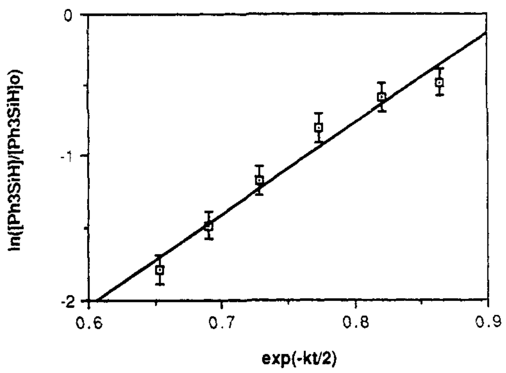

Figure 1. Plot of ln ($[Ph_3SiH]/[Ph_3SiH]_o$) versus $e^{-k_1t/2}$ for the benzoyl peroxide initiated reduction of bromohexadecane in heptane solvent at 90 °C.

found for k_4 is close to the average of values (2×10^4 M^{-1} s^{-1} at 50 °C in benzene) reported by Newcomb and Park[13] who used a competition technique to estimate the rate constant.

From a practical perspective, the GC results indicated that 50% of bromohexadecane was reduced after 1.4 h and that the yield of the reaction was over 80% after 4 h. The chain length at the start of the experiment was 18, which is respectable for applications in synthesis.

The competition experiments involving Ph_2MeSiH or $PhMe_2SiH$ led to more reliable results since the ratio of the rate constants k_4/k'_4, eq 7, did not depend on data for k_1 and k_5. The values obtained, 1.60 ± 0.03 and 2.63 ± 0.14 for $R_3SiH = Ph_2MeSiH$ and $PhMe_2SiH$, respectively, show a noticeable decrease of the reaction rate when the number of phenyl groups bonded to the silicon atom decreases. The values obtained in the competition experiments can be combined with that for k_4 to give $k'_4 = (1.9 \pm 0.25) \times 10^4$ M^{-1} s^{-1} (Ph_2MeSiH) and $(1.1 \pm 0.15) \times 10^4$ M^{-1} s^{-1} ($PhMe_2SiH$). For $R_3SiH = Et_3SiH$, no significant reduction of bromohexadecane was observed under the same experimental conditions. The results indicate that Ph_2MeSiH and $PhMe_2SiH$ are probably impractical agents because reaction chain lengths would be unacceptably small.

$$\frac{\ln([Ph_3SiH]/[Ph_3SiH]_0)}{\ln([R_3SiH]/[R_3SiH]_0)} = \frac{k_4}{k'_4} \qquad (7)$$

In radical-based reductions of alkyl halides, rapidity of hydrogen transfer is not necessarily a virtue. If the synthesis requires that a radical rearrangement takes place before the transfer step, then slowness may be a desirable characteristic given the limitation that the reactions must proceed with reasonable chain length to give decent yields. It has been suggested[14,15] that tributylgermane is a suitable reagent for this purpose, although its high cost tends to make this application unattractive. The above results suggest that triphenylsilane may be a good alternative when primary alkyl radicals are involved in hydrogen abstraction at the Si-H bond.

Registry No. Ph_3SiH, 789-25-3; Ph_2MeSiH, 776-76-1; $PhMe_2SiH$, 766-77-8; bromohexadecane, 112-82-3.

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Exploratory Studies of the Photochemistry of *N*-Hydroxypyridine-2-thione Esters. Generation of Excited Radicals by Laser Flash Photolysis and in a Conventional Fluorescence Spectrometer[1]

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Introduction

Since their introduction by Barton et al., chain reactions of *N*-hydroxypyridine-2-thione esters have been extensively used for synthetic purposes.[4,5] The reaction (Scheme I) is initiated by addition of a radical, generated thermally or photochemically, to the thione's sulfur center. Normally, the $RCO_2^\bullet$ radical decarboxylates rapidly leading to $R^\bullet$, which either propagates the chain by adding to the thione, or undergoes other reactions (e.g. rearrangements, hydrogen abstraction, etc.), ultimately leading to a chain carrier radical.

Competitive studies have led to rate constants of 2×10^6 (50 °C) and 4.6×10^5 M^{-1} s^{-1} (30 °C) for the addition of primary and tertiary carbon radicals to their precursor, respectively.[6,7] The kinetics with which carbon-centered radicals react with their precursors are important when *N*-hydroxypyridine-2-thione esters are used for synthetic purposes, since this reaction will determine whether the chain carrier will give the desired product or not.

Little is known about the primary photochemistry of *N*-hydroxypyridine-2-thione esters, although it has been established that extensive cleavage of the N-O bond takes place. The esters are excellent precursors for free radicals for EPR work,[8] but an earlier attempt to monitor the radicals by laser flash photolysis was unsuccessful as a result of interference by the strong UV-visible absorption of the starting esters.[8]

This study was undertaken in an attempt to learn some of the details of the primary photochemistry of these compounds. The compounds in Scheme II were selected for study, since upon N-O cleavage they are expected to yield radicals with very different kinetic and spectroscopic characteristics. For the diphenylacetic acid derivative (I) we expect rapid decarboxylation of $Ph_2CHCO_2^\bullet$ to yield the readily detectable diphenylmethyl radical,[9] with a very strong absorption band at 330 nm. Cleavage of the *p*-methoxybenzoic acid derivative (II) should lead to *p*-$CH_3OC_6H_4CO_2^\bullet$ radicals with a characteristic absorption band at $\lambda > 600$ nm and lifetimes of several microseconds in solvents such as carbon tetrachloride, acetonitrile, and Freon-113.[10] Finally, the 2,2-dimethylvaleric acid derivative (III) was used as a control in laser experiments, since the 2-methyl-2-pentyl radical is not expected to show

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[1] Issued as NRCC-31523.

[2] NRCC.

[3] University of Ottawa.

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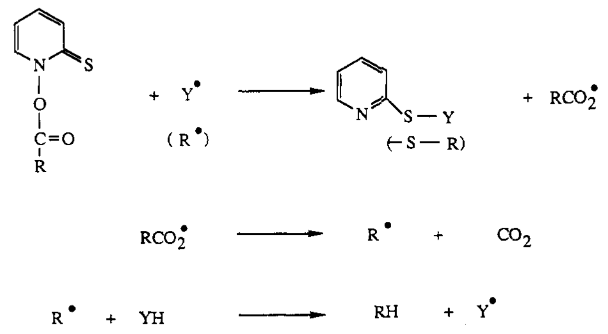
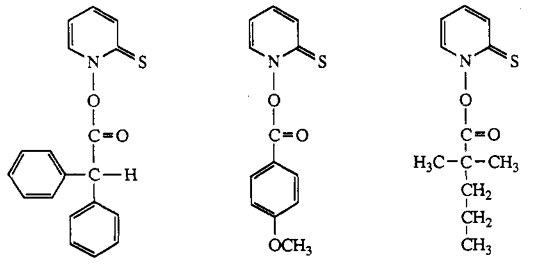
Scheme I



Scheme II



significant absorptions in the spectral region of interest.

Materials and Methods

Compounds I and II were prepared by a method similar to that reported in the literature.[4,6] The acid chlorides (from the acids from Aldrich) were dissolved in dry dichloromethane, and the solution was cooled to −10 °C and deaerated with nitrogen. *N*-Hydroxypyridine-2-thione sodium salt (Fluka, $^1/_2$ mol equiv to the acid chloride) was added slowly, and the mixture was warmed up to room temperature and stirred in the dark under nitrogen for 12 h; the formation of products was followed by TLC. The reaction mixture was then filtered, and the solvent was evaporated under reduced pressure. The solid obtained was purified by TLC on a silica gel spinning plate (Chromatotron Model 7924T).

Compounds I and II photodecompose readily, and in spite of careful protection from room lights, the presence of small concentration of products was unavoidable. In the case of I the product is the 2-pyridyl thioether and concentrations of I quoted are based on absorbances at 380 nm where both I and II have a characteristic absorption band which is absent in the products (i.e. after extensive photolysis). The extinction coefficient for I was determined by combining the UV–visible absorption spectra with thione-to-thioether ratios (i.e. precursor-to-product) determined by NMR. The ratio was determined from the signals at δ 5.69 (singlet) and 5.15 (singlet) corresponding to the thione and thioether, respectively, and the value of ϵ_{380} obtained is 4.5×10^3 M^{-1} cm^{-1}. The ϵ_{380} value determined for I was also used for II, due to the complex decomposition of the latter.[11,12] The ^1H NMR spectrum of I was obtained at the University of Ottawa, with a Varian-Gemini 200-MHz instrument and showed the following chemical shifts (δ) 5.46 (triplet, 1 H) and 6.17 (triplet, 1 H) corresponding to the hydrogens at the 4- and 5-positions and δ 6.47 (doublet, 1 H) corresponding to the hydrogen at the 6-position of the pyridinethione; δ 5.69 (singlet, 1 H) and 5.15 (singlet, 1 H) corresponding to the diphenylmethyl hydrogen of the thione and thioether, respectively. The multiplets observed between δ 7.00 and 7.45 correspond to the sum of the thioether (15 H) and thione (11 H) hydrogens (along with traces of residual benzene). Cyclohexane (Aldrich) was used as received. Freon-113 (Fluka) was treated on an alumina column to eliminate acid impurities. Compound III was a generous gift from Dr. J. Lusztyk (NRC, Ottawa), and 1,1,3,3-tetraphenylacetone (TPA) was prepared by a literature procedure.[13]

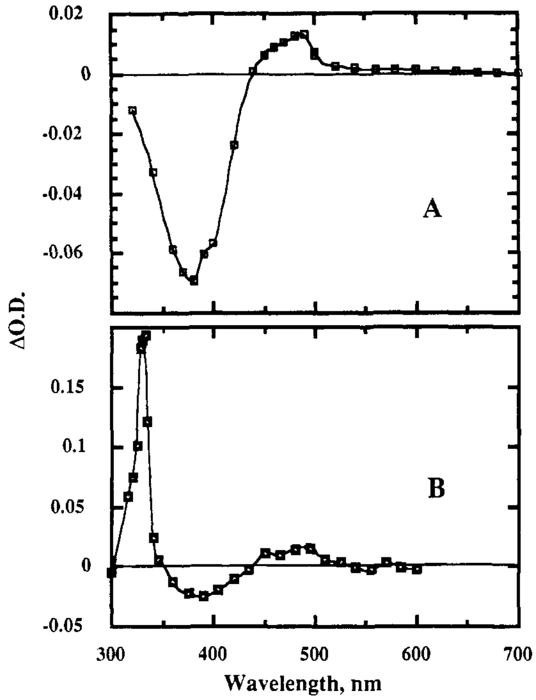


Figure 1. Transient absorption spectra from III (A, 9×10^{-5} M) and I (B, 8×10^{-5} M) in cyclohexane measured at 1.1 and 1.8 μs after the laser pulse, respectively.

Fluorescence spectra were recorded with a Perkin-Elmer LS-5 fluorescence spectrometer and UV–visible spectra with a Hewlett-Packard 8451-A diode array spectrometer. Laser photolysis experiments were carried out using 308 or 355 nm excitation, provided by a Lumonics Model TE-860 excimer laser (308 nm, ~30 mJ/pulse, ~5 ns) or by the third harmonic from a Lumonics Hyperyag-750 Nd/YAG laser (355 nm, ≤100 mJ/pulse, ~12 ns). The Nd/YAG laser was usually attenuated considerably. The detection systems which employ RCA-4840 photomultipliers, Tektronix-7912 digitizers, and PDP-11 computers for data acquisition and experiment control have been described in earlier publications.[9,14,15] The use of a flow system ensured that a fresh portion of solution was irradiated by each laser shot. The samples were deaerated by nitrogen bubbling in a light-protected container attached to the reaction cell with Teflon tubing. The reaction cell was constructed of 7 × 7 mm^2 Suprasil tubing.

Results and Discussion

Control Experiments with III. Laser excitation (308 nm) of our control molecule, III ($\leq 10^{-4}$ M), lead to the

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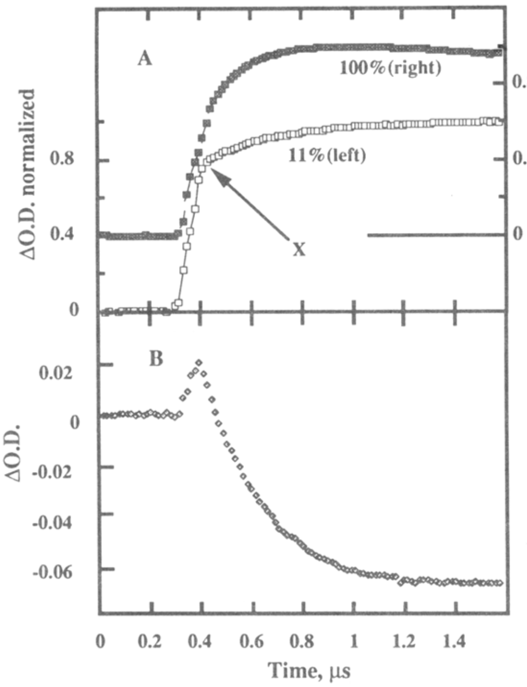
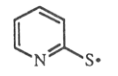


Figure 2. Transient absorption due to I (5×10^{-5} M in cyclohexane) monitored at 330 nm (a) with 100% or 11% of the 308-nm excitation dose, and at 380 nm (B) at 100% dose.

transient absorptions of Figure 1A. The presence of a band centered around 490 nm is a common feature of all the compounds studied here and is attributed to thiyl radical IV.



IV

In fact, the same species is also observed in the photolysis of *N*-hydroxypyridine-2-thione. The transient spectrum observed is in line with those observed for other arylthiyl radicals.[16] We note that in the case of III no other absorbing species are expected, i.e. alkyl radicals are transparent in this region and aliphatic acyloxyl radicals are expected to decarboxylate rapidly on our time scale.[17]

The thiyl radicals of Figure 1A are formed instantly on our time scale. Thus, any excited states of III involved in the reaction must be very short lived ($\tau \ll 10$ ns). The negative (bleaching) signals in the 380-nm region are due to destruction of the starting material (i.e. III in this case). These signals are essentially a "step" function, i.e. an instantaneous bleaching which occurs concurrently with the laser pulse and which is *not* followed by a slow component. Thus, the chain decomposition of III does not occur on our time scale, since such a contribution due to chain decomposition would require the initial rapid bleaching to be followed by a slow phase concurrent with the propagation of the chain. Given the low concentration involved and the values of propagation rate constants estimated by Newcomb et al.,[6,7] the absence of a contribution on our time scale is not surprising.

Formation of Diphenylmethyl Radicals from I. Laser excitation (308 nm) of I in cyclohexane or Freon-113 led to the characteristic absorption of the diphenylmethyl radical with $\lambda_{max} = 330$ nm, Figure 1B. Note also the signals due to the bleaching of I (~380 nm) and to the formation of IV (~490 nm).

To our surprise, the 330-nm signals due to $Ph_2\dot{C}H$ were not formed instantaneously under the conditions mentioned above (see Figure 2A). In fact, at full laser power, a smooth trace, showing no initial "jump", is obtained. This contrasts with the 490-nm thiyl signals which are formed instantaneously. The time evolution of the 330-nm signals, as well as observations at other wavelengths are all consistent with the involvement of excited diphenylmethyl radicals.[9] Thus, the lifetime for the signal growth of Figure 2A is ~150 ns but increases to 270 ns upon attenuation of the laser dose. When the laser pulse is 11% of the maximum dose one observes an initial "jump" in the signal (see point 'X' in Figure 2A). The signals in the 360–400-nm region clearly result from the superposition of at least two processes (Figure 2B); thus, the final bleaching can be attributed, just as in the case of III, to the partial depletion of precursor. The positive absorption signals observed initially are assigned to the excited diphenylmethyl radical, which is known to absorb in this region.[9,18,19] Kinetic analysis reveals that this process occurs concurrently with the growth observed at 330 nm. Further confirmation of the involvement of excited $Ph_2\dot{C}H$ radicals was obtained from fluorescence experiments. Thus, 308-nm excitation of I in cyclohexane leads to emission in the 540–580-nm region with a lifetime of ~210 ns.

The lifetimes for excited $Ph_2\dot{C}H$ mentioned above are somewhat shorter than the value of 255 ns reported in cyclohexane.[9] This may be the result of quenching by I and/or IV. Free radicals have been reported to be excellent quenchers of other excited radicals.[20,21]

Formation of excited diphenylmethyl radicals in single-pulse laser experiments is not unprecedented.[9] However, the high efficiency with which they are formed from I is rather surprising. The attenuation experiments mentioned above show that at least some of the excited radicals are formed in a two-photon process, as indicated by the appearance of a "jump" in the 330-nm signals upon attenuation (see Figure 2). This remarkable efficiency led us to explore whether excited $Ph_2\dot{C}H$ could be formed in a monophotonic process. The two experiments carried out are described below.

Experiments similar to those in Figure 2 were carried out using the 355-nm pulses from a Nd/YAG laser. This wavelength is sufficiently far from the absorption maximum of $Ph_2\dot{C}H$ (see Figure 1) so as to minimize reexcitation of $Ph_2\dot{C}H$ during the laser pulse. Under these conditions 70% of the signal is accounted for by the "jump" component, although a growth with a lifetime of 220 ns persists even at this excitation wavelength.

We reasoned that if a monophotonic source of excited radicals was involved, one should detect their luminescence in a conventional spectrofluorimeter, particularly taking into consideration their high quantum yield of fluorescence.[22]

The luminescence from $Ph_2\dot{C}H$ was readily detected (Figure 3) using a conventional fluorimeter.[23] However,

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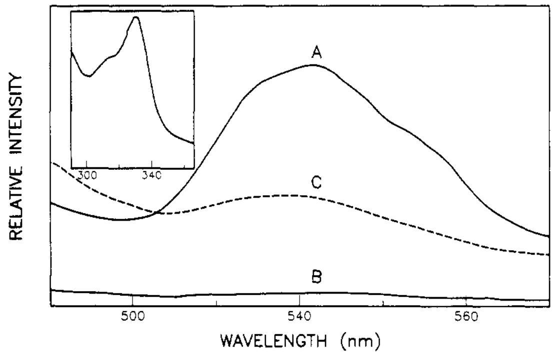

Figure 3. Fluorescence spectra of I (5×10^{-5} M in cyclohexane) excited at 330 nm with 100% (A) and 11% (B) excitation dose (using a 15 nm bandwith excitation slit). Spectrum C corresponds to B multiplied by 9.1, the ratio of excitation doses. The intense emission at $\lambda < 500$ nm at the lower excitation dose is due to the formation of products. The insert shows the excitation spectrum for the emission monitored at 540 nm.

the signals were strongly dose dependent, as illustrated by the spectra of Figure 3, where the trace obtained with 11% dose has been multiplied by 9.1 to make a direct comparison of the two spectra meaningful. This emission is identical with that recorded earlier in our laboratory for diphenylmethyl radicals employing the same instrument, albeit in a rather different type of experiment.[24] The emission from the radical is readily quenched by oxygen, as expected.[9] The insert in Figure 3 shows the excitation spectrum obtained monitoring the emission in cyclohexane at 540 nm which clearly matches that from $Ph_2\dot{C}H$. The radical must be reexcited by the instrument's lamp pulse, and therefore one must conclude that even under those conditions the emission from $Ph_2\dot{C}H$ results from a sequential two-photon process, consistent with the marked dependence on the excitation dose. We were surprised by the observation that two-photon processes could be initiated in a standard commercial fluorimeter in solution at room temperature, but our results seem to preclude any other interpretation. With hindsight it is perhaps not remarkable that under pulsed laser excitation at 308 nm essentially all the diphenylmethyl radicals formed in the initial N–O photocleavage are reexcited leading to the smooth full laser dose growth trace of Figure 2A.

A few exploratory experiments were also carried out to establish if the unusual ease with which two-photon processes occur is common under these conditions, or a peculiar characteristic of *N*-hydroxypyridine-2-thione esters. Experiments with 1,1,3,3-tetraphenylacetone as the radical source also show excited radical formation although the emission is weaker in this case.[25]

Formation and Decay of *p*-Methoxybenzoyloxyl Radicals from II. *p*-Methoxybenzoyloxyl radicals from the corresponding peroxide have lifetimes in the microsecond range in solvents such as acetonitrile and Freon-113. Laser photolysis[10,26] and EPR studies[27] have provided a wealth of data on the behavior of these radicals. The *N*-hydroxypyridine-2-thione ester II decomposes spontaneously in polar solvents; Freon-113 was our solvent of choice, since it leads to relatively long radical lifetimes. The radical $p\text{-}CH_3OC_6H_4CO_2^{\bullet}$ has a broad absorption band at $\lambda > 600$ and 720 nm is a convenient monitoring wavelength. A much faster flow than for I or III has to be employed when II is excited at 308 nm due to the formation of products that absorb strongly between 300 and 760 nm. Under conditions where no product accumulation is detected, a weak absorption (<10% of the bleaching at 380 nm) with a lifetime of ~5 μs is observed at 720 nm. The bleaching of II monitored at 380 nm does not appear to be instantaneous, in contrast with the observations for I and III. About 90% of the bleaching is accounted for by the "instantaneous" process; the remaining ~10% is a slow process (3.0 μs) probably due to the chain decomposition of II, which could involve either the benzoyloxy or the derived phenyl radical, that would need to react with II with a rate constant in excess of 10^7 M^{-1} s^{-1}.

p-Methoxybenzoyloxyl radicals add readily to unsaturated systems (e.g. for 1,3-cyclohexadiene $k = 5 \times 10^8$ M^{-1} s^{-1})[10] and react (presumably via electron transfer) with stable nitroxides.[10] The fact that products are readily formed in the photolysis of II suggests that some *p*-methoxybenzoyloxyl radicals react prior to decarboxylation. This radical could react with II and/or IV; the reaction with the former would lead to the thioperester and to the chain decomposition of II. Indeed, thioperesters were observed in product studies of the low-temperature photolysis of *N*-hydroxypyridine-2-thione esters; here the acyloxy radicals decarboxylate slowly and are trapped by their precursor.[12] Thus, the decarboxylation kinetics has important consequences in synthetic applications, and the reaction pathway could be controlled by the temperature at which the reaction is carried out, since decarboxylation should show a strong temperature dependence,[11] as well as by the concentration of reactants. We note that the concentration in the laser experiments are ca. 1000 times lower than in synthetic applications; this should favor decarboxylation in the laser work.

In conclusion, the laser photolysis of *N*-hydroxypyridine-2-thione esters leads to the cleavage of the N–O bond within the duration of the laser pulse (5–12 ns). The 2-pyridylthiyl radical (IV) has a characteristic absorption at 460–490 nm. N–O cleavage in the photolysis of I is followed by rapid loss of CO_2, and diphenylmethyl radicals are readily observed. The rapid and efficient formation of the radicals, as well as their ability to absorb the laser pulse, combine to make this system particularly prone to two-photon processes. This occurs to such a degree that under laser irradiation (308 nm) excitation of the radicals is almost quantitative. Even in the case of a spectrofluorimeter, the excitation source is sufficiently intense to lead to easily detectable radical emission.

When the decarboxylation of the radicals is slow, as in the case of II, several side reactions appear to occur. This observation is probably related to the low yield of synthetic procedures involving *N*-hydroxypyridine-2-thione esters when the decarboxylation is not rapid.

Chain reactions do not appear to play a significant role in the time scale of the laser experiments, with the only exception of the case of II, where some delayed bleaching suggests a minor involvement for this process.

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(23) It should be noted that the Perkin-Elmer LS-5 spectrofluorimeter is in fact a pulsed instrument. The excitation source is pulsed at 60 Hz and its pulse width is ca. 10 μs. All the experiments described herein were carried out in "fluorescence mode", i.e. with a 10-μs gate synchronized with the lamp pulse.

(24) Casal, H. L.; Scaiano, J. C.; Charette, G. M.; Sugamori, S. E. *Rev. Sci. Instr.* **1985**, *56*, 23.

(25) TPA's fluorescence in solution tails into the 500-nm region. When TPA was excited at 300 and 330 nm, an increased emission was observed at 550 nm at the latter excitation wavelength. Oxygen saturation essentially eliminates this new emission but does not affect the fluorescence (the excited lifetimes are ~250 ns[9] for the radical and only 1.5 ns for TPA). While detectable, radical emission using TPA as a precursor is much weaker than using I.

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Reinvestigation and Extension of the Aluminum Chloride Induced Reactions of Resorcinol and Hydroquinone with 3,6-Dichloropyridazine

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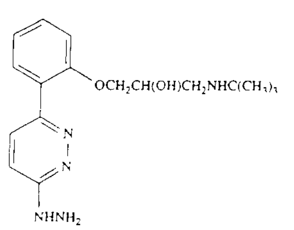

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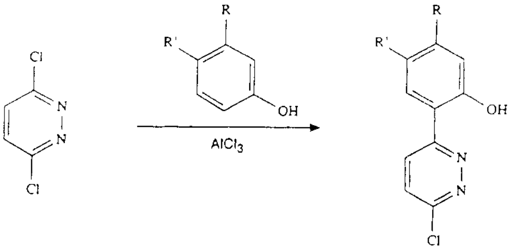
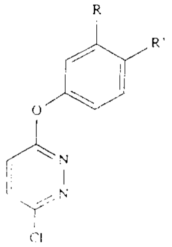
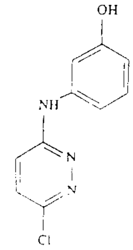


3a R = OH, R' = H
3b R = H, R' = OH
3c R = C(CH$_3$)$_3$, R' = H
3d R = H, R' = C(CH$_3$)$_3$



4a R = H, R' = OH
4b R = C(CH$_3$)$_3$, R' = H
4c R = H, R' = C(CH$_3$)$_3$



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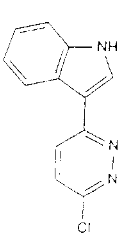

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During a study of methods for the preparation of the combined β-blocker/vasodilator prizidilol (3-[2-[3-(*tert*-butylamino)-2-hydroxypropoxy]phenyl]-6-hydrazinopyridazine, **1**) and analogues, our interest was aroused by a report that reaction of 3,6-dichloropyridazine (**2**) with resorcinol and hydroquinone in the presence of aluminum chloride gave the 3-chloro-6-(2,4- and 2,5-dihydroxyphenyl)pyridazines, **3a** and **3b**, respectively.[1] This reaction proved to be successful with resorcinol and was used for the preparation of analogues of prizidilol with 4-alkoxy substituents in the phenyl ring.[2] Reaction of **2** with hydroquinone also proceeded as described; the product (mp 196–197 °C; lit.[1] mp 195–196 °C), however, was readily shown by ^{1}H NMR spectroscopy to be the ether **4a**, and not the arylated pyridazine **3b** as claimed.

Further study of the arylation reaction **2** → **3** has revealed that it is of very limited scope. Phenol, 3- and 4-chlorophenol, catechol, and a variety of anisole derivatives failed to react with **2**, while 3- and 4-*tert*-butylphenol gave the ethers **4b** and **4c** in 15 and 9% yield, respectively, together with only very small amounts (<2%) of products tentatively identified (MS, NMR) as the C-arylated pyridazines **3c** and **3d**. 3-Aminophenol gave the anilino product **5** in 45% yield. Clearly, successful arylation of **2** under the present conditions requires a relatively powerful aromatic nucleophile. In support of this hypothesis, reaction of **2** with indole gave the 3-indolyl derivative **6** in 30% yield. This latter compound was also prepared by reaction of **2** with indolylmagnesium bromide.

Extension of the resorcinol reaction to 3,4,6-trichloropyridazine (**7**) gave the expected 3,6-dichloro-4-(2,4-dihydroxyphenyl)pyridazine (**8**) in 63% yield, which is consistent with a general reinforcement of the normal reactivity of the 4-chloro substituent in **7**,[3] rather than a specific effect ortho to the ring nitrogen atoms. The position of substitution in **8** was confirmed by hydrogenolysis to give 4-(2,4-dihydroxyphenyl)pyridazine (**12**) and spectral comparison of **12** with the 3-isomer **13**, prepared similarly from **3a**. The isomers **9** (3.5%) and **10** (3.5%) were also isolated from the reaction of resorcinol with **7**, together with a trace amount of a highly fluorescent compound. This latter product was also produced when **8** was heated at its melting point and was identified as 3-chloro-7-hydroxybenzofuro[2,3-*c*]pyridazine (**11**). Compound **11**, which was readily prepared from **8** by treatment with potassium carbonate in acetone, is acidic (pK_a = 7.5) and shows fluorescein-like fluorescence in aqueous alkaline solution. The properties of **11**–$\nu_{C=O}$ at 1630 cm^{-1}, failure to give a typical phenolic color reaction with diazotized sulfanilic acid—appear to reflect the importance of the vinylogous amide tautomer **11a**.

In mechanistic terms, the above aluminum chloride induced arylation reactions almost certainly proceed by initial complexation of the aluminum chloride with the di- or trichloropyridazine, which would result in enhanced activation of the chlorine substituent to nucleophilic displacement.

Experimental Section

NMR spectra were recorded with a Bruker 250AE spectrometer; DMSO-d_6 was used as solvent unless otherwise stated; δ_H values are in ppm relative to TMS. Mass spectra were registered on AEI 902 or VG 70-70F instruments; relative abundances of the ions are given in parentheses. Melting points are uncorrected. Column chromatography was carried out with silica gel (Merck SG 60, 0.063–0.2 mm) and TLC analysis with precoated plates (Merck SG 60 F$_{254}$).

3-Chloro-6-(4-hydroxyphenoxy)pyridazine (4a). Reaction of **2** with hydroquinone in the presence of AlCl$_3$ as described by Stanovnik[1] gave a solid, mp 196–197 °C (lit.[1] mp 195–196 °C), identified as **4a**: NMR δ 6.8 (AA', 2 H), 7.04 (BB', 2 H), 7.48 (d, 1 H, J = 9.2 Hz), 7.90 (d, 1 H, J = 9.2 Hz), 9.5 (br s, 1 H) ppm.

Reaction of 3-*tert*-Butylphenol with 3,6-Dichloropyridazine. A stirred mixture of AlCl$_3$ (3.58 g, 27 mmol), 3-*tert*-butylphenol (4.55 g, 30 mmol), and **2** (4.0 g, 27 mmol) in nitrobenzene (40 mL) was heated at 120 °C for 4 h, cooled, and poured into ice–water (200 mL) containing HCl (10 mL). The residue left after stream distillation was extracted with EtOAc, and the extract was evaporated to give 4.22 g of an oil. Column

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[2] Coates, W. J.; Roe, A. M.; Slater, R. A.; Taylor, E. M. British Patent 1,527,712 (to SK&F); *Chem. Abstr.* **1976**, *84*, 164819j.

[3] Aldous, D. L.; Castle, R. N. Halopyridazines. In *The Chemistry of Heterocyclic Compounds*; Castle, R. N., Ed.; Wiley: New York, 1973; Vol. 28.

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