations.[11]

Results and Discussion

4*H*-(1*H*-Benzotriazol-1-yl)-1-pyrans **10**, benzo[*b*]pyrans **16**, and xanthenes **23** were treated with a strong base (n-butyllithium) in dry THF at low temperature (−78 °C) to remove the α-proton. The generated eight π-electron heterocyclic anions, which show in THF solution deep blue colors, were trapped by a variety of electrophiles to give intermediates **14**, **21**, and **25**. Without isolation, these intermediates were treated with mineral acids (usually perchloric acid) to induce removal of the benzotriazole and generate pyrylium salts **11**–**13**, benzo[*b*]pyrylium salts **17b**, **18b**, **19a**–**d**, or **20b**, or the xanthylium salt **24** in good to excellent yields.

Varying the chain length of the electrophile, we synthesized as examples 4-methyl-, 4-benzyl-, 4-(n-butyl)-, 4-(n-dodecyl)-, and 4-(n-octadecyl)pyrylium, benzo[*b*]pyrylium, and xanthylium salts. 4-Methyl- and 4-arylpyrylium and 4-methyl- and 4-arylbenzo[*b*]pyrylium salts are known and can be synthesized by condensations of various acetaldehydes or aryl aldehydes and aryl methylene ketones (pyrylium salts).[1] Starting materials for 4-substituted benzo[*b*]pyrylium salts are 2-hydroxyaryl methyl ketones or 2-hydroxyaryl aryl ketones together with aryl methylene ketones.[2] Significantly, *O*-heterocycles of types **13**, **19**, **20**, and **24** with a long-chain alkyl group in the *para*-position to the oxygen of the heterocycle were not previously described. However, Balaban *et al.* have recently reported the synthesis of pyrylium salts with long alkyl chains in the 2- and 6-positions by standard methods, in 22% yield.[12] Our new methodology allows the synthesis of hitherto unknown long-chain derivatives in good to excellent yields.

Aryl aldehydes (p-tolylaldehyde) and ketones (benzophenone) have also been used as electrophiles but gave a complex mixture of products. Attempts to use cyclic ketones (cyclopentanone and cyclohexanone) as electrophiles in these reactions were also unsuccessful, the only products isolated being the parent unsubstituted pyry-

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Table 1. Yields, Melting Points, and Elemental Analysis Data of 10−13, 15−20, and 22−24

				anal. calcd (%)			found (%)		
compd	yield (%)	mp (°C)	molecular formula	C	H	N	C	H	N
10	76	205	$C_{27}H_{21}N_3O$	80.37	5.25	10.41	80.37	5.28	10.48
11	86	312	$C_{22}H_{19}ClO_5$	66.25	4.80		66.28	4.90	
12	89	306	$C_{28}H_{23}ClO_5$	70.81	4.88		70.37	5.10	
13	88	191	$C_{33}H_{41}ClO_5$	71.66	7.47		71.38	7.42	
15a	81	191	$C_{17}H_{13}BF_4O$	63.79	4.09		63.49	4.07	
15b	70	223	$C_{18}H_{15}BF_4O_2$	61.75	4.32		*a*	*a*	
15c	87	201	$C_{21}H_{22}BF_4NO$	64.47	5.67	3.58	64.54	5.74	3.52
15d	65	248	$C_{22}H_{24}BF_4NO_2$	62.73	5.74	3.33	62.77	5.47	3.26
16a	82	118	$C_{23}H_{17}N_3O$	78.61	4.88	11.96	78.79	5.15	11.98
16b	96	176	$C_{24}H_{19}N_3O_2$	75.57	5.02	11.02	75.56	4.95	11.05
16c	93	150	$C_{27}H_{26}N_4O$	76.75	6.20	13.26	76.78	6.43	13.34
16d	96	154	$C_{28}H_{28}N_4O_2$	74.31	6.24	12.38	73.93	6.29	12.43
17b	90	235	$C_{25}H_{21}ClO_6$	66.30	4.67		65.81	4.69	
18b	92	188	$C_{22}H_{23}ClO_6$	63.08	5.53		62.84	5.48	
19a	94	116	$C_{29}H_{37}ClO_5$	69.52	7.44		69.83	7.80	
19b	87	106	$C_{30}H_{39}ClO_6$	67.85	7.40		67.82	7.56	
19c[b]	83	141	$C_{33}H_{46}ClNO_5$	69.27	8.10	2.45	*b*	*b*	*b*
19d	33	116	$C_{34}H_{48}ClNO_6$	67.85	8.04	2.33	67.55	8.44	2.05
20b	79	134	$C_{36}H_{51}ClO_6$	70.28	8.36		70.07	8.68	
22	92	216	$C_{21}H_{20}BF_4NO$	64.81	5.18	3.60	64.68	5.13	3.52
23	91	205	$C_{27}H_{24}N_4O$	77.12	5.75	13.32	76.96	5.87	13.34
24	87	171	$C_{33}H_{34}ClNO_5$	69.52	7.78	2.46	69.05	7.85	2.40

[a] HRMS calcd 263.1072, found 263.1080. [b] HRMS calcd 472.3579, found 472.3566.

lium **9** and benzo[*b*]pyrylium salts **15**. This may also be the case for other α-methylene aldehydes or ketones.

Conclusions

We have realized a previously unknown general method to allow electrophilic substitutions of electron deficient *O*-heterocycles by the use of benzotriazole-mediated methodology. The compounds produced are of interest as long-wave absorbing and highly fluorescent compounds. The easy preparation of hitherto inaccessible long chain derivatives opens new applications, especially in the area of Langmuir−Blodgett films or in analytical chemistry as membrane probes due to their amphiphilic nature.[13]

Experimental Section

General Methods. Melting points were determined on a Koefler hot-stage apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$, $CDCl_3$/DMSO-d_6 or $CDCl_3/CF_3CO_2D$ referenced to Me_4Si for the proton spectra and the solvent for the carbon spectra. Tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone immediately before use. All reactions with water-sensitive compounds were carried out in dry nitrogen atmospheres. 5,6,8,9-Tetrahydro(dinaphtho[1,2-*b*;2,1-*e*]pyrylium) perchlorate (**9**) was prepared according to a literature procedure.[14]

General Procedure for the Preparation of the 5,6-Dihydro(naphtho[1,2-*b*]-benzo[*e*]pyrylium) Tetrafluoroborates 15a−d. The corresponding 2-hydroxybenzaldehyde (20 mmol) and 1-tetralone (20 mmol) were dissolved in acetic acid (50 mL) and refluxed in the presence of HBF_4 (2 mL, 48−50%) for 30 min. The precipitate separating soon after was filtered off and recrystallized from glacial acetic acid/nitromethane (10/1, v/v); see Table 1.

Preparation of the 9-(Diethylamino)(benzo[*a*]xanthylium) Tetrafluoroborate (22). 4-(Diethylamino)-2-hydroxybenzaldehyde (3.86 g, 20 mmol) and 2-naphthol (2.92 g, 20 mmol) were dissolved in acetic acid (40 mL) and refluxed in the presence of HBF_4 (2 mL, 48−50%) for 30 min. The precipitate separating soon after was filtered off and recrystallized from glacial acetic acid; see Table 1.

Preparation of the 4*H*-(1*H*-Benzotriazol-1-yl)pyran (10). To a solution of benzotriazole (1.19 g, 10 mmol) dissolved in dry acetone (40 mL) was added K_2CO_3 (0.69 g, 5 mmol). The reaction mixture was refluxed for 30 min before addition of the 5,6,8,9-tetrahydro(dinaphtho[1,2-*b*;2,1-*e*]pyrylium) perchlorate (**9**) (3.85 g, 10 mmol) portionwise. After addition of **9**, the reaction mixture was refluxed for 1 h (until the fluorescence disappeared) and poured into water (100 mL). The colorless product was filtered off and recrystallized from methanol; see Table 1.

General Procedure for the Preparation of the 4*H*-(1*H*-Benzotriazol-1-yl)benzo[*b*]pyrans 16a−d and the 9*H*-(1*H*-Benzotriazol-1-yl)xanthene (23). To a solution of benzotriazole (1.19 g, 10 mmol) dissolved in dry THF (50 mL) was added NaH (0.40 g of 60% in mineral oil, 10 mmol). The reaction mixture was stirred at rt for 20 min before addition of the corresponding 5,6-dihydro(naphtho[1,2-*b*]benzo[*e*]pyrylium) tetrafluoroborate (**15**) or xanthylium tetrafluoroborate (**22**) (10 mmol) portionwise. The reaction mixture was left stirring for 20 min before the precipitating inorganic byproduct was filtered off. After evaporation of the solvent, the crude product was purified by recrystallization from methanol; see Table 1.

General Procedure for the Preparation of the Salts 11−13, 17−20, and 24. To a solution of the corresponding 4*H*-(1*H*-benzotriazol-1-yl)pyran (**10**), benzo[*b*]pyran (**16**), or 9*H*-(1*H*-benzotriazol-1-yl)xanthene (**23**) (1.25 mmol) in dry THF (30 mL), at −78 °C, was added *n*-BuLi (0.78 mL, 1.25 mmol, 1.6 M in hexane). The solution was stirred at −78 °C for 0.5 h before addition of the electrophile (1.25 mmol) as a solution in dry THF (10 mL). The reaction mixture was stirred overnight and allowed to warm to rt before being quenched with saturated aqueous NH_4Cl solution (40 mL) and extracted with diethyl ether (2 × 30 mL). The combined organic extract was washed with brine and water and dried with $MgSO_4$. The solvent was removed *in vacuo*, and to the resulting oil, acetic acid (20 mL) and $HClO_4$ (0.4 mL, 70%) were added. The precipitate separating after addition of water (50 mL) was filtered off and recrystallized from glacial acetic acid/nitromethane (10/1, v/v); see Table 1.

Acknowledgment. We gratefully acknowledge the financial support of DFG for a stipend to P.C.

Supporting Information Available: ^1H and ^{13}C NMR spectra for all 22 compounds in Table 1 (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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