Synthesis and Photochromic Properties of Fulgides with a *t*-Butyl Substituent on the Furyl- or Thienylmethylidene Moiety

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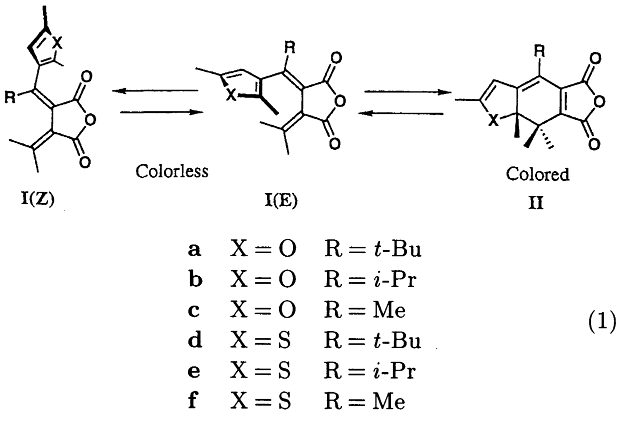
2,6,6-Trimethyl-5-(2,5-dimethyl-3-furyl and -3-thienyl)-3-heptyn-2,5-diols were carbonylated in benzene in the presence of 1 : 1 — $Pd(OAc)_2/I_2$ as the catalyst. The reaction at 90 °C under 80 atm of carbon monoxide for 5 h directly gave both *E* and *Z* isomers of *t*-butyl-substituted furyl- or thienyl fulgides. The former had been reported impossible to synthesize by the Stobbe condensation. Similarly, furyl- and thienylfulgides with an isopropyl group were synthesized by this method. The fulgides were isolated by column chromatography in 37—75% yields. Coloring quantum yields of *t*-butyl-furyl- and -thienylfulgides are 0.79 and 0.73, respectively, which are the greatest in each series of fulgides with the same heteroaromatic ring.

Fulgide is a term used to describe derivatives of bis(methylene)succinic anhydride.[1] Thermally irreversible, photochromic heterocyclic fulgides such as I have been synthesized from the viewpoint of a photochemical memory device.[2—8] In recent years, remarkable efforts have been made to produce better fulgides which possess high quantum yields in the coloration process (Eq. 1) and longer absorption maximum wavelengths. It has been pointed out that the rate of photochemical cyclization is accelerated when the bulkiness of the alkyl substituent (R) increases.[4a]



I(Z) I(E) II

a X = O R = *t*-Bu
b X = O R = *i*-Pr
c X = O R = Me
d X = S R = *t*-Bu
e X = S R = *i*-Pr
f X = S R = Me (1)

In general, fulgides have been synthesized by the successive condensation of two carbonyl compounds with a succinate in the presence of base (the Stobbe condensation). This method, however, is problematic because it requires many steps and the yield of each step is usually low. Moreover, when the substituent, which corresponds to R in Eq. 1, of the second ketone is bulky, the condensation occurs with difficulty under the usual conditions. The isopropyl derivative (**Ib**) of furylfulgide was prepared for the first time by the use of lithium diisopropylamide in the second condensation.[4a] Later synthesis of the corresponding thienyl derivative was also reported.[5] Fulgides (**Ia** and **Id**) with R = *t*-butyl have not been synthesized so far. Therefore, simpler and more efficient synthetic methods are desired.

In 1969, Tsuji and Nogi[9] reported the carbonylation of propargyl compounds. Among a variety of experimental results, the formation of bis(isopropylidene)-

Table 1. Synthesis of Heterocyclic Fulgides (**I**) by Palladium-Catalyzed Carbonylation of Substituted 2-Pentyne-1,4-diol (**III**)[a)]

Entry	Substituted 2-pentyne-1,4-diol (**III**)	Yields/%[b)] Fulgide (**I**) *E*	*Z*	Diacid (**VI**)
1	a X=O, R=*t*-Bu	10	49	<23
2	b X=O, R=*i*-Pr	24	13	<29
3	d X=S, R=*t*-Bu	43	10	<27
4	e X=S, R=*i*-Pr	25	50	<12

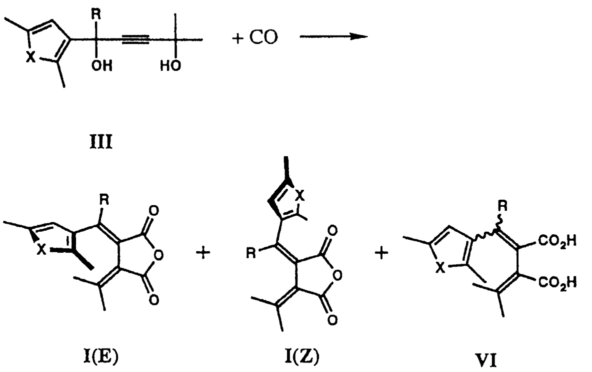
a) Reaction conditions: 4 mmol of diol (Entry 1, 5.7 mmol); 0.2 mmol of $Pd(OAc)_2$; 0.2 mmol of I_2; 10 ml of benzene; CO, 80 atm; 90 °C, 5 h. b) After separation by column chromatography.

Table 2. Spectroscopic Data and Quantum Yields of Fulgides[a)]

		λ_{max}/nm (ε_{max}/mol^{-1} dm^3 cm^{-1})			Φ_{EC}	Φ_{CE}	Φ_{EZ}	Φ_{ZE}	Φ_{CE}
	R	E	Z	C	366 nm				492 nm
Ia	*t*-Bu	350 (3000)	—	492 (7700)	0.79	0.082	0.00	—	0.034
Ib	*i*-Pr	342 (4200)	354 (4100)	494 (9200)	0.58	0.00	0.00	b)	0.043
Ic	Me	343 (6700)	353 (8400)	494 (9200)	0.18	0.00	0.13	0.11	0.048
Id	*t*-Bu	331 (2900)	ca.330 (sh)	509 (6400)	0.73	0.12	b)	b)	0.095
Ie	*i*-Pr	b)	b)	524[c)]	0.54[c)]	0.10[c)]	0.015[c)]	0.030[c)]	0.10[c,d)]
If	Me	335[e)]	b)	520[e)]	0.13[c)]	0.08[c)]	b)	b)	0.14[d,e)]

a) In toluene at room temperature. b) Not determined. c) In CH_2Cl_2. From Ref. 5. d) 546 nm. e) From Ref. 11.

succinic anhydride (**IV**) by the carbonylation of 2,5-dimethyl-3-hexyn-2,5-diol was presented. We applied this reaction to the synthesis of fulgides and succeeded in developing a one-step synthesis of photochromic furyl and thienyl fulgides. A preliminary paper on this subject has been published.[10)] We extended the carbonylation method to the synthesis of fulgides with a bulky substituent on the furyl- or thienylmethylidene moiety, and found that the palladium-catalyzed carbonylation of substituted 2-pentyne-1,4-diols (**III**) gave fulgides (**I**) possessing the bulky substituents in reasonable yields (Eq. 2). The present paper is concerned with the synthesis of the *t*-butyl and isopropyl derivatives of **I** by the carbonylation method.

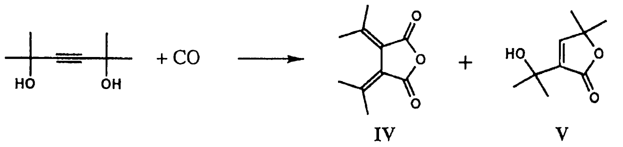


(2)

Results and Discussion

Optimization of the Carbonylation. Tsuji's research was done in a HCl-saturated benzene solution at 100 °C in the presence of $PdCl_2$ (20 mol%). Compound **IV** was obtained in a 49% yield, accompanied by a dilactone. Although the carbonylation seemed to offer a highly promising route to fulgides, the HCl-saturated benzene solution was somewhat troublesome to handle. Moreover, the activity of the catalyst was not efficient enough. Consequently, we attempted to make the carbonylation reaction more efficient.

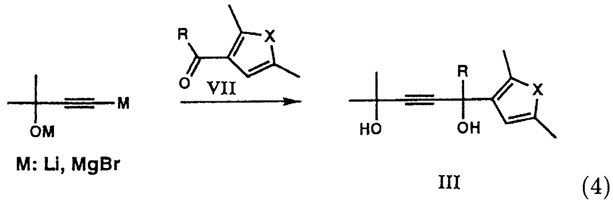
We first tried to optimize the reaction conditions using 2,5-dimethyl-3-hexyn-2,5-diol (Eq. 3). As described in our previous paper,[10)] the presence of a halogen as a catalyst component is essential for this carbonylation. Palladium chloride, palladium acetate, or palladium on carbon combined with iodine possessed catalytic activities. In terms of the solubility of the catalyst in organic solvents, the combined use of $Pd(OAc)_2$ and iodine seemed to be the most effective catalyst. Use of $PdCl_2(PPh_3)_2$ as the catalyst lowered the yield of **IV**, but increased that of lactone **V**.



(3)

The reaction (CO, 80 atm) at 50—130 °C for 5 h gave **IV** in 74—83% yields using 1 : 1 — Pd $(OAc)_2/I_2$ (5 mol%) as the catalyst. Even at 20 °C, **IV** was obtained in a 50% yield. It was concluded that a reaction temperature around 90 °C was the favorable choice.

Synthesis of Substituted 2-Pentyne-1,4-diols (III). Diols **IIIa**, **b**, **d**, and **e** were synthesized by the reaction of 2-methyl-3-butyn-2-ol with the corresponding ketones (**VII**). The yields of the diols based on the ketones were 54—91%.



(4)

Synthesis of Furyl or Thienyl Fulgides. The carbonylation was performed under pressure (80 atm) in benzene at 90 °C for 5 h, using $Pd(OAc)_2/I_2$ as the catalyst. The dark brown solution was filtered through a short silica gel column to remove the catalyst. After evaporation of the benzene, the resulting viscous oil or solid mass showed strong IR bands due to acid anhydride. Thin-layer chromatography of the products showed two purple to purplish-red spots on UV irradiation, which were attributable to the presence of the *Z* and *E* isomers. The products were purified by column chromatography. The yields of the products are shown in Table 1. It is noteworthy that the carbonylation of **IIIa** and **d**, which have *t*-butyl R substituents, proceeded readily and fulgides **Ia** and **d** were synthesized in reasonable yields. The configurations of the substituent (R) were assigned on the basis of ^{1}H NMR spectra; in the *Z* isomer the isopropylidene methyl groups appear around 2.1—2.4 ppm, while one of the isoproylidene methyl groups of the *E* isomer appears around 1.3—1.4 ppm due to the shielding effect of the furan or thiophene ring.

In all cases, the last eluate of the column chromatography using 1 : 1 — benzene/methanol as the solvent did not show photochromism, but possessed a strong IR absorption around 1685 cm^{-1}, presumably due to a carbonyl group. It seemed reasonable to assume that the eluate contained diacid **VI**. Attempted isolation of this postulated acid in a pure form was unsuccessful. However, this acid was converted into photochromic compounds by treatment with trifluoroacetic anhydride. This fact implies that a part of the carbonylation product exists in the acid form which can be converted into **I**.

The TLC analysis of the carbonylation product of **IIIa** showed the presence of two photochromic molecules due to the *E* and *Z* isomers. Immediately after separation by column chromatography, the eluates corresponding to the *E* and *Z* isomers possessed different R_f values on TLC. It seemed likely that no appreciable isomerization of *Z* to *E* took place during the column treatment. But after the usual isolation workup (evaporation of the solvent under reduced pressure around 60 °C and recrystallization from hexane), the *Z* isomer showed the same NMR spectrum in $CDCl_3$ as that of the *E* isomer. It was thus revealed that the *Z* isomer readily isomerizes to the *E* isomer on standing in room light at room temperature, presumably due to the steric hindrance of the *t*-butyl group.

Photochromic Reaction of Fulgides with the *t*-Butyl Group. We have already clarified that a bulky alkyl substituent on the furylmethylidene moiety increases the cyclization quantum yield (Φ_{EC}) and decreases the *E*-to-*Z* isomerization quantum yield (Φ_{EZ}) upon irradiation with 366 nm light. For fulgide **Ib**, Φ_{EC} is 0.58 and Φ_{EZ} is zero in toluene. Recently, Ulrich and co-workers obtained similar results for thienylfulgides.[5] The steric effect of the bulky alkyl groups on the quantum yields of the photoreactions of the *E* isomer have thus been established. We therefore examined the photochromic properties of fulgides **Ia** and **Id** which have the larger *t*-butyl group.

As shown in Table 2, Φ_{EC} is 0.79 and Φ_{EZ} is zero for **Ia**, and Φ_{EC} is 0.73 for **Id** (Φ_{EZ} of **Id** was too small to determine). The *t*-butyl group enhanced the properties of the fulgides having the isopropyl group.

The molar absorption coefficients of the *E*-forms of **I** decreased as the bulkiness of the alkyl group increased. As the mass rate of the photoreaction is, roughly saying, proportional to the product of Φ_{EC} and ε, the decrease in ε is a negative factor for the acceleration of the cyclization reaction. However, as the product of Φ_{EC} and ε at 366 nm for **Ia** ($\varepsilon_{366}=2430$) was 1.35 times of that for **Ib** ($\varepsilon_{366}=2450$), the steric bulkiness of the *t*-butyl group was found to effectively accelerate the cyclization reaction. The longer maximum absorption wavelength of **Ia**(*E*) than that of **Ib**(*E*) compensated for the smallness of the absorption coefficient at the absorption maximum.

Experimental

General Remarks. Melting points were determined using a MEL-TEMP II (Laboratory Devices) melting point apparatus and were uncorrected. Infrared spectra were recorded on a Perkin–Elmer FT-IR 1600. ^{1}H NMR spectra were measured on JEOL JNM-PMX60 (60 MHz) and JNM-GX270 (270 MHz) spectrometers. Electronic spectra were recorded on Shimadzu UV-260, Hitachi V-2000, or JASCO Ubest 50 spectrophotometers. The quantum yields of the photochromic reactions were determined according to procedures described elsewhere.[12] All solvents were stored under an argon atmosphere after purification by standard techniques. Commercially available 2,5-dimethyl-3-hexyn-2,5-diol, 2-methyl-3-butyn-2-ol, 2,5-dimethylfuran, acetyl, pivaloyl, and isobutyroyl chlorides, palladium acetate, and iodine were used without further purification. 2,5-Dimethylthiophene was prepared by the reaction of 2,5-hexanedione with diphosphorus pentasulfide. The reactions of the isopropyl derivatives were representative.

Synthesis of 2,6-Dimethyl-5-(2,5-dimethyl-3-furyl)-3-heptyne-2,5-diol (IIIb). To an ether solution (20 ml) of 2-methyl-3-butyn-2-ol (14.6 mmol) was added 1.6 mol dm^{-3} *n*-BuLi (29.2 mmol) in hexane at 0 °C under argon and stirring was continued at room temperature for 1.5 h. To this resulting solution was added a solution of ketone **VIIb** (7.3 mmol) in ether (20 ml) dropwise and the mixture was refluxed for 5 h. After cooling, 10% aqueous NH_4Cl (100 ml) was added. The organic layer was washed with water and dried over Na_2SO_4. Distillation under reduced pressure gave **IIIb** as a pale yellow liquid (1.46 g, 80% yield).

Synthesis of 2,6,6-Trimethyl-5-(2,5-dimethyl-3-furyl)-3-heptyne-2,5-diol (IIIa). Under the same conditions described above, 2.72 g (15 mmol) of **VIIa** gave 2.17 g (54.4% yield) of **IIIa** as a pale yellow solid.

Synthesis of 2,6-Dimethyl-5-(2,5-dimethyl-3-thienyl)-3-heptyne-2,5-diol (IIIe). Butyllithium (80.0 mmol) in hexane was added dropwise to an ether solution (40 ml) of 2-methyl-3-butyn-2-ol (40 mmol) at 0 °C under an atmosphere of argon. Stirring was continued for 1.5 h. To this solution was slowly added a mixture of 3-isobutyroyl-2,5-dimethylthiophene (**VIIe**, 20 mmol) and ether (50 ml). The solution was refluxed for 7 h. Aqueous NH_4Cl (10%, 100 ml) was added. The organic layer was washed with water three times and dried over Na_2SO_4. Evaporation of ether gave a liquid, which was treated under vacuum at 70 °C to give a pale yellow viscous liquid (4.94 g, 86.6% yield).

Synthesis of 2,6,6-Trimethyl-5-(2,5-dimethyl-3-thienyl)-3-heptyne-2,5-diol (IIId). Under the same conditions used for **IIIe**, 20 mmol of 2-methyl-3-butyn-2-ol and 10 mmol of **VIId** gave **IIId** in a 91.3% yield.

General Precedure for the Carbonylation of III

(Synthesis of I). In a 40 ml stainless autoclave were placed diol **III**, benzene, 1 : 1 — $Pd(OAc)_2/I_2$ (5 mol%), and a stirring bar. The air was purged with carbon monoxide. The autoclave was pressurized at 80 atm and heated at 90 °C with magnetic stirring for 5 h. The reaction solution was then filtered through a short silica gel column. Benzene was evaporated under reduced pressure to give a colored viscous oil or solid mass, which was purified by column chromatography. The isolated products were recrystallized from hexane. A typical procedure was conducted as follows. The reaction conditions and yields are summarized in Table 1.

Synthesis of 3-Isopropylidene-4-[1-(2,5-dimethyl-3-thienyl)-2-methylpropylidene]dihydrofuran-2,5-dione (Ie).[5] In an autoclave were placed **IIIe** (4 mmol), benzene (10 ml), $Pd(OAc)_2$ (0.2 mmol), I_2 (0.2 mmol), and a stirring bar. The autoclave was charged with 80 atm of carbon monoxide, placed in an oil bath, and heated at 90 °C for 5 h. The autoclave was then disassembled and the reaction solution was filtered through a glass filter filled with silica gel (Wakogel C-200) 2 cm in height. After the removal of most of the benzene in a rotary evaporator, the residue was heated at 70 °C under vacuum to give a dark viscous oil (1.1 g). The oil (0.51 g) was dissolved in a mixture of 1 : 1 — hexane/benzene and chromatographed on 36 ml of Wakogel C-200 using hexane (90 ml), 1 : 1 — hexane/benzene (100 ml), 1 : 2 — hexane/benzene (45 ml), benzene (70 ml), and 1 : 1 — benzene/methanol (25 ml) as the eluent in this order. The eluate of 1 : 1 — hexane/benzene and 1 : 2 — hexane/benzene gave **Ie**(*E*) (137 mg) and **Ie**(*Z*) (279 mg), respectively, which were recrystallized from hexane.

3-Isopropylidene-4-[1-(2,5-dimethyl-3-furyl)-2,2-dimethylpropylidene]dihydro-2,5-furandione (Ia). *E* Isomer, orange needles; mp 108.0—108.5 °C; ^{1}H NMR ($CDCl_3$) $\delta=1.32$ (9H, s), 1.50 (3H, s), 1.90 (3H, s), 2.17 (3H, s), 2.22 (3H, s), and 5.81 (1H, s); IR (KBr) 1767.0 and 1813.6 cm^{-1} (C=O).

Z Isomer, orange needles; mp 107—108 °C.

Found: C, 71.45; H, 7.40%. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33%.

3-Isopropylidene-4-[1-(2,5-dimethyl-3-thienyl)2,2-dimethylpropylidene]dihydro-2,5-furandione (Ie). *E* Isomer, fine pale yellow crystals; mp 122—123 °C; ^{1}H NMR ($CDCl_3$) $\delta=1.31$ (9H, s), 1.38 (3H, s), 2.03 (3H, s), 2.14 (3H, s), 2.39 (3H, s), and 6.37 (1H, s). IR (KBr) 1766.7 and 1811.3 cm^{-1} (C=O). Found: C, 67.97; H, 6.90; S, 10.09%. Calcd for $C_{18}H_{22}O_3S$: C, 67.90; H, 6.96; S, 10.07%.

Z Isomer, white needles; mp 140—141 °C; ^{1}H NMR ($CDCl_3$) $\delta=1.19$ (9H, s), 2.19 (3H, s), 2.21 (3H, s), 2.32 (3H, s), 2.41 (3H, s), and 6.27 (1H, s); IR (KBr) 1769.0 and 1833.4 cm^{-1} (C=O). Found: C, 67.28; H, 6.86; S, 10.11%.

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