s), 2.18 (1 H, m); IR 1778 cm^{-1} (C=O, lactone); $[\alpha]_D$ = +11.0° (c = 1.30, CH_2Cl_2).

(*R*)-(+)-γ-(*p*-Methoxyphenyl)-γ-butyrolactone (5h): ^1H NMR δ 7.25 (2 H, d, J = 8.6 Hz), 6.89 (2 H, d, J = 8.6 Hz), 5.45 (1 H, t, J = 6.5 Hz), 3.79 (3 H, s), 2.54-2.88 (2 H, m), 2.11-2.31 (2 H, m); IR 1778 cm^{-1} (C=O, lactone); $[\alpha]_D$ = +4.9° (c = 1.30, CH_2Cl_2).

(*R*)-(+)-γ-(*p*-Bromophenyl)-γ-butyrolactone (5i): ^1H NMR δ 7.49 (2 H, d, J = 8.4 Hz), 7.18 (2 H, d, J = 8.4 Hz), 5.44 (1 H, t, J = 6.9 Hz), 2.61-2.88 (3 H, m), 2.09-2.16 (1 H, m); IR 1778 cm^{-1} (C=O, lactone); $[\alpha]_D$ = +14.4° (c = 1.30, CH_2Cl_2).

Enzymatic Lactonization of γ-Hydroxypimelates (8b-e) (Representative Procedure). Porcine pancreatic lipase (PPL) (360 mg) was added to a 100 mM solution of diethyl γ-hydroxypimelate (**8c**) (140 mg) in hexane (6 mL), and the suspension was shaken on a reciprocal shaker at 40 °C. Reaction progress was monitored by NMR, following the gradual replacement of the multiplet at 3.65 ppm (corresponding to the C-4 proton in the γ-hydroxy diester) by a multiplet at 4.48 ppm (corresponding to this proton in the lactone **9c**). The reaction was terminated after 44 h, by filtering off the enzyme and evaporating the solvent. The lactone was purified by preparative TLC eluting with diethyl ether-hexane, 80:20 (R_f = 0.45).

Using this procedure the lactones **9b-e** were obtained in ca. 80% yields. Their structures and absolute configurations were confirmed by NMR and measurements of optical rotation.

Methyl (*R*)-(-)-γ-Butyrolactone-γ-propionate (9b). The reaction proceeded to 100% conversion in 21 h: ^1H NMR δ 4.50 (1 H, m), 3.67 (3 H, s), 2.49 (5 H, m), 1.90 (3 H, m); IR 1770 (C=O, lactone), 1730 cm^{-1} (C=O, ester); $[\alpha]_D$ = -48.8° (c = 2.26, CH_2Cl_2). Considering that in this experiment the product contained ca. 15% of racemic lactone as a result of spontaneous reaction, the ee of enzymatic product is at least 93%.

Ethyl (*R*)-(-)-γ-Butyrolactone-γ-propionate (9c). The reaction proceeded to 100% conversion in 44 h: ^1H NMR δ 4.50 (1 H, m), 4.10 (2 H, q, J = 7 Hz), 2.48 (4 H, m), 2.35 (1 H, m), 1.88 (3 H, m), 1.26 (3 H, t, J = 7 Hz); IR 1770 (C=O, lactone), 1730 cm^{-1} (C=O, ester); $[\alpha]_D$ = -60.86° (c = 0.58, CH_2Cl_2). This corresponds to ee >98%.

Isopropyl (*R*)-(-)-γ-Butyrolactone-γ-propionate (9d). The reaction proceeded to 33% conversion in 68 h: ^1H NMR δ 5.00 (1 H, m), 4.52 (1 H, m), 2.49 (5 H, m), 1.94 (3 H, m), 1.22 (6 H, d, J = 6 Hz); IR 1770 (C=O, lactone), 1730 cm^{-1} (C=O, ester); $[\alpha]_D$ = -26.85° (c = 0.51, CH_2Cl_2). This corresponds to ee 46%.

Benzyl (*R*)-(-)-γ-Butyrolactone-γ-propionate (9e). The substrate **8e** is poorly soluble in hexane, but the lactone **9e** is soluble so progressive dissolution occurs as lactonization proceeds. The reaction proceeded to 100% conversion in 52 h: ^1H NMR δ 7.33 (5 H, s), 5.11 (2 H, s), 4.50 (1 H, m), 2.50 (4 H, m), 2.35 (1 H, m), 1.95 (3 H, m); IR 1770 (C=O, lactone), 1730 cm^{-1} (C=O, ester); $[\alpha]_D$ = -40.86° (c = 0.74, CH_2Cl_2). This corresponds to ee >95%.

(*S*)-(-)-Lactonic Acid (9a). The foregoing lactone benzyl ester (**9e**) (54 mg, 0.22 mmol) was dissolved in glacial acetic acid, mixed with activated palladium oxide on charcoal (32 mg, 10% Pd), and hydrogenated at atmospheric pressure for 3 h. Filtration of the catalyst and evaporation of the acetic acid in vacuum afforded the lactonic acid **9a** as white crystalline material (30 mg, 87% yield): ^1H NMR δ 4.54 (1 H, m), 2.53 (4 H, m), 2.34 (1 H, m), 1.91 (3 H, m); $[\alpha]_D$ = -39.86° (c = 0.77, H_2O).

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Registry No. **4a**, 925-57-5; **4b**, 126252-14-0; **4c**, 87241-91-6; **4d**, 126135-36-2; **4e**, 126135-37-3; **4f**, 126252-15-1; **4g**, 126135-38-4; **4h**, 126135-39-5; **4i**, 126135-40-8; **5a**, 96-48-0; *S*-**5b**, 19041-15-7; *R*-**5b**, 58917-25-2; **5c**, 41035-07-8; **5d**, 107797-27-3; **5e**, 69830-92-8; **5f**, 111138-03-5; **5g**, 126135-41-9; **5h**, 126135-42-0; **5i**, 126135-43-1; **6b**, 111043-99-3; **7a**, 502-50-1; **7b**, 22634-92-0; **7c**, 6317-49-3; **7d**, 117726-76-8; **7e**, 70957-27-6; **8b**, 126135-44-2; **5b** lactone derivative, 126252-16-2; **8c**, 58262-40-1; **8d**, 122950-94-1; **8e**, 122950-95-2; **9a**, 98611-83-7; **9b**, 111070-69-0; *R*-**9c**, 99438-12-7; *S*-**9c**, 99438-11-6; *R*-**9d**, 122950-97-4; *S*-**9d**, 122950-96-3; **9e**, 99393-14-3; PPL, 9001-62-1; methyl γ-oxo-γ-phenylbutyrate, 25333-24-8; methyl γ-oxo-γ-tolylbutyrate, 57498-54-1; methyl 3-(*p*-methoxybenzoyl)propionate, 5447-74-5; furylacrylic acid, 539-47-9.

A Novel Aromatic Iodination Method Using F_2

Shlomo Rozen* and Dov Zamir

School of Chemistry, Raymond and Beverly Sackler Faculty of Exact Sciences, Tel-Aviv University, Tel-Aviv 69978, Israel

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A new method for direct aromatic iodination with IF, made in situ from the corresponding elements, is described. Depending on the reaction time and temperature, mono- or polyiodination can be achieved. Even deactivated aromatic rings can be directly iodinated without the presence of any Friedel-Crafts catalyst. Sensitive groups such as aromatic aldehydes are not affected by the reagent.

During the last 10 years elemental fluorine has gained increasing popularity as a fluorinating agent.[1] We and others have shown that F_2 can be a source of electrophilic,[2] nucleophilic,[3] and radical[4] fluorine species. Despite this remarkable versatility it was not anticipated that fluorine would also play a role in general organic chemistry by participating in the syntheses of fluorine-free compounds which are otherwise difficult to prepare. But it seems that this surprising element can indeed do just that, and, since we believe that F_2 has a considerable general synthetic potential, we have channeled most of our efforts toward this new area. Thus in the last few years we have used fluorine to activate alkanes by converting them to alkenes,[5] to substitute very resistant heterocyclic hydrogens by acetoxy,[6] chlorine, bromine, or various ethers,[7] to epoxidize a whole spectrum of olefins,[8] to hydroxylate molecules at regions remote from activating groups,[9] and to brominate

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most aromatic rings without using any catalyst.[10] We describe in this work yet another use of fluorine which makes synthesis of aryl iodides a relatively simple and easy task.[11]

Iodo aromatic compounds have considerable importance in metabolism and radiolabeling studies. Thyroid hormones, amphetamines, and corticosteroids have been investigated by using radio-iodine derivatives.[12] A method which directly inserts an iodine isotope into the aromatic ring late in the synthetic process is thus highly desirable.

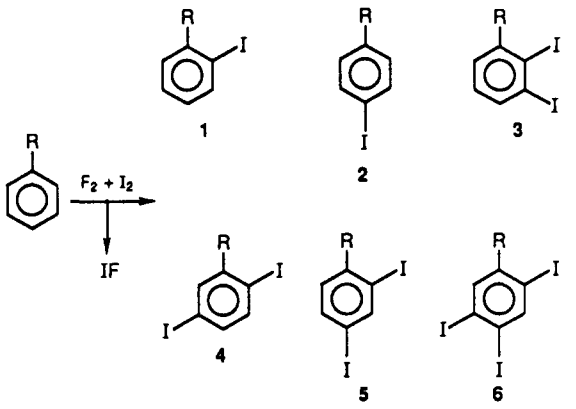
Aryl iodides are usually more difficult to prepare than the other aryl halogens, and synthetic methods leading to them are relatively few.[13] Because of the low electrophilic strength of iodine, direct iodination methods usually can be performed only on strongly activated aromatic rings. In general, this is done under harsh conditions in the presence of powerful oxidants such as nitric acid or liquid SO_3.[14] However, with a good source of electrophilic iodine and a strong binding acceptor for the leaving proton, mild direct aryl iodination, even on unreactive substrates, should be possible. Unsolvated iodine monofluoride seems to be the ideal candidate since it satisfies both requirements by offering a highly positively polarized iodine with no bulky ligands and the formation of HF which has one of the strongest known bonds.

There are several methods which produce complexes that add the elements of iodine and fluorine across simple double bonds. The most popular involves mixing an *N*-iodo compound with anhydrous HF or its complexes with various amines.[15] Other methods utilize silver salts and iodine[16] or mercury derivatives and silica gel supported iodine.[17] In these examples the iodine is not sufficiently polarized and the fluoride ion is usually strongly solvated, thereby reducing the ability for direct iodination of aromatic rings.

One of the best methods for making the real IF is by direct reaction of the elements. This reaction has been studied previously,[18] but because of low stability and tedious isolation, the method was not attractive. In organic synthesis, however, this isolation step is unnecessary and most of the technical difficulties disappear. We have prepared and used this reagent in situ on several occasions[3,19] and found the whole operation to be very easy indeed.

IF is usually prepared at −78 °C, and at this temperature its reaction with benzene is very slow. When the mixture is warmed to −25 °C, an almost quantitative yield of iodobenzene (**1a**) is obtained, but in rather low 30% conversion. At room temperature, however, and in the absence of any Friedel–Crafts catalyst, a full conversion was achieved, and in addition to **1a**, both *o*-diiodo- (**3a**) and *p*-diiodobenzene (**4a**) were isolated.

The degree of polyiodination is temperature and time dependent. When the more activated ring in toluene reacted with IF at −78 °C for 5 h, a 1:1 mixture of *o*- and *p*-iodotoluene (**1b** and **2b**) was obtained. By allowing the reaction to proceed at room temperature for an hour, a considerable amount of 2,4-diiodotoluene (**5b**) was also formed. After 4 h at room temperature the monoiodo derivatives disappeared and the two major products were **5b** and 2,4,5-triiodotoluene (**6b**). Traces of the tetra- and pentaiodo derivatives were also detected in low yields but not isolated. With the more bulky *tert*-butylbenzene, the low temperature monoiodination was directed exclusively to the para position (**2c**), but at higher temperatures (−20 °C) 2,4-diiodo-*tert*-butylbenzene (**5c**) was also formed.



R: **a** = H; **b** = Me; **c** = *t*-Bu; **d** = Cl; **e** = Br; **f** = F; **g** = OAc; **h** = *p*-OC_6H_4I; **i** = NHAc; **j** = $NHCOCF_3$

The aromatic ring in chlorobenzene is less activated than in the previous cases, and indeed the reaction with IF was very slow at −78 °C. Raising the temperature to −20 °C resulted in a relatively fast reaction, and after 1 h, *p*-iodochlorobenzene (**2d**) was obtained in greater than 95% yield. As with the alkylbenzenes, at room temperature polyiodination occurred and 2,4,5-triiodochlorobenzene (**6d**) was formed and isolated. Similar yields and parallel behavior were observed with bromobenzene which failed to react at −78 °C, but using 1 molar equiv of IF at −20 °C gave an excellent yield of 4-bromoiodobenzene (**2e**). With excess IF a mixture of two unknown diiodobromobenzenes (**5e** and 3,4-diiodobromobenzene) was also obtained in 30% yield along with the triiodo derivative **6e** (see Table I).

Similar behavior was observed with other mildly activated rings. At low temperature, fluorobenzene reacts very slowly, but after 30 min at −25 °C, the iodination was complete to give *p*-iodofluorobenzene (**2f**). Here too we were able to push the reaction toward polyiodination. Thus using a large excess of IF at room temperature for more than 6 h resulted mainly in the formation of 2,4-diiodofluorobenzene (**5f**) along with the triiodo derivative **6f** and a small amount of pure but not fully identified tetraiodofluorobenzene. Phenyl acetate also reacted rapidly at room temperature to yield the *p*-iodo product (**2g**), while diphenyl ether was iodinated on both rings to produce bis(4-iodophenyl) ether[20] (**2h**). In the last case no polyiodo derivative were obtained since forcing conditions gave unidentified high molecular weight insoluble material.

Direct iodination can also be performed on aniline derivatives although the reaction has to be more finely tuned than usual. Acetanilide reacts extremely slowly at −78 °C but produces tars above 0 °C. It seems that the best

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Table I

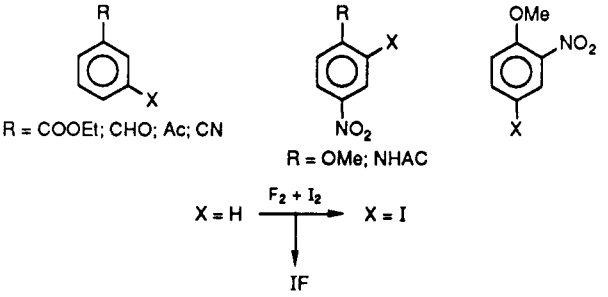
starting material	product (yield, %)	temp, °C	reactn time, h
C_6H_6	**1a** (95)[a]	−78	24
C_6H_6	**1a** (30), **3a** (30), **4a** (40)	25	5
$C_6H_5CH_3$	**1b** (35), **2b** (35)	−78	5
$C_6H_5CH_3$	**1b** (20), **2b** (20), **5b** (40)	25	1
$C_6H_5CH_3$	**5b** (40), **6b** (35)	25	4
C_6H_5t-Bu	**2c** (65)[b]	−78	7
C_6H_5t-Bu	**2c** (35), **5c**[c] (30)	−20	2
C_6H_5Cl	**2d** (98)	−20	3
C_6H_5Cl	**6d**[d] (50)	25	12
C_6H_5Br	**2e** (90), **1e** (5)	−20	0.5
C_6H_5Br[e]	**5e**:3,4-$I_2C_6H_3Br$ (2.5:1) (30),[f] **6e** (10)[g]	25	6
C_6H_5F	**2f** (85)	−20	0.5
C_6H_5F[e]	**5f**[h] (30), **6f** (15),[i] I_4C_6HF (>10)[j]	25	6
C_6H_5OAc	**2g** (40)	25	1
$C_6H_5OC_6H_5$	**2h** (45)	−78	0.25
C_6H_5NHAc	**2i** (55)	−20	0.5
$C_6H_5NHCOCF_3$	**2j**[k] (35)	−20	1
C_6H_5COOEt	3-IC_6H_4COOEt (85)	25	16
C_6H_5CHO	3-IC_6H_4CHO (85)	25	3
$C_6H_5COCH_3$	3-$IC_6H_4COCH_3$ (35)	25	3
C_6H_5CN	3-IC_6H_4CN (90)[a]	25	16
2-$O_2NC_6H_4OMe$	4-I-2-$O_2NC_6H_3OMe$ (90)	−78[l]	4
4-$O_2NC_6H_4OMe$	2-I-4-$O_2NC_6H_3OMe$ (80)	25	12
4-$O_2NC_6H_4NHAc$	2-I-4-$O_2NC_6H_3NHAc$ (22)	25	24

[a] 30% conversion. [b] 50% conversion. [c] $Bp_{0.01mm}$ 89–91 °C; ^1H NMR 7.8 (1 H, d, ^4J = 2 Hz), 7.7 (1 H, d, ^3J = 6.5 Hz), 7.0 (1 H, dd, ^4J = 2 Hz, ^3J = 6.5 Hz), 1.26 ppm (9 H, s); MS *m/e* 386 (M^+). Anal. Calcd for $C_{10}H_{12}I_2$: C, 31.09; H, 3.11. Found: C, 31.32; H 3.02. [d] Mp (EtOH) 145 °C; ^1H NMR 8.19 (1 H, s), 7.81 ppm (1 H, s); MS *m/e* 490, 492 (M^+). [e] 5-fold excess of IF. [f] These two diiodobromo isomers were identified through their ^1H NMR spectra using proton decoupling experiments. **5e**: 8.1 (1 H, d, J = 2 Hz), 7.5 (1 H, dd, J_1 = 8.7, J_2 = 2 Hz), 7.3 ppm (1 H, d, J = 8.7 Hz). The 3,4-diiodobromobenzene isomer: 8.0 (1 H, d, J = 2 Hz), 7.7 (1 H, d, J = 8.2 Hz), 7.1 ppm (1 H, dd, J_1 = 8.2, J_2 = 2 Hz); MS *m/e* 408, 410 (M^+). [g] Mp (EtOH) 190 °C; ^1H NMR 8.2 (1 H, s), 8.0 ppm (1 H, s); MS *m/e* 534, 536 (M^+). [h] Although not isolated in analytical purity the spectral properties of **5f** are: ^1H NMR 8.0 (1 H, dd, J_1 = 6, J_2 = 2 Hz), 7.5 (1 H, m), 6.8 ppm (1 H, t, J = 8 Hz); ^{19}F $NMR_{(CFCCl_3)}$ −95.6 ppm (octet, J_1 = 8, J_2 = 7, J_3 = 6 Hz); MS *m/e* 348 (M^+). [i] Mp (EtOH) 128 °C; ^1H NMR 8.1 (1 H, d, J = 6.4 Hz), 7.5 ppm (1 H, d, J = 7.2 Hz); ^{19}F $NMR_{(CFCCl_3)}$ −94.95 ppm (dd, J_1 = 6.4, J_2 = 7.2 Hz); MS *m/e* 474 (M^+). [j] Mp (EtOH) 167 °C; ^1H NMR 8.3 (d, J = 7 Hz); ^{19}F NMR −65.7 ppm (d, J = 7 Hz); MS *m/e* 600 (M^+). [k] Mp (PhH) 142 °C; ^1H NMR 7.9 (1 H, bs), AB centered at 7.52 ppm (4 H); MS *m/e* 315 (M^+). [l] A similar yield was obtained also at room temperature.

temperature in this case is around −20 °C where *p*-iodoacetanilide (**2i**) is formed in reasonable yields, but with considerable amounts of dark insoluble materials as well. Protecting the aniline with the trifluoroacetyl group did not much change the outcome.

The power of this direct iodination method can be best appreciated when aromatic rings deactivated toward electrophilic attack are used. With chlorine and bromine such molecules require at least 1 molar equiv of strong Friedel–Crafts catalyst in order to increase the electrophilicity of the halogen. Such additives do not help iodine, and up to now, in order to iodinate deactivated rings, one had to search for indirect methods. Iodine fluoride, we believe, is a significant step in this direction, since it offers a simple and mild route for the purpose.

Ethyl benzoate was iodinated at room temperature to form ethyl 3-iodobenzoate in excellent yield. No signs of attack at the ester moiety were observed. Since IF is but a weak oxidizer, even the more sensitive aldehyde group remained intact and 3-iodobenzaldehyde was formed from benzaldehyde. In both cases the regioselectivity seems to be complete, providing strong support for the electrophilic nature of the reagent. Other deactivated derivatives, such as acetophenone and benzonitrile were also successfully iodinated in a matter of a few hours at room temperature (see Table I).



Nitrobenzene was unreactive after 24 h at room temperature, while with strongly activated rings, such as phenol or anisole, there was total destruction of the substrate even at −78 °C. By placing the two groups on a single ring the reaction with IF proceeds quite smoothly. Thus, 2-nitroanisole reacts cleanly at −78 °C as well as at room temperature to produce 4-iodo-2-nitroanisole, while 4-nitroanisole was transformed into 2-iodo-4-nitroanisole but only at room temperature, illustrating that most ortho iodinations are considerably slower. Similarly 4-nitroacetanilide produced the expected 2-iodo-4-nitroacetanilide.

In conclusion this method affords a rare opportunity to directly iodinate almost any type of aromatic compound under mild conditions, when helped by the first member of the family, F_2.

Experimental Section

^1H NMR spectra were recorded with a Bruker WH-360 at 360 MHz with $CDCl_3$ as a solvent and Me_4Si as internal standard. Mass spectra were measured with a DuPont 21-491B instrument, and IR spectra were recorded on a Perkin-Elmer 177 spectrometer.

General Fluorination Procedure. A description of the set up and the procedure for working with elemental fluorine has previously been given.[21] Although we have mentioned it several times in the past, it still should be remembered that F_2 is a strong oxidant and the reactions described herein should be conducted with care. If elementary precautions are taken, work with fluorine and its derivatives is safe, relatively simple, and so far we have never had an accident while working with it.

Preparation and Reactions of IF. For preparation, behavior and properties of IF in general, see ref 18. For iodination of the compounds listed in the table, the following procedure was used. A suspension of 25 g (100 mmol) of well-ground iodine was dispersed in 500 mL of $CFCl_3$. It is recommended, if possible, to sonify the mixture for 15 min to obtain a better suspension. The reaction mixture was cooled to −78 °C and agitated with the aid of a vibromixer; 1.1 molar equiv of nitrogen diluted F_2 (10%) was bubbled through the suspension. It has been previously concluded that the yield of IF is practically quantitative in respect to both iodine and fluorine. When monoiodination was desired, excess of the reagent was usually about 40–70%, while much larger excesses of 3–5 molar equiv was used when aiming at polyiodination. The parent aromatic compound was dissolved in about 30–50 mL of precooled $CHCl_3$ and added in one portion to the reaction vessel. The reactions were monitored by GC and TLC and usually stopped when practically full conversion was achieved. The reaction mixture was then poured into dilute thiosulfate solution; the organic layer was washed with water and $NaHCO_3$ until neutral, dried over $MgSO_4$, and evaporated. Products that are commercially available were usually compared with authentic samples. All the physical and spectral properties of compounds previously described in the literature were in complete agreement

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with the structure and the data published. Unless otherwise indicated new compounds were fully characterized by all the usual spectroscopy methods and confirmed by microanalysis.

Registry No. **1a**, 591-50-4; **1b**, 615-37-2; **1e**, 583-55-1; **2b**, 624-31-7; **2c**, 35779-04-5; **2d**, 637-87-6; **2e**, 589-87-7; **2f**, 352-34-1; **2g**, 33527-94-5; **2h**, 28896-49-3; **2i**, 622-50-4; **2j**, 126063-08-9; **3a**, 615-42-9; **4a**, 624-38-4; **5b**, 32704-08-8; **5c**, 126063-03-4; **5e**, 126063-04-5; **5f**, 126063-06-7; **6b**, 32704-10-2; **6d**, 126082-46-0; **6e**, 126063-05-6; **6f**, 126063-07-8; C_6H_6, 71-43-2; C_6H_5Me, 108-88-3; C_6H_5t-Bu, 98-06-6; C_6H_5Cl, 108-90-7; C_6H_5Br, 108-86-1; C_6H_5F, 462-06-6; C_6H_5OAc, 122-79-2; $C_6H_5OC_6H_5$, 101-84-8; C_6H_5NHAc, 103-84-4; $C_6H_5NHC(O)CF_3$, 404-24-0; $C_6H_5CO_2Et$, 93-89-0; C_6H_5CHO, 100-52-7; C_6H_5Ac, 98-86-2; C_6H_5CN, 100-47-0; $2\text{-}O_2NC_6H_4OMe$, 91-23-6; $4\text{-}O_2NC_6H_4OMe$, 100-17-4; $4\text{-}O_2NC_6H_4NHAc$, 104-04-1; $3,4\text{-}I_2C_6H_3Br$, 21521-54-0; I_4C_6HF, 126063-09-0; $3\text{-}IC_6H_4CO_2Et$, 58313-23-8; $3\text{-}IC_6H_4CHO$, 696-41-3; $3\text{-}IC_6H_4Ac$, 14452-30-3; $3\text{-}IC_6H_4CN$, 69113-59-3; 4-iodo-2-nitroanisole, 52692-09-8; 2-iodo-4-nitroanisole, 5399-03-1; 2-iodo-4-nitroacetanilide, 19591-18-5.

Diels–Alder Reactions of Dieno-Pyranosides. Anomeric vs Allylic Stereoselection‡

Robert M. Giuliano,* John H. Buzby, and Nicholas Marcopulos

Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

James P. Springer

Merck Institute for Therapeutic Research, P.O. Box 2000, Rahway, New Jersey 07065

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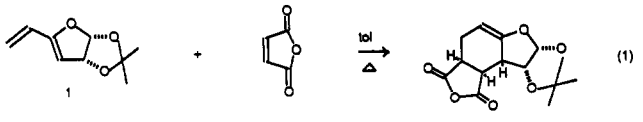
A series of carbohydrate-derived dienes with different patterns of substitution on the pyranose ring were synthesized and their Diels–Alder reactions investigated. The diene moiety was incorporated into the pyranose ring by oxidation of 4-*O*-methanesulfonate esters of sugar derivatives to enals, followed by Wittig alkenation. This new class of dienes underwent cycloaddition with maleimide or its *N*-phenyl derivative to give annulated pyranosides. The Diels–Alder reactions were highly stereoselective, giving single products in some cases. Structural analysis of the reaction products was carried out by NMR spectroscopy and X-ray crystallography. The results indicated a strong preference for the formation of the products resulting from addition of the dienophile to the face of the diene opposite the anomeric center. In cases where the anomeric and allylic substituents on the diene occupied opposite faces, addition of the dienophile occurred predominantly from the face opposite the more remote anomeric center. This result was contrary to expectations based on the reported effects of allylic groups on the diastereofacial selectivity of Diels–Alder reactions.

Introduction

Diels–Alder reactions of carbohydrate derivatives constitute a useful methodology for the synthesis of carbocyclic compounds in optically active form. In recent studies, Diels–Alder adducts obtained from sugar substrates have been used as intermediates in approaches to complex natural products that contain cycloalkyl rings, for example, the aureolic acid antibiotic olivin,[1] the antibiotic actinobolin,[2] the diterpene forskolin,[3] and prostaglandins.[4] While carbohydrate derivatives have functioned both as dienes and dienophiles in the Diels–Alder reaction, in most applications, the dienophile has been derived from the carbohydrate. The first examples of the synthesis of carbocyclic compounds with carbohydrate-derived dienes were reported from the laboratories of Fraser-Reid.[5] Dieno-furanoside **1** and related systems underwent cycloaddition to maleic anhydride, giving annulated furanosides in high stereoselectivity (eq 1). In spite of these promising

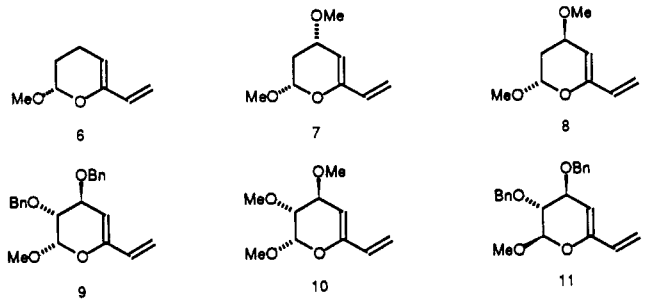


(1)

results, only a few other examples of carbohydrate-derived dienes have been reported.

In a recent communication[6] from our laboratory, we described the synthesis and Diels–Alder reactions of

Table I. Dieno-Pyranosides



analogous six-membered dieno-pyranosides **2**, the prototypes of a new class of dienes which contain a pyranose ring. Since the publication of our results, structurally related dieno-pyranosides in which the diene moiety occurs at a different position have also been reported.[7,8] In

‡ Taken in part from the Ph.D. thesis of J. H. Buzby, Villanova University, 1987; *Diss. Abstr. Int. B* **1987**, DA8720636.

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