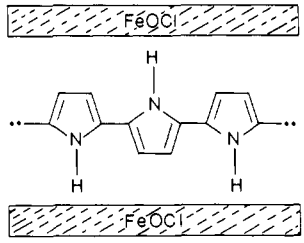
for **1** (B). Additional support for B is derived from the observation



B

of a larger 5.84-Å interlayer expansion for the intercalative polymerization of *N*-methylpyrrole and from the observation that 2,5-dimethylpyrrole fails to intercalate in FeOCl. This latter inertness parallels the electrochemical behavior of 2,5-dimethylpyrrole.[1]

Further evidence that a relatively high molecular weight, conductive polypyrrole has formed in the FeOCl van der Waals gap is derived from several lines of chemical and spectroscopic/charge transport evidence. (i) Pyrolysis mass spectra (up to 350 °C) of chemically prepared[13] $[Ppy(NO_3)_{0.27}]_n$ and **1** show no evidence of pyrrole or pyrrole oligomers.[14a] This is in contrast to results[14b] for $(pyridine)_{0.33}FeOCl$[11a] and $(pyridine)_{0.50}TaS_2$[11a-c] where pyridine and pyridine oligomers are readily detected. (ii) Thermal gravimetric analysis (TGA) traces of $[Ppy(NO_3)_{0.27}]_n$[13] and **1** (He, up to 550 °C) are similar and evidence very high thermal stability (in contrast to the aforementioned pyridine intercalates). (iii) FT-IR spectra of polypyrroles[1] and **1** (Figure 1A,B) are very similar, differing principally in modes (500-700 cm^{-1}) known to be sensitive to polymerization conditions and counterion.[1,7c,15] The corresponding spectra of pyrrole, bipyrrole, and terpyrrole are radically different.[1b] (iv) The ^{57}Fe Mössbauer spectrum of **1** (IS = 0.41 mm/s, QS = 0.86 mm/s at 25 °C) is similar to other FeOCl redox intercalation compounds, indicating partial reduction of the FeOCl layers (cf., IS = 0.42 mm/s, QS = 0.73 mm/s for $(pyridine)_{0.33}FeOCl$).[11d,16] (v) In contrast to other FeOCl intercalation compounds, **1** exhibits relatively high electrical conductivity. Furthermore, the temperature dependence of charge transport in polycrystalline samples (Figure 2) closely parallels that of $[Ppy(NO_3)_{0.27}]_n$.[1] The lower conductivity of the intercalate appears to reflect both volume and interparticle contact effects[17] in these necessarily isotropic measurements on a highly anisotropic material. The thermoelectric power of **1** is similar to that of polypyrroles[1] with predominant hole transport near room temperature, $S(T) > 0$ reaching a maximum near 260 °C and falling at lower temperatures. Above 340 K, **1** exhibits negative $S(T)$ which may indicate increasingly important valence-to-conduction band carrier excitation within the FeOCl layers. In contrast, $(pyridine)_{0.33}FeOCl$ is a less conductive n-type material[14,18] at room temperature. Finally, the inorganic matrix of **1** can be removed with phenanthroline/NH_2OH·HCl to yield a black polymer exhibiting an IR spectrum similar to that of chemically or electrochemically prepared polypyrrole (Figure 1C). Further characterization of this polymer is in progress.

These results demonstrate that intercalative polymerization can yield unusual and informative new forms of conductive polymers. In the present case, polypyrrole can now be studied within the stringently ordered constraints of a well-defined van der Waals gap. In addition, a novel polymer-inorganic laminate has been produced. Elaboration and characterization of such materials is continuing.

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Registry No. Ppy, 30604-81-0; FeOCl, 13870-10-5.

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(18) Kanamaru, F.; Koizumi, M. *Jpn. J. Appl. Phys.* **1974**, *13*, 1319-1320.

Selective Steroid Chlorinations Directed by Attached Pyridine Ester Templates

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We have described the process of remote chlorination of steroids and other substrates by the radical relay process.[1,2] *m*-Iodobenzoic acid or related substances were esterified to the steroids to act as templates. Under free radical chain conditions a chlorine atom becomes attached to the iodine of the template by transfer from a radical such as $PhICl^{\bullet}$ or $ClSO_2^{\bullet}$ and is then relayed to a geometrically accessible hydrogen of the substrate. We have also used the sulfur of diaryl sulfide templates[3] or of thiophene ester templates[4] to perform the radical relay process. These methods have been taken up in other laboratories as well.[5]

The use of an iodine or a sulfur to accept and deliver atomic chlorine is related to known free radical complex chemistry, in particular to the work of Russell[6] and of others[7] on the complexing of chlorine atoms by aromatic solvents. Although many such complexing effects have been examined, no studies have been done of chlorine atom binding to *pyridine* derivatives.[8] We now wish to report that the pyridine rings of nicotinic or isonicotinic acid steroid esters can geometrically direct the free radical chlorinations of the substrates. For practical applications such pyridine templates seem preferable to the iodine or sulfur template systems described previously.

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(3) Breslow, R.; Wife, R. L.; Presant, D. *Tetrahedron Lett.* **1976**, 1925-1926.

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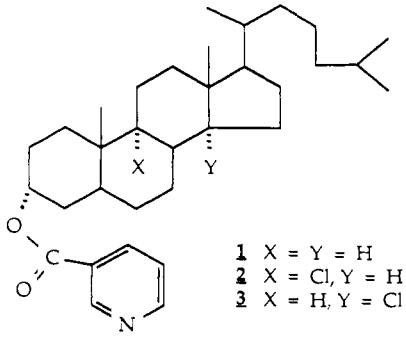
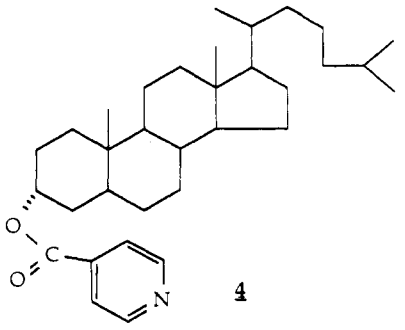
On 15-min irradiation with 1.2 equiv of $PhICl_2$ and 6 equiv of 1,2-epoxybutane, under conditions we have described previously,[9] 3-α-cholestanyl nicotinate (*1*) at 20 mM was quantitatively chlorinated[10] to the 9-chloro derivative **2**, contaminated by the



1 X = Y = H
2 X = Cl, Y = H
3 X = H, Y = Cl

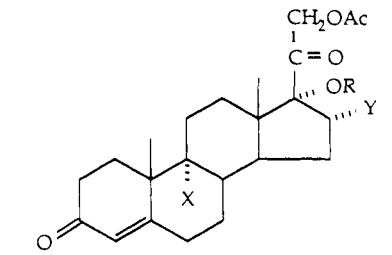
14-chloro derivative **3**. The mixture was analyzed by hydrolysis/dehydrochlorination with KOH to form the known[1] 9(11) olefin (92% isolated yield) and Δ14 olefin (3% yield), respectively. With the isonicotinate ester **4**,[12] the changed geometry led to 44% recovered starting material, 37% 9(11) olefin, 14% Δ14 olefin, and 5% of a product formed by double chlorination.

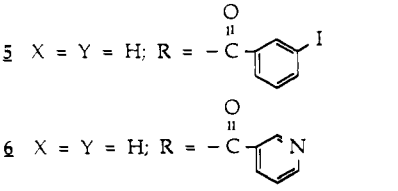


4

The most useful application of template methods so far is the chlorination at C-9 directed by the template attached at C-17 in cortexolone *m*-iodobenzoate (**5**) and related corticosteroid precursors.[13] The template-directed chlorination is so effective that the unactivated C-H at C-9 is attacked in preference to reaction with bonds in or next to the enone system. The 9(11) olefins prepared from these 9-chloro steroids can be converted to such useful compounds as betamethasone or dexamethasone. We find the same remarkable selectivity with cortexolone nicotinate (**6**) or with 16-α-methylcortexolone nicotinate (**7**).

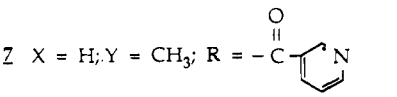
Irradiation of **6** (3 mM) with 1.5 equiv of $PhICl_2$ and 5 equiv of finely powdered K_2CO_3 in CH_2Cl_2 for 30 min produced the 9-chloro derivative **8** in >98% yield. This was dehydrochlorinated to the 9(11) olefin with $AgBF_4$ in acetone, and the product was converted by hydrolysis (K_2CO_3 in MeOH) and reacetylation to the 21-acetate **9** whose NMR spectrum was identical with that



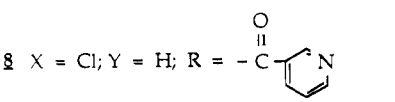


5 X = Y = H; R = –C(=O)–C$_6$H$_4$–I

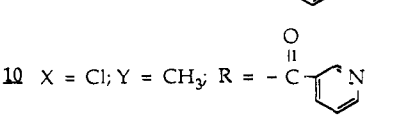
6 X = Y = H; R = –C(=O)–C$_5$H$_4$N



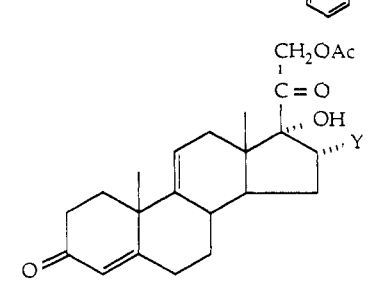
7 X = H; Y = CH_3; R = –C(=O)–C$_5$H$_4$N



8 X = Cl; Y = H; R = –C(=O)–C$_5$H$_4$N



10 X = Cl; Y = CH_3; R = –C(=O)–C$_5$H$_4$N



9 Y = H

11 Y = CH_3

published.[14] In a similar fashion the corresponding 16-α-methyl steroid **7** was converted to the chloro derivative **10** and the 9(11) olefin **11**, which was identical with an authentic sample. When the reaction of **6** was performed at a higher concentration (21 mM), a side reaction resulting in allylic chlorination competed with the template-directed process and led to a 1:2 ratio of C-6 to C-9 chloro steroid.

The geometries observed in the reactions of **1**, **4**, **6**, and **7** are those expected if a chlorine atom becomes attached to the pyridine nitrogen atom. In the radical relay mechanism[1,2] this chlorine is transferred from PhICl$^\bullet$ and after hydrogen abstraction the steroid carbon radical accepts Cl from $PhICl_2$ to regenerate PhICl$^\bullet$. With an approximately tetrahedral nitrogen the chlorine attached to a nicotinate ester is in almost the same position as is a chlorine on the iodine of *m*-iodobenzoate esters, which chlorinate at the same steroid positions. If the chlorine were fully bonded in a covalent σ-complex **12**, the radical would be greatly stabilized by conjugation of the radical center with the nitrogen lone pair of electrons.[15] The situation would be even better with the radical **13** derived from a nicotinate ester (forming an enamino ester) and better still in the isonicotinate radical **14** (with captodative sta-

(9) Maitra, U.; Breslow, R. *Tetrahedron Lett.* **1986**, *27*, 3087–3090.
(10) Recently we described (ref 11) experiments in which remarkably low concentrations of template catalysts were transiently coordinated to steroid derivatives such as **1** via mixed metal complexes. We reported that **1** underwent selective chlorination at C-9 to form **2** when various catalysts were present but *not in their absence*. This critical control reaction had seemingly been confirmed by others, but it is not correct. Furthermore, the claim (ref 11) that the chlorination goes to only partial conversion when the "catalyst" concentration is decreased below a critical level had been confirmed by one of us in four separate instances, but this is also not correct. When he repeats them under secure conditions he finds no such catalyst dependence, although the reactions are not capricious. For these reasons among others, the papers have been retracted.
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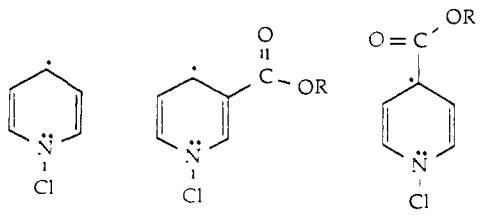

12 13 14

bilization).[15,16] Such stabilization should make these radicals relatively selective.

We are pursuing the questions of the chemical selectivity and spectroscopy of these novel radical species. However, even at this stage the selectivities observed and the ready availablility of pyridine derivatives suggest that they will prove to be the templates of choice for directed radical relay reactions.

Acknowledgment. Support of this work by the NSF, and by an NIH Postdoctoral Fellowship to A. Adams, is gratefully acknowledged.

(15) Simple HMO calculations predict this stability sequence, but higher level calculations are in progress. For a relevant calculation, see: Yonezawa, T.; Nakatsuji, H.; Kawamura, T.; Kato, H. *Mol. Phys.* **1967**, *13*, 589–590.
(16) For a related radical, see: Kosower, E. M.; Poziomek, E. J. *J. Am. Chem. Soc.* **1964**, *86*, 5528–5533 and later publications.

Dithiatopazine:[1] The First Stable 1,2-Dithietane

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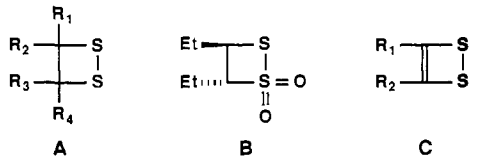
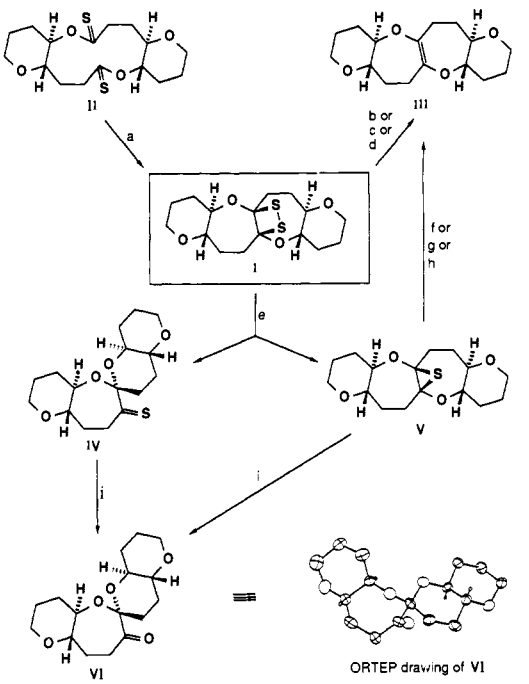
1,2-Dithietanes (A) are of fundamental theoretical, chemical, and biological interest.[2–4] Although postulated as transient in-



A B C

termediates,[5] to the best of our knowledge, no representative of this class of compounds has yet been isolated. Their hypothesized unstable nature has been attributed largely to the expected destabilizing repulsion between the lone pairs of electrons on the adjacent sulfur atoms imposed by the geometrical constraints of the 4-membered ring.[6] Replacement of the lone pairs in one of the sulfurs with oxygen atoms removed this destabilizing effect and resulted in the first isolable example of the 1,2-dithietane 1,1-dioxide B as recently reported by Block.[7] Aromatic systems with 6π electrons of type C (1,2-dithietenes) have also been reported as stable compounds.[8] We now report the synthesis, some physical and chemical properties, and the X-ray crystallographic analysis of the first stable 1,2-dithietane system, dithiatopazine[1] (I, Scheme I).

Scheme I[a]



[a] (a) *hν* (Hanovia UV lamp), toluene, ambient temperature, 15 min, I (65%), II (10%), III (13%); (b) as in (a), 1 h, 90%; (c) heat neat, 140 °C, 45 min, 95% or heat in xylene, 140 °C, 1 h, 95%; (d) 2 equiv of n-Bu_3SnH, AIBN catalyst, toluene, 110 °C, 15 min, 97%; (e) 1.2 equiv of PPh_3, CH_2Cl_2, 15 min, 25 °C, IV (46%), V (45%); (f) same as (c), 1 h, 93%; (g) 10 equiv of $(EtO)_3P$, toluene, 110 °C, 1 h, 94%; (h) heat in xylene, 160 °C, sealed vessel, 2 h, 88%; (i) 2 equiv of mCPBA, 10 equiv of H_2O, CH_2Cl_2, 25 °C, 2 h, 55%; (j) ozone, CH_2Cl_2, −78 °C then 10 equiv of Me_2S, −78 → 25 °C, 1 h, 85%.

Scheme I summarizes the synthesis and a number of selected reactions of the title compound (I). Irradiation of dithionolactone II[9,10] (toluene, Hanovia, UV lamp, ambient temperature) for 15 min resulted in a mixture of I (65%), II[10] (10%), and III[9,10] (13%) which were easily separated by flash column chromatography (silica, 15% EtOAc in benzene; R_fs, I, 0.42, II, 0.70, III, 0.32). Longer irradiation times resulted in the complete consumption of II and I and the exclusive formation of olefin III (1 h, 85% yield). Dithiatopazine (I) is a stable yellow-orange compound forming beautiful topazlike crystals from hexane, mp 134–135 °C.[11] Its structure was based on its spectroscopic and chemical

(1) The name dithiatopazine is suggested for compound I for its beautifully yellow-orange topazlike crystalline form. The preferred name according to the IUPAC rules for this compound is (4a*R*,5a*S*,7a*R*,11a*S*,12a*S*,14a*S*)-dodecahydro-6*H*,13*H*-5a,12a-epidithiopyrano[3,2-*b*]pyrano[2′,3′,:6,7]oxepino[2,3-f]oxepin.
(2) For some intriguing properties of the disulfide linkage, see: Guttenberger, H. G.; Bestmann, H. J.; Dickert, F. L.; Jorgensen, F. S.; Snyder, J. P. *J. Am. Chem. Soc.* **1980**, *103*, 159.
(3) For a monograph on sulfur chemistry, see: Block, E. In *Reactions of Organosulfur Compounds*; Blomquist, A. T., Wasserman, H. H., Eds.; Academic: New York, 1978.
(4) Cyclic disulfides have been associated with biological activity; for some examples, see glyotoxin and α-lipoic acid: *Merck Index*, 10th ed.; 1983, entries 4301 and 9166, respectively, and references cited therein.
(5) See, for examples: (a) Steliou, K.; Salama, P.; Brodeur, D.; Gareau, Y. *J. Am. Chem. Soc.* **1987**, *109*, 926. (b) Orahovatz, A.; Levinson, M. I.; Carroll, P. J.; Lakshmikanthan, M. V.; Cava, M. P. *J. Org. Chem.* **1985**, *50*, 1550. (c) Jahn, R.; Schmidt, U. *Chem. Ber.* **1975**, *108*, 630. (d) Ishibe, N.; Odani, M.; Teramura, K. *J. Chem. Soc., Chem. Commun.* **1970**, 371.
(6) 1,2-Dioxetanes, however, are isolable, see: Bartlett, P. D.; Landis, M. E. In *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic: New York, 1979. Also, 3,3,4,4-tetramethyl-1,2-oxathietane has recently been reported: Lown, J. W.; Koganty, R. R. *J. Am. Chem. Soc.* **1986**, *108*, 3811.
(7) Block, E.; Bazzi, A. A.; Revelle, L. K. *J. Am. Chem. Soc.* **1980**, *102*, 2490.
(8) See, for example: Boar, R. B.; Hawkins, D. W.; McGhie, J. F.; Barton, D. H. R. *J. Chem. Soc., Perkin Trans.* **1977**, *1*, 515. de Mayo, P.; Weedon, A. C.; Wong, G. S. K. *J. Org. Chem.* **1979**, *44*, 1977. Krebs, A.; Colberg, A.; Hopfner, U.; Kimling, H.; Odenthal J. *Heterocycles* **1979**, *12*, 1153. For a review on four- and five-membered cyclic disulfides, see: Vasil'eva, T. P.; Lin'kova, M. G.; Kil'disheva, O. V. *Russ.* Chem. *Rev.* (*Engl. Transl.*) **1976**, *45*, 639.
(9) Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E.; Reddy, K. B.; Marron, B. E.; McGarry, D. G. *J. Am.* Chem. *Soc.* **1986**, *108*, 6800.
(10) Compounds II and III have C_i symmetry and are, therefore, meso, whereas compounds I and V are racemic.

0002-7863/87/1509-3801$01.50/0