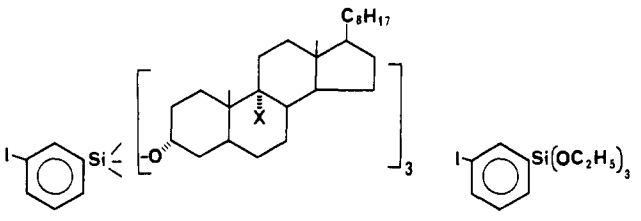
directs attack on one after another. Furthermore, the reaction is still so selective that only one product can be detected. Once the selective attack on one substrate nucleus has occurred the geometric relationships prohibit further attack on that nucleus, so multiple reactions within a single system do not lead to loss of selectivity.

Two examples have been examined so far. In the best of these, a *m*-iodophenyl template was attached to 3$\alpha$-cholestanol by preparing the silyl ether **1**. Reaction of *m*-diiodobenzene with

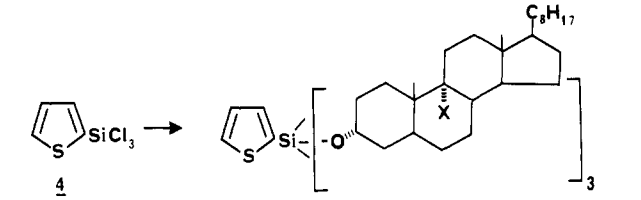


**1** X:H
**3** X:Cl

**2**

1 equiv of butyllithium at −78 °C followed by tetraethoxysilane at 0 °C afforded (*m*-iodophenyl)triethoxysilane (**2**).[6] This was converted to the cholestanyl ether **1**[7] by heating with 3$\alpha$-cholestanol in xylene with a catalytic amount of camphorsulfonic acid. When **1** was irradiated in methylene chloride solution at 25 °C with 3.6 equiv (1.2 equiv/steroid) of sulfuryl chloride[8] and a catalytic amount (5–10 mol %) of AIBN, followed by alkaline hydrolysis accompanied by HCl elimination as we have described previously,[4] the product was 9(11) cholesten-3$\alpha$-ol in 75–83% yield, with the remainder being unfunctionalized 3$\alpha$-cholestanol. The material balance was better than 98%, and no other steroid product was detectable. Thus the exclusive functionalization in this case must have been at C-9 to produce the tris(9-chloro) derivative **3**. This is as expected if a chlorine atom becomes attached to the iodine of **1** and then relayed to the hydrogen at C-9. The resulting C-9 radical is then chlorinated by $SO_2Cl_2$. 3$\alpha$-Cholestanyl *m*-iodobenzoate used this mechanism[4,5] to direct chlorination to C-9, and models show that the same selectivity is expected for the silyl ether **1**. The high yield, exceeding 66%, indicates that *all three* steroid rings in any given molecule of **1** are being chlorinated as the regenerated template directs a second and then a third selective functionalization.

A related compound was prepared with a thiophene template. We reported earlier[9] that the sulfur atom of diphenyl sulfide could serve as a template for radical-relay chlorinations and also found[10] that the sulfur of thiophene can play such a role. 2-Bromothiophene was converted to the Grignard reagent, and this was reacted with silicon tetrachloride. The resulting trichlorosilane **4** was reacted with 3$\alpha$-cholestanol to produce the cholestanyl silyl



**4**

**5** X:H
**6** X:Cl

ether **5**.[11] When this was irradiated for 2 h in methylene chloride solution with 2 equiv of sulfuryl chloride (with AIBN), it produced a 45% yield of the 9(11)-olefin after alkaline hydrolysis and elimination and 55% recovered cholestanol. Here too no significant formation of any other chlorinated product was observed, and the yield is high enough to indicate that more than one steroid nucleus is being attacked by template control to form **6** and **5**/**6** hybrids. However, it is apparent that at least under these conditions the thiophene template is not as useful as the iodophenyl template, which gives higher yields with less chlorinating agent.

In both of these cases a template-directed reaction is certainly occurring, since halogenations in the absence of a template effect would have led[4] to significant amounts of attack at C-14 and other positions and not just at C-9. Furthermore, the thiophene results indicate that it can be a specific halogen-delivering template, presumably by coordinating a chlorine atom to the sulfur on the thiophene ring. However, the principal importance of our findings is the demonstration that templates can indeed act repeatedly to functionalize several substrate molecules, without any loss of specificity. In addition, since all the previous examples of template-directed halogenation have involved the attachment of the template to the substrate as a simple carboxylic ester, it is interesting to see that this is not necessary for selective reaction to occur. Silyl ethers are frequently preparable from hindered alcohols in which esterification is difficult, so the observation that silicon-based templates can be used may broaden the scope of these methods. The finding that three substrates can be attacked for each template used may also make the methods even more attractive for practical application.[12,13]

(6) Bp 94–96 °C (0.2 mm); M + 1 366; anal. C, H, S, Si; $^1$H NMR $\delta$ 7.97–7.07 (4 H), 3.84 (q, 6 H), 0.71 (t, 9 H).

(7) Mp 167–168 °C; M$^+$ 1394; $^1$H NMR $\delta$ 4.23 (3$\beta$-H), 0.75 (18-Me), 0.63 (19-Me).

(8) We have described[4] the use of either $SO_2Cl_2$ or phenyliodine dichloride as chlorine sources for radical-relay chlorinations. Usually the two were equally useful, but in the present case $SO_2Cl_2$ is the superior reagent.

(9) Breslow, R.; Wife, R. L.; Prezant, D. *Tetrahedron Lett.* **1976**, 1925.

(10) Prezant, D., unpublished work.

(11) Mp 123–126 °C; M$^+$ 1274; anal. C, H, S, Si; $^1$H NMR $\delta$ 7.65–7.20 (3 H), 4.25 (3-$\beta$-H), 0.75 (18-Me), 0.63 (19-Me).

(12) For a recent example of such applications in other laboratories, see: Kerb, U.; Stahnke, M.; Schulze, P.-E.; Wiechert, R. *Angew. Chem., Int. Ed., Engl.* **1981**, *20*, 88–89.

(13) Support of this work by the National Science Foundation is gratefully acknowledged.

## Studies in Macrolide Synthesis: Lactones by S to O Acyl Transfer of Hydroxyalkyl Thiol Lactones

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*Received December 14, 1981*

We report a new method for the synthesis of medium-ring lactones from cyclic sulfide precursors. The essential features of this technique are illustrated in a synthesis of phoracantholide I (**11**, Scheme I).[1]

In the first nontrivial step, **5a** is converted into **7a**[2] (83%) by heating with $K_2CO_3$ in acetonitrile. This step is based on analogous ring-forming reactions that have been studied in our laboratory and is believed to occur by 2,3 sigmatropic shift of an intermediate ylide **6**.[3]

After double-bond reduction (diimide) and protecting-group manipulation, the phosphine oxide **8a** is converted into the key thiol lactone **9a**[4] (62%) by reaction with $C_4H_9Li$ followed by

(1) Previous syntheses of phoracantholide I: Gerlach, A.; Kunzler, P.; Ortle, K. *Helv. Chim. Acta* **1978**, *61*, 1226. Malherbe, R.; Bellus, D.; *Ibid.* **1978**, *61*, 3096. Petrzilka, M. *Ibid.* **1978**, *61*, 3075. Takahashi, T.; Hashiguchi, S.; Kasuga, K.; Tsuji, J. *J. Am. Chem. Soc.* **1978**, *100*, 7424. Trost, B. M.; Verhoeven, T. R. *Ibid.* **1979**, *101*, 1595.

(2) **7a** (mixture of diastereomers), major diastereomer: mp 184–185 °C (crystallized from ethyl acetate–hexane); NMR spectrum (vinyl region) shows two atropisomers frozen out on NMR time scale, 270 MHz ($CDCl_3$) $\delta$ 5.7 (1 H, both atropisomers overlapping, m), 5.47 (0.33 H, ddd, $J$ = 15.4, 9.7, 4.1 Hz), 5.13 (0.67 H, $J$ = 15.4, 10.7, 4.8 Hz).

(3) Vedejs, E.; Gapinski, D. M.; Hagen, J. P. *J. Org. Chem.* **1981**, *46*, 5452.

(4) **9a** (oil after preparative TLC): NMR (270 MHz) $\delta$ 4.05 (1 H, m), 3.69 (1 H, dt, $J$ = 11.0, 4.0 Hz), 2.78 (1 H, ddd, $J$ = 12.9, 8.8, 4.0 Hz), 2.61 (1 H, ddd, $J$ = 12.9, 7.7, 4.0 Hz), 1.2–2.13 (11, H, complex), 1.23 (3 H, d, $J$ = 6.6); IR (neat) 1660 cm$^{-1}$.

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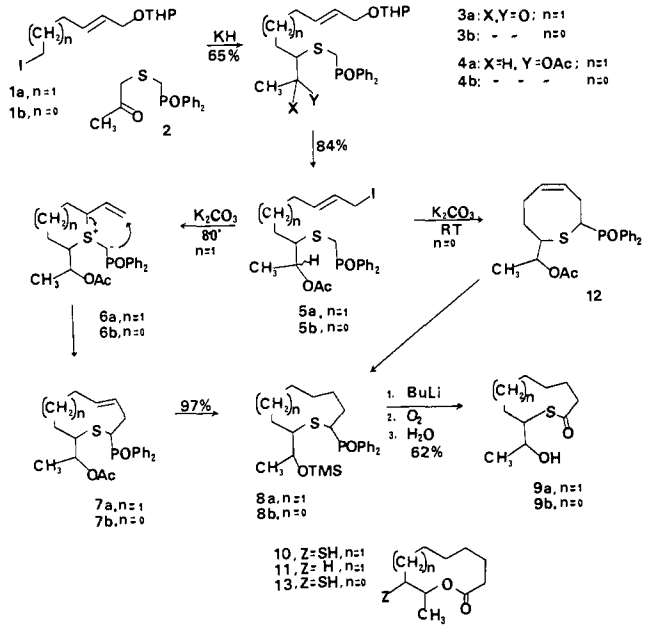
Scheme I



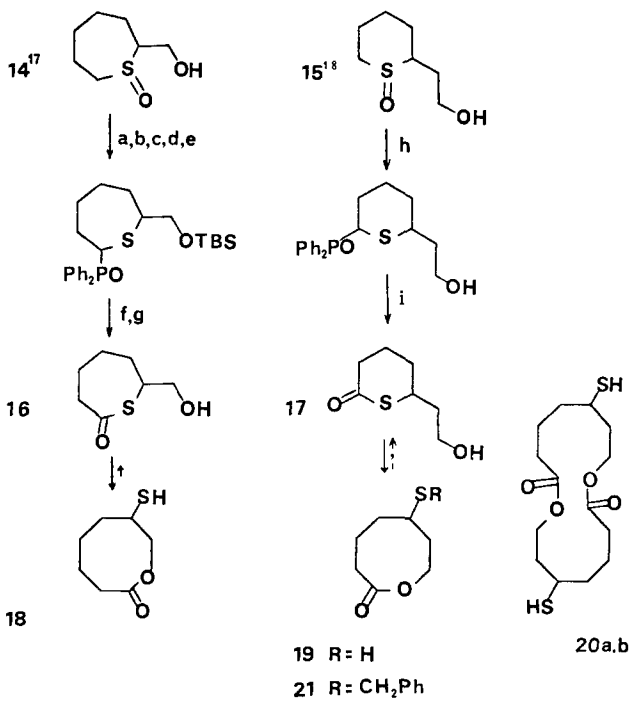
oxygenation. In the presence of camphorsulfonic acid (CSA) in methylene chloride, **9a** rearranges to mercapto lactone **10**[5] (91% isolated) by an S to O acyl transfer process.

To complete the synthesis of phoracantholide I (**11**), desulfurization is accomplished by heating **10** with 2.1 equiv of $(C_4H_9)_3SnH$/AIBN (80% yield).[6] The same procedure has been found to reduce other secondary mercaptans in useful yield.[7] The corresponding methyl sulfides are significantly less reactive.[8,9]

Acyl transfer from sulfur to oxygen is well known in acyclic compounds, and the *O*-acyl isomers are clearly favored.[10] In the phoracantholide sequence, there is the additional factor of ring size to consider. Corey et al. have shown that analogous intramolecular oxygen to oxygen acyl transfers will take place starting with hydroxyalkyl lactones of 8 and 9 members if the product lactone is a relatively strain-free 11- or 12-membered lactone.[11] In one case, a 7-membered hydroxyalkyl lactone did not rearrange to the isomeric 10-membered lactone. In view of these results, we have examined several hydroxyalkyl thiol lactones to determine whether the formation of a mercapto lactone provides sufficient driving force to overcome unfavorable ring size effects. The answer is yes (almost)!

The 8-membered thiol lactone **9b** is prepared by methods that closely parallel those used for the homologous phoracantholide series (Scheme I). The ring-expansion step in this case occurs at room temperature to give *cis*-thiacyclooctene **12**, 80% from **3b**, as well as a small amount of the trans olefin isomer **7b**.[12] After the usual redox and protection steps, phoshine oxide oxygenation affords **9b**[13] in 73% yield. The acyl transfer process to give **13**[13] (70%) is somewhat slower (4 days, room temperature, CSA, >95% conversion) than **9a** → **10**, but the reaction does go to completion within the limits of NMR analysis. In this respect **9a** and **9b** behave similarly.

Scheme II[a]



[a] Key: (a) TBSCl/DMAP/THF, 92%; (b) $C_4H_9Li$; $ClPPh_2$; (c) $TiCl_4$/Zn; (d) $H_2O_2$; (e) 33% overall yield, steps b–d; (f) $C_4H_9Li$, −78 °C; $O_2$, −130 to −45 °C, 53%; (g) HCl/$H_2O$–THF, 83%; (h) steps a–d, g, 46% overall; (i) 2 equiv of BuLi, −78 °C; $O_2$, −130 °C, 65%.

Two additional hydroxyalkyl thiol lactones, **16**[13] and **17**,[13] have been prepared from sulfoxide alcohols **14** and **15** via reaction of α-lithio sulfoxides with $ClPPh_2$ followed by redox manipulations (Scheme II, nonoptimized).[14] Both **16** and **17** undergo S to O acyl transfer, but neither reaction goes to completion. In the case of **16**, acyl transfer is exceptionally facile (partial conversion to **18**[13] during refrigerator storage or $SiO_2$ chromatography), but the ratio of **18**:**16** is no higher than 2.5–3:1 upon CSA treatment (ca. 70% **18** isolated from **16**). When pure **18** is resubjected to CSA, minor NMR absorptions due to **16** gradually appear. A true equilibrium has not been observed due to competing decomposition, but isomer interconversion is not in doubt.

In the case of **17**, CSA-catalyzed acyl transfer requires several days at room temperature, and two significant decomposition products (dimers) (30%) are formed along with **19** (ca. 20%) and a trace of recovered **17**. One of the dimers can only be separated from **19** after *S*-benzylation, but sufficient NMR data have been obtained to allow tentative assignment of the meso and dl structures **20a,b** to the dimers (symmetrical $OCH_2$ and *CH*SH NMR signals). The *S*-benzyl derivative **21**[15] has been used for

(5) **10** (oil): NMR (270 MHz) δ 4.75 (1 H, dq, $J$ = 10.3, 6.3 Hz), 2.83 (1 H, m), 2.47 (1 H, ddd, $J$ = 15.4, 6.1, 3.7 Hz), 2.25 (1 H, ddd, $J$ = 15.4, 11.4, 3.3 Hz), 2.09 (1 H, m), 1.9 (1 H, m), 1.54 (8 H, m), 1.48 (1 H, d, $J$ = 8.1 Hz), 1.42 (3 H, d, $J$ = 6.3 Hz); IR (neat) 1740 cm$^{-1}$.

(6) We thank Professor B. M. Trost for comparison spectra of phoracantholide I.

(7) 1-Dodecylthiol + 2.2 equiv of $Bu_3SnH$ → dodecane (65%); cyclododecylthiol + 2.2 equiv of $Bu_3SnH$ → cyclododecane (59%) (both with AIBN catalyst, 14 h at 80 °C in benzene, 0.2 M).

(8) For example, the mercaptan $C_6H_5CH_2CH_2CO_2CH(CH_3)CH(CH_3)SH$ + 2.1 equiv of $Bu_3SnH$ → $C_6H_5CH_2CH_2CO_2CH(CH_3)CH_2CH_3$ (90%) after 5 h, while the sulfide $C_6H_5CH_2CH_2CO_2CH(CH_3)CH(CH_3)SCH_3$ + 2.1 equiv of $Bu_3SnH$ → partial conversion after 42 h to a mixture including $C_6H_5CH_2CH_2CO_2H$ as the major product as well as a small amount of desulfurized ester.

(9) Other examples of sulfide + tin hydride; Pang, M.; Becker, E.; *J. Org. Chem.* **1964**, *29*, 1948. Noltes, J. G.; Van der Kerk, G. J. M. *Chem. Ind. (London)* **1959**, 294. Kuivila, H. G. *Synthesis* **1970**, 499. Gutierrez, C. G.; Stringham, R. A.; Nitasaka, T.; Glasscock, K. G. *J. Org. Chem.* **1980**, *45*, 3393. Ueno, Y.; Sano, H.; Okawara, M. *Synthesis* **1980**, 1011.

(10) See for example: Reid, E. E. *Am. Chem. J.* **1910**, *43*, 489. Harding, J. S.; Owen, L. N. *J. Chem. Soc.* **1954**, 1528, 1536. Jenks, W. P.; Cordes, S.; Corrinolo, J. *J. Biol. Chem.* **1960**, *235*, 3608. Seliger, H. *Synth. Commun.* **1980**, *10*, 175. Tanaka, K.; Yamagishi, N.; Tanikaga, R.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3619.

(11) Corey, E. J.; Brunelle, D. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1977**, *99*, 7359.

(12) **12**: mp 210–217 dec (crystallized from ethyl acetate–hexane); NMR (270 MHz) δ 7.89 (4 H, m), 7.51 (6 H, m), 5.75 (1 H, td, $J$ = 10.8, 7.5 Hz), 5.64 (1 H, td, $J$ = 10.8, 5.5 Hz), 4.9 (1 H, m), 3.13 (1 H, dd, $J$ = 15.4, 10.3 Hz), 2.9 (3 H, m), 2.75 (1 H, m), 2.1 (1 H, m), 1.94 (3 H, s), 1.7 (2 H, m), 1.07 (3 H, d, $J$ = 6.3 Hz).

(13) Carbonyl frequencies of lactones and thiol lactones: **9b**, 1650 cm$^{-1}$; **13**, 1740 cm$^{-1}$; **16**, 1660 cm$^{-1}$; **18**, 1740 cm$^{-1}$; **17**, 1670 cm$^{-1}$.

(14) Vedejs, E.; Mastalerz, H.; Meier, G. P.; Powell, D. W. *J. Org. Chem.* **1981**, *46*, 5253.

characterization of **19**, and mono- or dibenzyl derivatives have been prepared and characterized from **20a,b**.[16]

These results show that the greater stability of ester relative to thiol ester is sufficient to dominate over ring size effects. In the most demanding 6- to 8-membered ring conversion **17** → **19**, the result is somewhat obscured by competing dimer formation, but the trends are clear. Differences in ring strain between thiol lactone and mercapto lactone isomers are only important in the reactions **17** → **19** and **16** → **18**. In larger rings, the lactone is favored by a clear margin. Synthetically useful conversions of hydroxyalkyl thiol lactones to mercapto lactones are expected in the absence of drastic changes in strain or transannular interactions.

**Acknowledgment.** This work was supported by the National Science Foundation (Grant CHE-8113026).

**Registry No. 1a**, 79815-79-5; **1b**, 79815-88-6; **3**, 81044-80-6; **3a**, 81044-81-7; **3b**, 81044-82-8; **4a**, 81044-83-9; **4b**, 81098-22-8; **5a**, 81044-84-0; **5b**, 81044-85-1; **7a**, 81044-86-2; **7b**, 81044-87-3; **8a**, 81044-88-4; **8b**, 81064-08-6; **9a**, 81044-89-5; **9b**, 81044-90-8; **10**, 81044-91-9; **11**, 61448-27-9; **13**, 81044-92-0; **14**, 81044-93-1; **15**, 81044-94-2; **16**, 81044-95-3; **17**, 81044-96-4; **18**, 81044-97-5; **19**, 81044-98-6; **20a**, 81044-99-7; **20b**, 81045-00-3; **21**, 81045-01-4; 2-diphenylphosphinyl-7-(dimethylbutyl)silyloxymethylthiepane, 81064-09-7; 2-diphenylphosphinyl-6-(2-hydroxy)ethyl-tetrahydrothiopyran, 81045-02-5.

(15) **21** (oil): NMR (270 MHz, $CDCl_3$) $\delta$ 7.3 (5 H, m), 4.3 (1 H, ddd, $J$ = 11.4, 5.9, 4.0 Hz), 4.1 (1 H, ddd, $J$ = 11.4, 5.5, 4.0 Hz), 3.7 (2 H, s), 2.57 (1 H, m), 2.15 (2 H, two overlapping dt, $J$ = 15.4, 6.6 Hz and $J$ = 15.4, 6.3 Hz), 1.8 (2 H, $J_{AB}$ = 5.5 Hz), 1.67 (2 H, m), 1.48 (4 H, m); IR (neat) 1740 $cm^{-1}$.

(16) Satisfactory exact mass data have been obtained for all lactones and dilactones.

(17) A solution of 2-lithiothiepane *S*-oxide was added to excess dimethyl carbonate in THF (at 20 °C, 45% yield of 2-carbomethoxythiepane *S*-oxide). Reduction with $NaBH_4$ in ethanol-THF (1.5 h, 20 °C) gave **14** (82%).

(18) Cerè, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1978**, *43*, 4826.

## Suicidal Inactivation of Cytochrome P-450 by Cyclopropylamines. Evidence for Cation-Radical Intermediates

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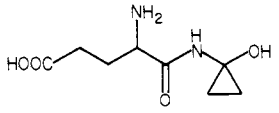
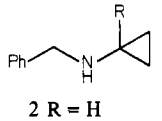
*Received November 17, 1981*

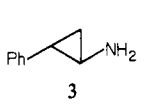
Cyclopropylamine derivatives are known to have interesting and sometimes useful properties as enzyme inhibitors. For example Coprine (**1**), a constituent of inky-cap mushrooms (*Coprinus* sp.),



**1**



**2** R = H
**6** R = $CH_3$



**3**

is hydrolyzed in vivo to 1-hydroxycyclopropylamine and cyclopropanone hydrate, which inhibit aldehyde dehydrogenase.[1,2] This in turn gives rise to a disulfiram-like reaction if these mushrooms are ingested with ethanol. *N*-Benzylcyclopropylamine (BCA, **2**)[3] and related arylalkyl cyclopropylamines[4] are inhibitors of mitochondrial monoamine oxidase (MAO, E.C. 1.4.3.4) and tranylcypromine (**3**) is a therapeutically useful MAO inhibitor. We recently reported that **2** and a number of its derivatives were potent inhibitors of cytochrome P-450 enzymes.[5] Several characteristics of the inhibition process suggested that it might involve suicide inactivation of the enzyme via a metabolite of the parent amine. Thus, loss of enzyme activity followed first-order kinetics, required oxygen and NADPH, and was inhibited by carbon monoxide but *not* by glutathione. In this communication we report further studies that firmly establish the suicidal nature of the enzyme inactivation process and suggest the involvement of a novel mechanism for the enzymatic activation of cyclopropylamines by cytochrome P-450.

Table I. Covalent Binding of Radioactivity to Microsomal Proteins[a]

| incubation conditions | time, min | nmol bound $^3H$ | nmol bound $^{14}C$ |
|---|---|---|---|
| expt A, [7-$^3$H,7-$^{14}$C]-**2** | | | |
| standard | 10 | 2.49 ± 0.09 | 2.03 ± 0.50 |
| −NADPH | 10 | 0.20 ± 0.05 | 0.10 ± 0.05 |
| standard | 60 | 6.63 ± 1.24 | 6.54 ± 0.89 |
| −NADPH | 60 | 0.16 ± 0.03 | 0.22 ± 0.04 |
| expt B, [7-$^3$H,7-$^{14}$C]-**2** | | | |
| standard | 60 | 3.74 ± 0.27 | 3.86 ± 0.40 |
| +glutathione (1 mM) | 60 | 0.92 ± 0.05 | 1.11 ± 0.17 |
| +semicarbazide (0.1%) | 60 | 2.56 ± 0.13 | 2.60 ± 0.14 |
| expt C, [7-$^3$H]-**6** | | | |
| standard | 60 | 0.88 | |
| +glutathione (1 mM) | 60 | 0.48 | |

[a] Standard conditions were as described in ref 6. Each experiment used a different preparation of microsomes, but these results are typical of several such experiments. At the indicated times aliquots of incubation mixture were withdrawn and covalently bound radioactivity was measured by using method A (ref 9). Results are net binding after correction for a small zero-time background and are expressed as the mean ±SD ($n$ = 3) or averages of duplicates.

Under standard conditions,[6] incubation of **2** with rat liver microsomes leads to a first-order loss of aminopyrine demethylase activity with a half-life of 14.9 min,[7] as shown in Figure 1a. So that it could be determined whether the inactivation of P-450 by **2** involved covalent modification of the enzyme, [7-$^3$H]-**2** was prepared[8] and incubated with microsomes under the standard

(1) Tottmar, O.; Lindberg, P. *Acta Pharmacol. Toxicol.* **1977**, *40*, 476-481.

(2) Wiseman, J. S.; Abeles, R. H. *Biochemistry* **1979**, *18*, 427-435.

(3) Silverman, R. B.; Hoffman, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 884.

(4) (a) Murphy, D. L.; Donnelly, C. H.; Richelson, E.; Fuller, R. W. *Biochem. Pharmacol.* **1978**, *27*, 1767. (b) Fuller, R. W.; Hemrich, D. K.; Mills, J. *Ibid.* **1978**, *27*, 2255. (c) Long, R. F.; Mantle, T. J.; Wilson, K. *Ibid.* **1976**, *25*, 247. (d) Winn, M.; Horrom, B. W.; Rasmussen, R. R.; Chappel, R. B.; Plotnikoff, N. P. *J. Med. Chem.* **1975**, *18*, 437.

(5) Hanzlik, R. P.; Kishore, V.; Tullman, R. *J. Med. Chem.* **1979**, *22*, 759.

(6) Liver microsomes were prepared from male rats (200-300 g) and washed by resuspension in 1.15% KCl and recentrifugation at 105000*g*. Incubations contained 100 mg of microsomes (ca. 8 mg of protein)/mL in 0.1 M NaK phosphate buffer (pH 7.6) containing 1 mM EDTA, 7 mM $MgCl_2$, 6.6 mM glucose-6-phosphate, 0.65 mM NADP, and 1-2 IU of glucose 6-phosphate ddehydrogenase/mL. Incubations were carried out at 33 °C under air. Aminopyrine was added at 3.5 mM (along with 0.1% semicarbazide) and incubated for 5 min; formaldehyde was measured by the Nash procedure. Cyclopropylamines **2** and **6** were added to incubations to a concentration of 1 mM.

(7) It is probable that the total inhibition observed at a given time includes a reversible component as well as that due to enzyme inactivation by **2** or **6** and that significant inactivation of cytochrome P-450 by **2** or **6** occurs even during the 5-min assay with aminopyrine. Hence the exact amount of enzyme remaining at a given time is somewhat ambiguous, and inactivation plots tend to be shifted to the right of the covalent binding plots. However, neither of these eventualities interfere with measurement of the *rate of change* in enzyme activity with time and the associated half-life for inactivation under standard conditions.

(8) Amines **2** and **6**, tritiated on the benzylic carbon, were prepared by reduction of the corresponding benzylidene Schiff bases in absolute ethanol with [$^3$H]$NaBH_4$. For incubations they were diluted with cold carrier to final specific activities of 2-6 Ci/mol. Carbon-14 labeled **2** was prepared from [*carboxyl*-$^{14}$C]benzoic acid by successive treatment with oxalyl chloride in benzene, excess cyclopropylamine in ether, and excess $BH_3$-tetrahydrofuran at 25 °C for 24 h. For incubations [$^{14}$C]-**2** was used at a specific activity of 0.7 Ci/mol.

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