Quantum yields for **14** and **17** were determined in a similar way with **4** as an actinometer: $\phi^{254\text{nm}}(-\mathbf{14}) = 0.0.0094 \pm 0.001$; $\phi^{300\text{nm}}(-\mathbf{17}) = 0.083 \pm 0.004$.

**Flash Photolysis Experiments.** Triplet absorption spectra were obtained at 25 °C on ~3 mL of acetonitrile solutions of **5** (0.0087 M) and **14** (0.010 M) and benzophenone (0.005 M) that were thoroughly purged with argon. Benzophenone triplet decay ($2.78 \times 10^5$ s$^{-1}$) was monitored at 480 nm. The absorption spectra were generated by measuring absorbances at 5-nm intervals in the range 290–580 nm. Because of photochemical instability, the triplet absorption spectrum of isoxazole **5** was a composite of measurements taken from different samples. In addition, the spectrum was recorded in both sweep directions in which case small differences in optical densities were observed. Both compounds had a strong absorption peak at ca. 320 nm, and in addition, **5** showed a broad maximum at 480 nm and **14** showed a shoulder at 410 nm. The transient lifetimes in the absence of biphenyl were 276 and 48 ns, respectively. In the presence of 0.01 M biphenyl a new absorption appeared at 360–365 nm. Quenching rates were calculated from lifetime measurements in the presence and absence of biphenyl: **5**, $8.3 \times 10^8$ M$^{-1}$ s$^{-1}$; **14**, $2.0 \times 10^9$ M$^{-1}$ s$^{-1}$.

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# Photochemical Reactivity of Halofuran and Halothiophene Derivatives in the Presence of Arylalkenes and Arylalkynes

Maurizio D'Auria* and Giovanni Piancatelli

*Centro CNR per lo Studio della Chimica delle Sostanze Organiche Naturali, Dipartimento di Chimica, Università di Roma "La Sapienza", P.le A. Moro, 2, I-00185 Roma, Italy*

Tommaso Ferri

*Dipartimento di Chimica, Università di Roma "La Sapienza", P.le A. Moro 2, I-00185 Roma, Italy*

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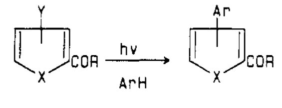
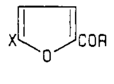
The photochemical reactions of 5-iodothiophene-2-carbaldehyde (**4a**), 2-acetyl-5-iodothiophene (**4b**), 5-bromofuran-2-carbaldehyde (**3a**), and 5-iodofuran-2-carbaldehyde (**3b**) with arylalkenes **5** (styrene), **7** (2-vinylthiophene), **10** (2-vinylfuran), **12** (4-methyl-5-vinylthiazole), and **16** (benzofuran) are reported. All of the reactions give the corresponding substitution products as a cis–trans mixture. The photochemical reaction of **4a** and **4c** (methyl 5-iodothiophene-2-carboxylate) with arylalkynes is also reported: in this case the reaction of **4a** and **4c** with phenylacetylene (**18**) furnishes the substitution products (**19** and **26**, respectively) deriving from an attack on the alkyne moiety, while the reaction with 2-ethynylthiophene (**20**) and 2-ethynylfuran (**23**) furnishes a mixture deriving from the attack both on the alkyne and on the heterocyclic ring. The ratio between these two products can be modified by changing the concentrations of the reagents. The mechanism of these reactions is discussed on the basis of photochemical and electrochemical properties of the reagents in terms of an electron-transfer process. The experimental results are explained in terms of $\Delta G$ values, and they are in agreement with the formation of both a solvent-separated pair and a contact radical ion pair.

In our previous papers we described the photochemical behavior of halofuran[1] and halothiophene[2] derivatives when irradiated in the presence of an aromatic or heteroaromatic compound. Under these conditions, compound **1** is converted into the corresponding aryl or heteroaryl derivative **2** in high yields.



1 2

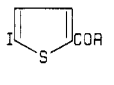
In this paper we report our results on the photochemical reactivity of 5-halofuran-2-carbaldehyde **3** and 5-iodothiophene-2-carbaldehyde, methyl ketone, or methyl carboxylate **4** when they are irradiated in the presence of aryl- and heteroarylalkenes and -alkynes. In fact, it is well-known that both aryl-substituted alkenes, such as styrene, and alkynes, such as phenylacetylene, give the photoaddition products.[3,4]



3

a: X = Br

b: X = I



4

a: R = H

b: R = $CH_3$

c: R = $OCH_3$

In our case we wanted to verify whether photochemical reactions occur on the aromatic ring or whether the presence of an unsaturated side chain could influence the reaction pattern giving photoaddition products.

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(1) (a) Antonioletti, R.; D'Auria, M.; De Mico, A.; Piancatelli, G.; Scettri, A. *Tetrahedron* **1985**, *41*, 3441. (b) Antonioletti, R.; D'Auria, M.; De Mico, A.; Piancatelli, G.; Scettri, A. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1285. (c) D'Auria, M.; D'Onofrio, F. *Gazz. Chim. Ital.* **1985**, *115*, 595. (d) D'Auria, M.; Antonioletti, R.; De Mico, A.; Piancatelli, G. *Heterocycles* **1986**, *24*, 1575.

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(3) (a) Casals, P. F.; Ferard, J.; Ropert, R. *Tetrahedron Lett.* **1976**, 3077. (b) Sano, T.; Horiguchi, Y.; Tsuda, Y.; Itatani, Y. *Heterocycles* **1978**, *9*, 161. (c) Oda, M.; Oikawa, H.; Kanao, Y.; Yamamuro, A. *Tetrahedron Lett.* **1978**, 4905. (d) Carless, H. A. J.; Kumar Maitra, A.; Trivedi, H. S. *J. Chem. Soc., Chem. Commun.* **1979**, 984. (e) Chandra, H.; Gowenlock, B. G.; Pfab, J. *J. Chem. Soc., Chem. Commun.* **1979**, 392.

(4) (a) Yamazuchi, K.; Cvetanovic, R. J. *J. Am. Chem. Soc.* **1969**, *91*, 502. (b) Sket, B.; Zupan, M. *J. Am. Chem. Soc.* **1977**, *99*, 3504. (c) Lippke, W.; Ferree, W. I.; Morrison, H. *J. Am. Chem. Soc.* **1974**, *96*, 2134.

Scheme I

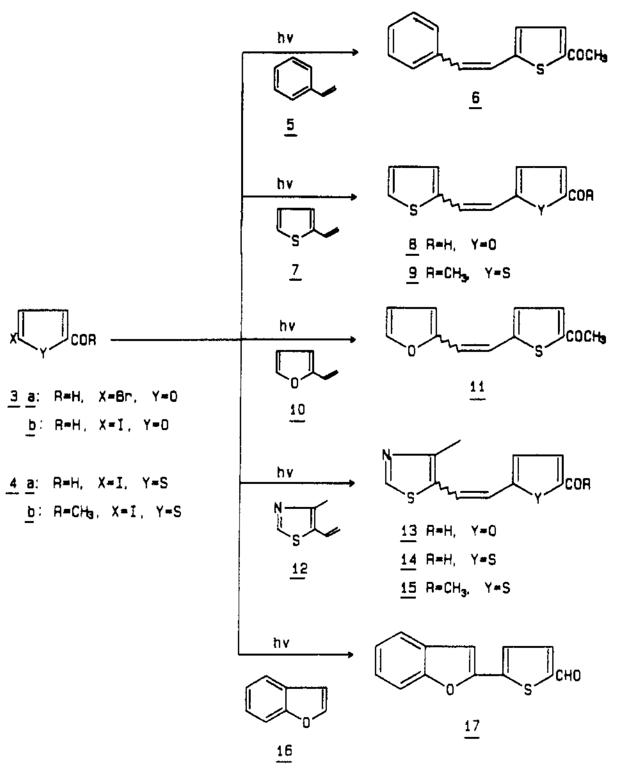

Table I. Photochemical Coupling of Haloheteroaryl Derivatives with Vinyl Compounds

| sub-strate | vinyl compd | reactn time, h | product | yield,$^a$ % | cis/trans ratio |
|---|---|---|---|---|---|
| **4b** | styrene | 3 | **6** | 98 | 1.4 |
| **4b** | 2-vinylthiophene | 1.5 | **9** | 97 | 2 |
| **4b** | 2-vinylfuran | 1.5 | **11** | 98 | 1.0 |
| **4b** | 4-methyl-5-vinylthiazole | 4 | **15** | 68 | 3 |
| **4a** | 4-methyl-5-vinylthiazole | 4 | **14** | 70 | 6 |
| **3b** | 2-vinylthiophene | 1 | **8** | 71 | 5.3 |
| **3b** | 4-methyl-5-vinylthiazole | 1 | **13** | 56 | 1 |
| **3a** | 2-vinylthiophene | 1 | **8** | 61 | 5 |

$^a$ All yields refer to isolated chromatographically pure products.

## Results and Discussion

We have studied the reaction of 5-iodothienyl derivatives (**4a,b**) with styrene (**5**) as well as with the vinyl compounds 2-vinylthiophene (**7**), 2-vinylfuran (**10**), and 4-methyl-5-vinylthiazole (**12**). The irradiation ($\lambda > 300$ nm) of **4a,b** in a degassed acetonitrile solution in the presence of a large excess of the selected olefin furnished high yields of cis–trans mixtures of the corresponding substitution products **6**, **9**, **11**, **14**, and **15** (Scheme I).

It is noteworthy that the reaction furnished almost quantitative yields of the photosubstitution product even with highly unstable vinyl compounds such as 2-vinylfuran (**10**).

Furthermore, **4a** reacted with cyclic vinyl compounds such as benzofuran (**16**) to give **17** in 70% yield.

Finally, the same trend of reactivity was observed with furan derivatives as substrate: both 5-bromo- and 5-iodofuran-2-carbaldehyde (**3**) reacted with **7** and **12** to give the corresponding substitution products (**8** and **13**) (Scheme I).

All of the products obtained were isolated as a cis–trans mixture. The cis–trans ratio was determined via GLC, and it is reported for each isolated compound in Table I. The cis–trans ratio is very variable, probably depending on the photostationary equilibrium constant of each compound.

Scheme II

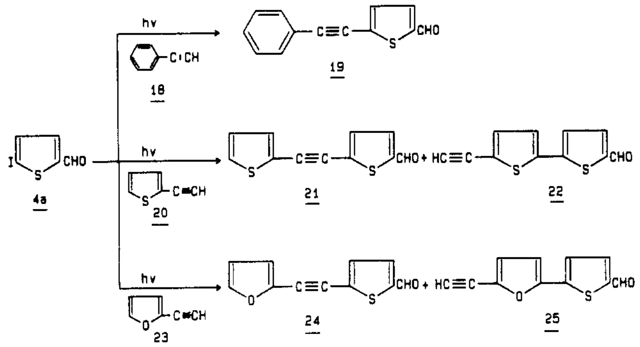

Table II. Photochemical Reaction of 4a and 4c with Alkynes

| substrate | alkyne | exptl cond | reactn time, h | product | yield,$^a$ % |
|---|---|---|---|---|---|
| **4a** | **18** | A, B$^b$ | 1.5 | **19** | 54 |
| **4a** | **20** | A | 3 | **21** | 68 |
|  |  |  |  | **22** | 30 |
| **4a** | **20** | B | 3 | **21** | 22 |
|  |  |  |  | **22** | 72 |
| **4a** | **23** | A | 1 | **24** | 33 |
|  |  |  |  | **25** | 25 |
| **4a** | **23** | B | 3 | **24** | 22 |
|  |  |  |  | **25** | 60 |
| **4c** | **18** | B | 1 | **26** | 52 |
| **4c** | **20** | B | 3 | **27** | 70 |
|  |  |  |  | **28** | 20 |

$^a$ All yields refer to isolated chromatographically pure products $^b$ A: [**4a**] = 0.0035 M; B: [**4a**] = [**4c**] = 0.007 M.

This behavior was tested by irradiating a small amount (3 mg) of the pure cis isomer of **14** under the same photochemical conditions. After 1 h of irradiation, the cis–trans ratio was identical with that obtained in the preparative experiment. However, the equilibrium is shifted to the cis isomer in most of the examples.

To our knowledge, this is the first reported photochemical substitution reaction on styrene and related structures. Substitution reactions can be obtained chemically by using palladium compounds.[5] Palladium acetate, palladium chloride, tetrakis(triphenyl)phosphine, palladium acetate in the presence of triphenylphosphine, palladium–graphite, and diacetatobis[tri(*o*-tolyl)phosphine]palladium are the most common catalysts. However, the yields are very variable, and there are very few examples in the heteroaromatic area.

The irradiation of **4a** in the presence of phenylacetylene (**18**) showed a photochemical behavior in agreement with above reported results, giving the substitution product (**19**) on the alkyne (Scheme II, Table II).

When **4a** reacted with 2-ethynylthiophene (**20**) we obtained a mixture of two products, one (**21**) deriving from the attack of **4a** on the alkyne, the other (**22**) deriving from a substitution reaction on the thiophene ring. Interestingly, we observed that by using a solution of **4a** and **20** where [**4a**] = $3.5 \times 10^{-3}$ M and [**20**] = $1.4 \times 10^{-2}$ M, we

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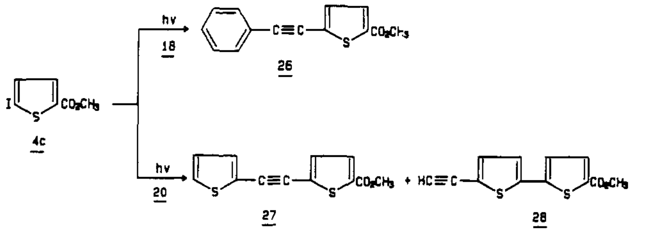
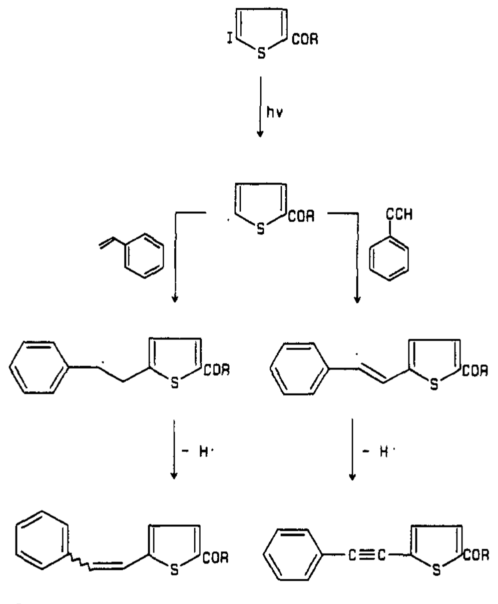
(5) (a) Asano, R.; Moritani, I.; Fujiwara, Y.; Teranishi, S. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 663. (b) Mori, K.; Mizoroki, T.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1505. (c) Fijiwara, Y.; Asano, R.; Moritani, I.; Teranishi, S. *J. Org. Chem.* **1976**, *41*, 1681. (d) Heck, R. F. *Pure Appl. Chem.* **1978**, *50*, 691. (e) Edo, K.; Sakamoto, T.; Yamanaka, H. *Heterocycles* **1979**, *12*, 383. (f) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146. (g) Savoia, D.; Trombini, C.; Umani-Ronchi, A.; Verardo, G. *J. Chem. Soc., Chem. Commun.* **1981**, 541. (h) Fujiwara, Y.; Maruyama, O.; Yoshidomi, M.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 851. (i) Horino, H.; Inoue, N.; Asao, T. *Tetrahedron Lett.* **1981**, 741. (j) Blaser, H. U.; Spencer, A. *J. Organomet. Chem.* **1982**, *233*, 267. (k) Spencer, A. *J. Orgnomet. Chem.* **1982**, *240*, 209; **1983**, *258*, 101; **1984**, *270*, 115.

**Scheme III**



**Scheme IV**



obtained **21** in 68% yield and **22** in 30%. On the contrary, when we used as starting material a solution where [**4a**] = $7.0 \times 10^{-3}$ M and $[^{20}]$ = $2.8 \times 10^{-2}$ M, the irradiation furnished a 22% yield of **21** and a 72% yield of **22**. The same results were obtained by using 2-ethynylfuran (**23**) as alkyne: in this case the reaction gave a mixture of two products, the ratio depending on the concentration of the reagents (Table II).

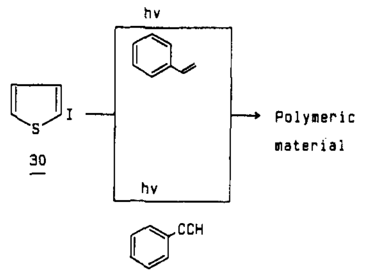
The reaction of methyl 5-iodothiophene-2-carboxylate (**4c**) with both **18** and **20** showed the same trend of reactivity (Scheme III): while **4c** reacted with **18** giving **26** in 52% yield, the reaction of the same substrate ([**4c**] = $7.0 \times 10^{-3}$ M) with **20** ([**20**] = $2.8 \times 10^{-2}$ M) furnished a mixture of **27** and **28** in a 3.5:1 ratio (90% yield, Table II).

It is noteworthy that, to the best of our knowledge, the conversions **4a** → **19** and **4c** → **26** are the first examples of a photosubstitution reaction on an alkyne moiety, as well as the above-described reaction with arylalkenes.

We have described that the photosubstitution of halofuran and halothiophene derivatives with an aromatic compound probably occurs through the formation of an exciplex as intermediate.[1c,2g]

In this case, the conversion **4b** → **6** and **4a** → **19** can evolve through a homolytic cleavage of a C–I bond and subsequent reaction of the radical with the alkene and the alkyne, respectively (Scheme IV). This scheme is not consistent with experimental results. In fact, the irradiation of 2-iodothiophene (**30**), a compound able to furnish 2-thienyl radical under photochemical conditions,[6] in the presence of styrene (**5**) or phenylacetylene (**18**) did not give any interesting result, yielding only polymeric materials (Scheme V).

**Scheme V**



On the other hand, above we have described the reaction of 5-bromofuran-2-carbaldehyde (**3a**) with heteroarylalkenes, while we have previously reported[1c] that this compound (**3a**) shows $E_T$ = 54 kcal mol$^{-1}$, which is insufficient for homolytic C–Br fission (the bond dissociation energy is about 70 kcal mol$^{-1}$). Thus, we think that also in the above-described reactions the mechanism involves a single electron transfer between halofuran or halothiophene derivatives (acceptors) or aryl- or heteroarylalkenes and -alkynes (donors).

The production of radical ions via photoinduced electron transfer can be predicted by using the Weller equation (1),[7]

$$\Delta G = F[E_{1/2}{}^{\mathrm{Ox}}(\mathrm{D}) - E_{1/2}{}^{\mathrm{Red}}(\mathrm{A})] - \Delta E_{\mathrm{exc}} + (e^2N/4\pi\epsilon_0 a)\,[(1/\epsilon) - (2/37.5)] \quad (1)$$

where $E_{1/2}{}^{\mathrm{Ox}}(\mathrm{D})$ and $E_{1/2}{}^{\mathrm{Red}}(\mathrm{A})$ are the oxidation and reduction potentials of the donor and acceptor molecules, respectively, and $\Delta E_{\mathrm{exc}}$ is the excitation energy. We have calculated $\Delta G$ values for the reaction of **4a** with styrene (**5**) and 4-methyl-5-vinylthiazole (**12**) on the one hand and with phenylacetylene (**18**) and 2-ethynylthiophene (**20**) on the other.

5-Iodothiophene-2-carbaldehyde (**4a**) showed in the UV spectrum an absorption at 306 nm ($\epsilon$ = 12100). Compound **4a** did not show a fluorescence spectrum. This behavior can be explained by considering a quantitative intersystem crossing to the lowest excited triplet state. The triplet state of compound **4a** did not show a phosphorescence spectrum: therefore, the $E_T$ value for this compound was estimated by using photoisomerization of *trans*-stilbene in benzene.[8] Because **4a** reacted with stilbene, we used thiophene-2-carbaldehyde as substrate, obtaining $E_T$ = 60 kcal mol$^{-1}$. In fact, using both furan and thiophene derivatives, we have found[1c,9] that the presence of a halogen atom on the heteroaromatic ring does not influence the triplet energy.

The $E_{1/2}{}^{\mathrm{Red}}$ value for 5-iodothiophene-2-carbaldehyde (**4a**) was −0.66 V. This datum was calculated from the pulsed polarographic curve (vs SCE), adding 0.5 mL of a $10^{-3}$ M solution of **4a** in MeOH in 15 mL of phosphate buffer (pH = 7). Styrene shows $E_{1/2}{}^{\mathrm{Ox}}$ = 1.90 V vs SCE.[10]

Concerning the electrochemical behavior of 4-methyl-5-vinylthiazole (**12**), phenylacetylene (**18**), and 2-ethynylthiophene (**20**), only information about phenylacetylene is available.[10] As is the case with phenylacetylene, **12** and **20** show voltammetric activity only in

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(6) (a) Wolf, W.; Kharasch, N. *J. Org. Chem.* **1965**, *30*, 2493. (b) Benati, L.; Tiecco, M. *Boll. Sci. Fac. Chim. Ind. Bologna* **1966**, *24*, 45, 225. (c) Martelli, G.; Spagnolo, P.; Tiecco, M. *J. Chem. Soc. B* **1966**, 901.

(7) (a) Gordon, M.; Ware, W. R. *The Exciplex*; Academic Press: New York, 1975. (b) Weller, A. *Pure Appl. Chem.* **1968**, *16*, 115; **1982**, *54*, 1885. (c) Mattay, J. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 825. (d) Mattay, J. *Synthesis* **1989**, 233.

(8) (a) Hammond, G. S.; Saltiel, J.; Lamola, A. A.; Turro, N. J.; Bradshaw, J. S.; Cowan, D. O.; Counsell, R. C.; Vogt, V.; Dalton, C. *J. Am. Chem. Soc.* **1964**, *86*, 3197. (b) Lamola, A. A.; Hammond, G. S. *J. Chem. Phys.* **1965**, *43*, 2129. (c) Herkstroeter, W. G.; Hammond, G. S. *J. Am. Chem. Soc.* **1966**, *88*, 4769.

(9) D'Auria, M., unpublished results.

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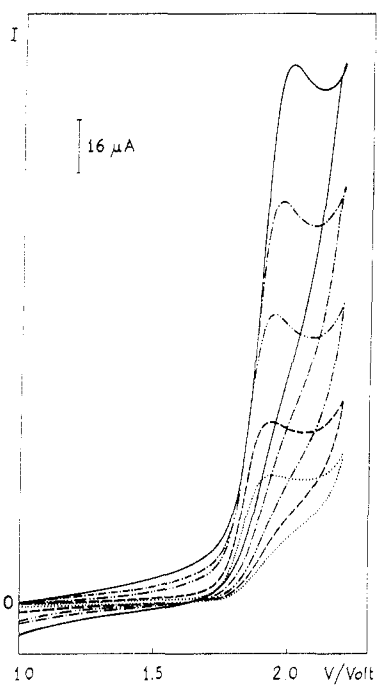


**Figure 1.** Cyclic voltammograms of a 6 × $10^{-4}$ M acetonitrile solution of **20**: (···) 10, (- - -) 20, (-··) 50, (-·-) 100, and (—) 200 mV/s. The electrode was cleaned after each run.

media capable of reaching very high positive potentials. We used acetonitrile with sodium perchlorate as supporting electrolyte.

In this medium, 4-methyl-5-vinylthiazole (**12**), 2-ethynylthiophene (**20**), and phenylacetylene (**18**) show an anodic signal whose peak potentials versus the adopted reference electrode are 1.78, 1.89, and 2.35 V, respectively (6 × $10^{-4}$ M, 20 mV $s^{-1}$). As evident from the peak potential values, the signals of **12** and **20** are much better defined than that of **18**, occurring at a higher value.

Cyclic voltammetric experiments showed that these compounds yield an irreversible electrode process: no cathodic peak is present, the $i/v^{1/2}$ ($v$ = potential scan rate) ratio is nearly constant, and the peak potential shifts toward more positive values with scan rate. In Figure 1, some curves relative to **20** are reported.

These are reports in the literature of the irreversibility, on a Pt electrode, of alkenes with formation of dimers[10–13] through a carbon ion. In our case, the formation of dimers or more probably polymeric species is evidenced by modification of the electrode surface. This modification is evident on a voltammogram recorded prior to any cleaning of the electrode surface: a signal much lower in intensity and shifted toward more positive values is obtained. If the electrode surface is cleaned by rinsing the electrode with dichloromethane (a good solvent of polymer species) after each voltammetric run, reproducible peaks (within ±10% for the intensity and ±10 mV for the peak potential) are obtained. The above-mentioned phenomenon is clearly seen by Figure 2.

On the basis of these results we can calculate $\Delta G$ values for selected reactions (Table III). For this purpose we have corrected the obtained potentials vs $Ag^+/Ag$ (see Experimental Section). Furthermore, correction of peak potentials as reported by Miller[14] was considered.

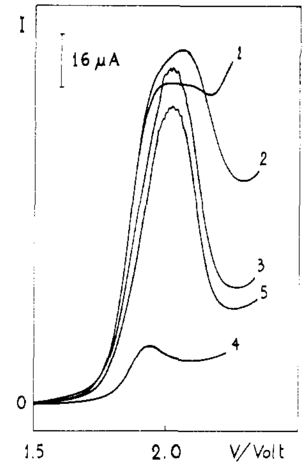
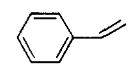
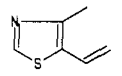
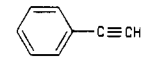
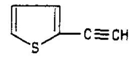
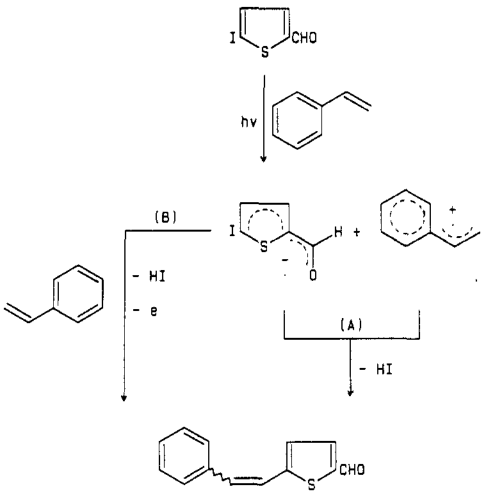


**Figure 2.** Linear sweep voltammograms performed on a 1.2 × $10^{-3}$ M acetonitrile solution of **20**. Curves 1–3 were recorded after the electrode was cleaned prior to each run, then curve 4 was recorded without any cleaning of the electrode, and finally curve 5 was obtained after the electrode was again cleaned.

**Table III.** $\Delta G$ **Values for the Reaction between 4a and Selected Alkenes and Alkynes**

| entry | alkene or alkyne | $\Delta G$, eV |
|---|---|---|
| 1 |  | −0.10 |
| 2 |  | −0.25 |
| 3 |  | 0.32 |
| 4 |  | −0.14 |

**Scheme VI**



$\Delta G$ values for the reaction of **4a** with alkenes are in agreement with the formation of a solvent-separated ion pair (Scheme VI). This radical pair can evolve to the product via a radical coupling with subsequent elimination of HI (path A). Alternatively, the ketyl **31** can react with another molecule of the alkene to give the product (path B). The formation of a benzylic radical (path B) or a carbonium ion (path A) as intermediates can explain the high observed regiospecificity.

The same reaction pattern can be formulated for the reaction with phenylacetylene. In this case the positive value of $\Delta G$ can be in agreement with the formation of a contact ion pair. Then the system evolves following path

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[11] Fritsch, J. M.; Weingarten, H. *J. Am. Chem. Soc.* **1968**, *90*, 793.

[12] O'Connor, J. J.; Pearl, I. A. *J. Electroanal. Chem.* **1965**, *111*, 335.

[13] Bond, A. M. *Modern Polarographic Methods in Analytical Chemistry*; Marcel Dekker: New York, 1980.

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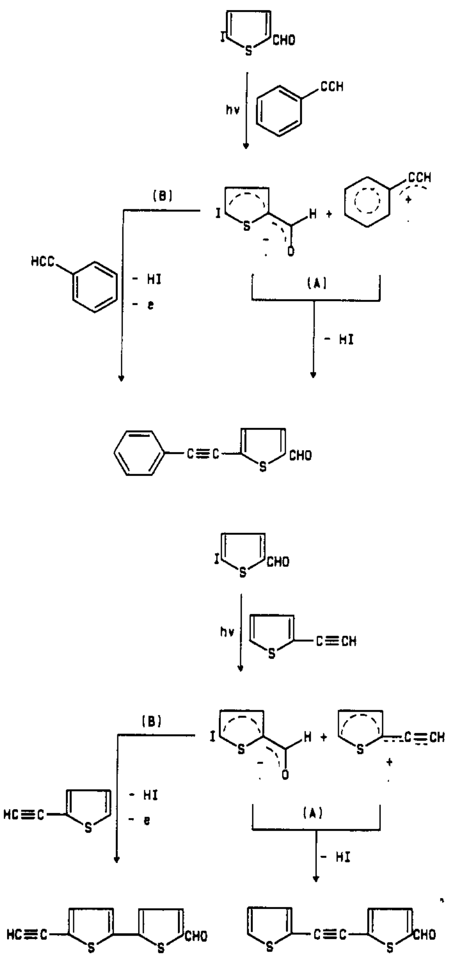
**Scheme VII**



A of Scheme VII. On the contrary, when the reaction is performed with **20**, a solvent-separated ion pair can be formed, and, in this case, the ketyl **31** and react following path B: since attack of the triple bond is not favored by formation of a benzyl type radical as well as in the case of arylalkenes, attack on the aromatic ring is possible. This scheme can explain the experimental results obtained at different concentrations. In fact, since the ketyl must encounter a molecule of the alkyne to react, by using diluted solutions, we can increase the reactions following path A.

In conclusion, we have described some interesting photochemical reactions of halothiophene and halofuran derivatives. With aryl- and heteroarylalkenes and -alkynes, the reactions furnish only photosubstitution products, never described before by using photochemical methods. Our results are in agreement with a mechanism involving a single electron transfer between halothiophene derivative (the acceptor) and alkene or alkyne (the donor).

## Experimental Section

$^1$H NMR spectra were recorded with Varian EM-360, Bruker W-80 SY, and Varian Gemini 200-MHz spectrometers, using $CCl_4$ or $CDCl_3$ as solvent with $Me_4Si$ as internal standard. IR spectra were obtained on a Perkin-Elmer 457 spectrometer. Mass spectra were obtained at 70 eV with a Kratos MS-80 instrument by direct insertion at a source temperature of 150 °C. Commercial Merck silica gel plates were used for TLC. UV spectra were recorded with a Varian DMS-90 spectrophotometer. GLC analyses were performed with Hewlett-Packard 5880A and 5890 instruments (flame ionization detector).

**Starting Materials.** 2-Iodothiophene (**30**) was prepared from thiophene by reaction with iodine and HgO.[15] The product was converted into 2-acetyl-5-iodothiophene (**4b**) by reaction with $Ac_2O$ in the presence of $H_3PO_4$.[16] 2-Vinylthiophene (**7**) was obtained from thiophene by reaction with $CH_3CHO$ and subsequent elimination.[17] 2-Vinylfuran (**10**) was obtained through decarbonylation of 3-(2-furyl)acrylic acid.[18] 5-Iodothiophene-2-carbaldehye (**4a**) was obtained from thiophene-2-carbaldehyde through reduction with $NaBH_4$, iodination of the corresponding alcohol with iodine and HgO, and subsequent oxidation of 5-iodothiophene-2-methanol with PCC (pyridinium chlorochromate).[2c] 5-Bromofuran-2-carbaldehyde (**3a**) was prepared by reacting furan-2-carbaldehyde with bromine in 1,2-dichloroethane.[19] This compound was converted into 5-iodofuran-2-carbaldehyde (**3b**) by reaction with KI in AcOH.[20] 2-Ethynylthiophene (**20**) was prepared from thiophene-2-carbaldehyde by reaction with $CBr_4/PPh_3$ in $CH_2Cl_2$ and subsequent reaction of the dibromoalkene with BuLi and then water.[21] The same procedure can furnish 2-ethynylfuran.[22] Methyl 5-iodothiophene-2-carboxylate (**4c**) was obtained from methyl thiophene-2-carboxylate[23] through reaction with iodine and iodic acid.[24]

**Photochemical Reaction of Halothiophene and Halofuran Derivatives with Alkenes. General Procedure.** The halothiophene (**4a,b**) or halofuran (**3a,b**) derivative (1 g) was dissolved in acetonitrile (300 mL) in the presence of a vinyl compound (**5**, **7**, **10**, **12**, or **16**) (3 g). The mixture was degassed with nitrogen for 1 h and then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. When the reaction was completed (Table I), the mixture was dissolved in chloroform and washed successively with 0.1 M $Na_2S_2O_3$ and then with brine. The organic phase was dried ($Na_2SO_4$) and evaporated to yield a crude product that was chromatographed on $SiO_2$. Elution with chloroform–*n*-hexane (2:1) gave pure products (Table I).

**(*E,Z*)-2-Acetyl-5-(β-phenylvinyl)thiophene (6)**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 7.8–7.0 (m, 7 H), 6.93 (d, 1 H, $J$ = 5 Hz), 6.71 (d, 1 H, $J$ = 5 Hz), 2.53 (s, 1 H), 2.44 (s, 2 H); IR ($CHCl_3$) $\nu_{max}$ 1715, 1455, 1100 cm$^{-1}$; mass spectrum, *m/z* 228 ($M^+$, 100), 213 (48); HRMS 228.3162 (calcd for $C_{14}H_{12}OS$, 228.3151).

**(*E,Z*)-5-[β-(2′-Thienyl)vinyl]furan-2-carbaldehyde (8)**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 9.51 (s, 1 H), 7.25 (d, 1 H, $J$ = 2.5 Hz), 7.17 (d, 1 H, $J$ = 2.5 Hz), 6.76 (d, 1 H, $J$ = 7.5 Hz), 6.55 (d, 1 H, $J$ = 2.5 Hz), 6.40 (d, 1 H, $J$ = 2.5 Hz), 6.25 (d, 1 H, $J$ = 7.5 Hz); IR ($CHCl_3$) $\nu_{max}$ 1680, 1460, 1380, 1020, 960 cm$^{-1}$; mass spectrum, *m/z* 206 ($M^+$ + 2, 6), 205 ($M^+$ + 1, 12), 204 ($M^+$, 100), 175 (25), 147 (60), 121 (10), 115 (10); HRMS 204.2484 (calcd for $C_{11}H_8O_2S$, 204.2492).

**(*E,Z*)-2-Acetyl-5-[β-(2′-thienyl)vinyl]thiophene (9)**: very dense oil; $^1$H NMR ($CCl_4$) $\delta$ 7.33 (d, 1 H, $J$ = 4 Hz), 7.20–6.57 (m, 5 H), 6.45 (d, 1 H, $J$ = 5 Hz), 2.36 (s, 3 H); IR ($CCl_4$) $\nu_{max}$ 1670, 1455, 1425, 1360, 1280, 700 cm$^{-1}$; mass spectrum, *m/z* 234 ($M^+$, 99), 220 (13), 219 (100), 190 (14), 158 (26), 147 (25); HRMS 234.3413 (calcd for $C_{12}H_{10}OS_2$, 234.3409).

**(*E,Z*)-2-Acetyl-5-[β-(2′-furyl)vinyl]thiophene (11)**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 7.50–6.70 (m, 4 H), 6.50–5.80 (m, 3 H), 2.40 (s, 1.5 H), 2.38 (s, 1.5 H); IR (film) $\nu_{max}$ 1665, 1435, 1360, 1280, 1150, 1075, 1015, 930, 780, 765, 740 cm$^{-1}$; mass spectrum, *m/z* 218 ($M^+$, 100), 203 (52); HRMS 218.2775 (calcd for $C_{12}H_{10}O_2S$, 218.2763).

**(*E,Z*)-5-[β-(4′-Methyl-5′-thiazolyl)vinyl]furan-2-carbaldehyde (13)**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 9.64 (s, 0.5 H), 9.61 (s, 0.5 H), 8.74 (s, 0.5 H), 8.62 (s, 0.5 H), 7.25 (m, 1 H), 6.72 (s, 0.5 H), 6.63 (s, 0.5 H), 6.50 (m, 2 H), 2.57 (s, 1.5 H), 2.48

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(s, 1.5 H); IR ($CHCl_3$) $\nu_{max}$ 1665, 1625, 1555, 1530, 1465, 1400, 1380, 1255, 1245, 1025, 975, 960, 945, 805, 755 cm$^{-1}$; mass spectrum, *m/z* 221 (M$^+$ + 2, 6), 220 (M$^+$ + 1, 13), 219 (M$^+$, 100), 218 (10), 191 (14), 190 (78), 174 (9), 173 (19), 172 (28), 163 (23), 162 (40), 161 (12), 149 (9), 148 (10), 136 (11), 135 (38), 134 (24), 102 (11), 91 (36), 77 (9), 69 (11); HRMS 219.2645 (calcd for $C_{11}H_9O_2SN$, 219.2639).

**(*E*,*Z*)-5-[$\beta$-(4′-Methyl-5′-thiazolyl)vinyl]thiophene-2-carbaldehyde (14)**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 9.80 (s, 1 H), 8.69 (s, 1 H), 7.61 (d, 1 H, *J* = 4 Hz), 7.06 (d, 1 H, *J* = 4 Hz), 6.94 (d, 1 H, *J* = 4.5 Hz), 6.72 (d, 1 H, *J* = 4.5 Hz), 2.35 (s, 3 H); IR ($CHCl_3$) $\nu_{max}$ 1675, 1455, 1320, 940 cm$^{-1}$; mass spectrum, *m/z* 237 (M$^+$ + 2, 9), 236 (M$^+$ + 1, 14), 235 (M$^+$, 100), 192 (18), 172 (7); HRMS 235.3298 (calcd for $C_{11}H_9OS_2N$, 235.3285).

**(*E*,*Z*)-2-Acetyl-5-[$\beta$-(4′-methyl-5′-thiazolyl)vinyl]thiophene (15)**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 8.78 (s, 1 H), 7.59 (d, 1 H, *J* = 5 Hz), 7.12 (d, 1 H, *J* = 4.5 Hz), 7.01 (d, 1 H, *J* = 5 Hz), 6.75 (d, 1 H, *J* = 4.5 Hz), 2.50 (s, 3 H), 2.40 (s, 3 H); IR (film) $\nu_{max}$ 1665, 1615, 1500, 1440, 1415, 1360, 1315, 1270, 1110, 1070, 1030, 940, 925, 910 cm$^{-1}$; mass spectrum, *m/z* 251 (M$^+$ + 2, 10), 250 (M$^+$ + 1, 14), 249 (M$^+$, 100), 235 (12), 234 (92), 162 (6); HRMS 249.3549 (calcd for $C_{12}H_{11}OS_2N$, 249.3556).

**5-[$\beta$-(2′-Benzofuryl)vinyl]thiophene-2-carbaldehyde (17)**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 9.88 (s, 1 H), 7.7 (m, 2 H), 7.5 (m, 2 H), 7.51 (s, 1 H), 7.34 (s, 2 H); IR ($CHCl_3$) $\nu_{max}$ 1670, 1440, 1145, 1110 cm$^{-1}$; mass spectrum, *m/z* 230 (M$^+$ + 2, 7), 229 (M$^+$ + 1, 14), 228 (M$^+$, 100), 227 (38); HRMS, 228.2730 (calcd for $C_{13}H_8O_2S$, 228.2715).

**5-(Phenylethynyl)-thiophene-2-carbaldehyde (19).** 5-Iodothiophene-2-carbaldehyde (**4a**) (0.5 g) was dissolved in acetonitrile (300 mL) in the presence of phenylacetylene (**18**) (3 g) and degassed with nitrogen for 1 h. The mixture was then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. After 1.5 h, the above-described workup yielded a crude product that was chromatographed on $SiO_2$. Elution with benzene gave pure **19** (240 mg): very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 9.80 (s, 1 H), 7.60 (d, 1 H, *J* = 3.3 Hz), 7.47 (m, 2 H), 7.32 (m, 3 H), 7.25 (d, 1 H, *J* = 3.3 Hz); IR ($CHCl_3$) $\nu_{max}$ 2215, 1675, 1445, 1410, 1105, 955, 910 cm$^{-1}$; mass spectrum, *m/z* 214 (M$^+$ + 2, 6), 213 (M$^+$ + 1, 17), 212 (M$^+$, 100), 211 (64), 139 (34); HRMS 212.2734 (calcd for $C_{13}H_8OS$, 212.2721).

**Photochemical Reaction of 4a with 2-Ethynylthiophene (20).** 5-Iodothiophene-2-carbaldehyde (**4a**) (0.5 g) was dissolved in acetonitrile (300 mL) in the presence of 2-ethynylthiophene (**20**) (3 g) and degassed with nitrogen for 1 h. The mixture was then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. After 3 h, the above-described workup yielded a crude product that was chromatographed on $SiO_2$. Elution with benzene gave pure **22** (330 mg) and **21** (100 mg). **22**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 9.93 (s, 1 H), 7.7 (m, 2 H), 7.3 (m, 2 H), 3.45 (s, 1 H); IR ($CHCl_3$) $\nu_{max}$ 3305, 2200, 1665, 1450, 1410, 910 cm$^{-1}$; mass spectrum, *m/z* 220 (M$^+$ + 2, 11), 219 (M$^+$ + 1, 19), 218 (M$^+$, 100), 217 (55), 189 (11), 145 (26). **21**: mp 78–79 °C; $^1$H NMR ($CDCl_3$) $\delta$ 9.83 (s, 1 H), 7.66 (d, 1 H, *J* = 5 Hz), 7.38 (m, 2 H), 7.29 (d, 1 H, *J* = 5 Hz), 7.03 (dd, 1 H, *J* = 4 Hz); IR ($CHCl_3$) $\nu_{max}$ 2720, 2200, 1670 cm$^{-1}$; mass spectrum, *m/z* 220 (M$^+$ + 2, 12), 219 (M$^+$ + 1, 19), 218 (M$^+$, 100), 217 (56), 190 (6), 189 (13), 145 (24); HRMS 218.2990 (calcd for $C_{11}H_6OS_2$, 218.2979). When the reaction was performed by using 0.25 g of **4a** and 1.5 g of **20**, 69 mg of **21** and 156 mg of **22** were obtained.

**Photochemical Reaction of 4a with 2-Ethynylfuran (23).** 5-Iodothiophene-2-carbaldehyde (**4a**) (0.5 g) was dissolved in acetonitrile (270 mL) in the presence of 2-ethynylfuran (**23**) (3 g) and degassed with nitrogen for 1 h. The mixture was then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. After 3 h, the above-described workup yielded a crude produced that was chromatographed on $SiO_2$. Elution with benzene gave pure **25** (254 mg) and **24** (95 mg). **25**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 9.86 (s, 1 H), 7.67 (d, 1 H, *J* = 4 Hz), 7.35 (d, 1 H, *J* = 4 Hz), 6.71 (d, 1 H, *J* = 4 Hz), 6.68 (d, 1 H, *J* = 4 Hz), 3.51 (s, 1 H); IR ($CHCl_3$) $\nu_{max}$ 3310, 2740, 2260, 1668, 1495, 1434, 1020, 960, 910 cm$^{-1}$; mass spectrum, *m/z* 204 (M$^+$ + 2, 7), 203 (M$^+$ + 1, 14), 202 (M$^+$, 100), 201 (37), 145 (19); HRMS 202.2327 (calcd for $C_{11}H_6O_23S$, 202.2333). **24**: very dense oil; $^1$H NMR ($CDCl_3$) $\nu$ 9.85 (s, 1 H), 7.64 (d, 1 H, *J* = 4 Hz), 7.46 (d, 1 H, *J* = 2 Hz), 7.30 (d, 1 H, *J* = 4 Hz), 6.74 (d, 1 H, *J* = 3 Hz), 6.44 (dd, 1 H, $J_1$ = 3 Hz, $J_2$ = 2 Hz); IR ($CHCl_3$) $\nu_{max}$ 2740, 2200, 1670, 1430, 1408, 1010, 910 cm$^{-1}$; mass spectrum, *m/z* 204 (M$^+$ + 2, 6), 203 (M$^+$ + 1, 13), 202 (M$^+$, 100), 201 (10), 173 (23), 145 (28), 102 (11). When the reaction was performed by using 0.25 g of **4a** and 1.5 g of **23**, 56 mg of **25** and 73 mg of **24** were obtained.

**Methyl 5-(Phenylethynyl)thiophene-2-carboxylate (26).** Methyl 5-iodothiophene-2-carboxylate (**4c**) (0.5 g) was dissolved in acetonitrile (300 mL) in the presence of phenylacetylene (**18**) (3 g) and degassed for 1 h. The mixture was then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. After 1.5 h, the above-described workup yielded a crude product that was chromatographed on $SiO_2$. Elution with $CHCl_3$–*n*-hexane (1:1) gave pure **26** (239 mg): very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 7.66 (d, 1 H, *J* = 4 Hz), 7.5 (m, 2 H), 7.3 (m, 3 H), 7.18 (d, 1 H, *J* = 4 Hz), 3.86 (s, 3 H); IR (film) $\nu_{max}$ 2200, 1670, 1600, 1525, 1490, 1448, 1432, 1405, 1350, 1323, 1285, 1250, 1240, 1095, 785, 750, 685 cm$^{-1}$; mass spectrum, *m/z* 244 (M$^+$ + 2, 6), 243 (M$^+$ + 1, 16), 242 (M$^+$, 100), 212 (16), 211 (96), 139 (50), 91 (13); HRMS 242.3002 (calcd for $C_{14}H_8O_2S$, 242.2986).

**Photochemical Reaction of 4c with 2-Ethynylthiophene (20).** Methyl 5-iodothiophene-2-carboxylate (**4c**) (0.5 g) was dissolved in acetonitrile (300 mL) in the presence of 2-ethynylthiophene (**20**) (3 g) and degassed with nitrogen for 1 h. The mixture was then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. After 3 h, the above-described workup yielded a crude product that was chromatographed on $SiO_2$. Elution with $CHCl_3$–*n*-hexane (1:1) gave pure **28** (323 mg) and **27** (96 mg). **28**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 7.25 (s, 4 H), 3.90 (s, 3 H), 3.33 (s, 1 H); IR (film) $\nu_{max}$ 3310, 2105, 1715, 1530, 1440, 1410, 1330, 1290, 1260, 1195, 1098, 855, 815, 745, 705 cm$^{-1}$; mass spectrum, *m/z* 250 (M$^+$ + 2, 8), 249 (M$^+$ + 1, 14), 248 (M$^+$, 100), 217 (94), 189 (8), 145 (51). **27**: very dense oil; $^1$H NMR ($CDCl_3$) $\delta$ 7.69 (d, 1 H, *J* = 4 Hz), 7.31 (m, 1 H), 7.21 (d, 1 H, *J* = 4 Hz), 7.05 (d, 1 H, *J* = 4 Hz), 6.98 (d, 1 H, *J* = 4 Hz), 3.90 (s, 3 H); IR $CHCl_3$) $\nu_{max}$ 2205, 1715, 1455, 1440, 1415, 1335, 1295, 1270, 1100 cm$^{-1}$; mass spectrum, *m/z* 250 (M$^+$ + 2, 9), 249 (M$^+$ + 1, 14), 248 (M$^+$, 100), 217 (98), 189 (6), 145 (50); HRMS 248.3257 (calcd for $C_{12}H_8O_2S_2$, 248.3244).

**Triplet Energy of Thiophene-2-carbaldehyde.** A benzene solution (50 mL) containing 0.05 mol dm$^{-3}$ of *trans*-stilbene and 0.05 mol dm$^{-3}$ of thiophene-2-carbaldehyde was irradiated with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket for 4 h under nitrogen in a quartz tube surrounded by a quartz water jacket connected to a Haake F3 thermostat to maintain the temperature at 28.0 ± 0.1 °C. The cis–trans ratio was determined via GLC.

**Voltammograms of 12, 18, and 20.** All voltammograms were obtained on an Amel Model 472 (Amel, Milano, Italy) polarograph equipped with a potentiostatic control, allowing potential scan rates up to 200 mV/s. As stationary working electrode the Metrohm 6.0302.000 platinum electrode was used, while a mercury pool was used as the counter electrode.[25] Finally, all of the potential values were referred to an Ag,AgCl/LiCl$_{satd}$ (in acetonitrile) reference electrode[26] whose potential value vs the aqueous SCE is −124 mV (at 27 °C). The experiments were carried out in acetonitrile containing $NaClO_4$ (0.114 M) as supporting electrolyte. All experiments were performed at room temperature (from 25 to 28 °C) on 25 mL of solution. The solutions to be processed were first bubbled with UPP nitrogen for a few seconds, and then a nitrogen atmosphere was maintained above the solution in order to prevent contact with air. The voltammograms were recorded at a 20 mV/s scan rate unless otherwise specified.

**Registry No. 3a**, 1899-24-7; **3b**, 2689-65-8; **4a**, 5370-19-4; **4b**, 30955-94-3; **4c**, 88105-22-0; **5**, 100-42-5; (*Z*)-**6**, 2689-65-8; (*E*)-**6**, 125972-78-3; **7**, 1918-82-7; (*Z*)-**8**, 125972-65-8; (*E*)-**8**, 125972-79-4;

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*J. Org. Chem.* **1990**, *55*, 4025-4033

(*Z*)-**9**, 125972-66-9; (*E*)-**9**, 125972-80-7; **10**, 1487-18-9; (*Z*)-**11**, 125972-67-0; (*E*)-**11**, 125972-81-8; **12**, 1759-28-0; (*Z*)-**13**, 125972-68-1; (*E*)-**13**, 125972-82-9; (*Z*)-**14**, 125972-69-2; (*E*)-**14**, 125972-83-0; (*Z*)-**15**, 125972-70-5; (*E*)-**15**, 125972-84-1; **16**, 271-89-6; **17**, 125972-71-6; **18**, 536-74-3; **19**, 17257-10-2; **20**, 4298-52-6; **21**, 36687-75-9; **22**, 125972-72-7; **23**, 18649-64-4; **24**, 125972-73-8; **25**, 125972-74-9; **26**, 125972-75-0; **27**, 125972-76-1; **28**, 125972-77-2; **30**, 3437-95-4.

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# Hydroxyl-Directing Effects on [1,7]-Sigmatropic Hydrogen Migrations[1]

Kuo-Ming Wu and William H. Okamura*

*Department of Chemistry, University of California, Riverside, California 92521*

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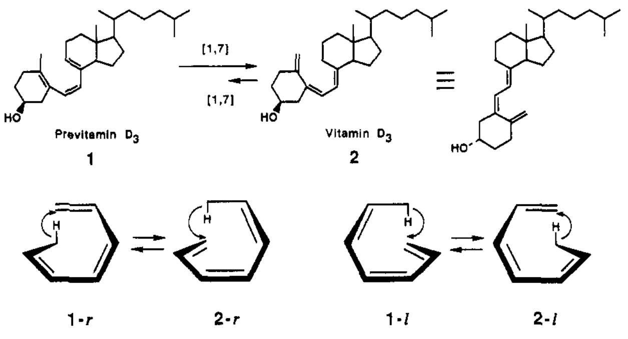
Previous stereomechanistic investigations of thermally induced [1,7]-sigmatropic shifts of *cis*-isotachysterol analogues **8** and **14** revealed that an allylic hydroxyl exerts a syn-directing effect on the helicity of this antarafacial process. Studies of *cis*-isotachysterols **17** and **18**, wherein the allylic hydroxyl control element at $C_1$ is relocated to a new position on the steroid, namely $C_4$, were undertaken to develop a better understanding of this eight-electron pericyclic reaction. The rearrangement in isooctane at 98.4 °C of **17** to **24** and **25** and of **18** to **26** and **27** and their equilibrations were studied quantitatively. The results reveal that the hydroxyl syn-facial directing effect on the antarafacial helicity of this rearrangement is retained for **17** and **18** and that the magnitude of this $\pi$-facial selectivity is similar to that observed for **8** and **14**.

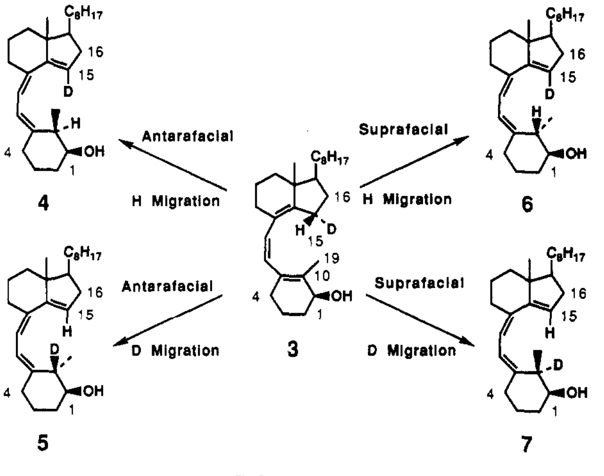
## Introduction

The intramolecular nature of the thermal equilibrium between previtamin $D_3$ (**1**) and vitamin $D_3$ (**2**)[2] involving a [1,7]-sigmatropic hydrogen migration[3] (Scheme I) was established in 1965 by a tritium-labeling experiment.[4] In the same year Woodward and Hoffmann on the basis of orbital symmetry considerations predicted that thermal [1,7]-sigmatropic hydrogen shifts should be an antarafacial, allowed and suprafacial, forbidden process.[5] Thus for the rearrangement of **1** to **2**, the hydrogen transfer may occur either via the right-handed or left-handed helical pathway depicted as **1**-*r* to **2**-*r* or **1**-*l* to **2**-*l*. However, it was not until recently that the antarafaciality of this rearrangement process was demonstrated[6a,b] wherein an appropriate deuterium-labeling experiment was carried out. The *cis*-isotachysterol analogue **3** and its hydroxyl epimer (both with deuterium label at the $C_{15}$-$\alpha$ position) were synthesized and then their thermal rearrangements were studied. The antarafacial nature of this rearrangement was established by the finding that only **4** and **5** (and no **6** and **7**) were observed within experimental error (>98%) from thermolysis of *cis*-isotachysterol analogue **3** (Scheme II). Parallel conclusions were reached for the $C_1$ epimer of **3**.

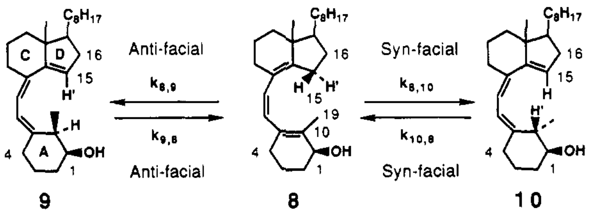
**Scheme I**



**Scheme II**



**Scheme III**



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(1) (a) This is Paper 36 in the series Studies of Vitamin D (Calciferol) and Its Analogues. For paper 35, see: Okamura, W. H.; Aurrecoechea, J. M.; Gibbs, R. A.; Norman, A. W. *J. Org. Chem.* **1989**, *54*, 4072. (b) This paper was taken in part from the Ph.D. Thesis submitted to the University of California, Riverside, by K.-M. Wu, September, 1989.

(2) For selected studies of the previtamin D–vitamin D system, see: (a) Verloop, A.; Koevoet, A. L.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1957**, *76*, 689. (b) Havinga, E.; Schlatmann, J. L. M. A. *Tetrahedron* **1961**, *16*, 146. (c) Velluz, L.; Amiard, G.; Petit, A. *Bull. Soc. Chim. Fr.* **1949**, 501. (d) Havinga, E. *Experientia* **1973**, *29*, 1181. (e) Jacobs, H. J. C.; Havinga, E. *Adv. Photochem.* **1979**, *11*, 305. (f) Schlatmann, J. L. M. A.; Pot, J.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1964**, *83*, 1173. (g) Holick, M. F.; Frommer, J. E.; McNeill, S. C.; Richtand, N. M.; Henley, J. W.; Potts, J. T., Jr. *Biochem. Biophys. Res. Commun.* **1977**, *76*, 107. (h) Hanewald, K. H.; Rappoldt, M. P.; Roborgh, J. R. *Recl. Trav. Chim. Pays-Bas* **1961**, *80*, 1003. (i) Sheves, M.; Berman, E.; Mazur, Y.; Zaretskii, Z. V. I. *J. Am. Chem. Soc.* **1979**, *101*, 1882.

(3) For a general review of [1,*j*]-sigmatropic shifts, see: Spangler, C. W. *Chem. Rev.* **1976**, *76*, 187.

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