coordinates but not the assigned isotropic temperature factor of 4.2 Å^2 for the hydrogens were also refined) converged the final R value to 0.09. The final atomic coordinates are given in Table V.

Acknowledgments. We are indebted to Mr. J. Alicino and Ms. Mary Young for microanalysis and to Ms. Virginia Shu for chemical synthesis.

Registry No. 1, 1072-72-6; 2, 17396-36-0; 3, 17396-35-9; 4, 70332-83-1; 5, 70332-84-2; 6, 70332-85-3; 7, 70355-01-0; 8a, 70355-02-1; 8b, 70355-03-2; 9, 70355-04-3; benzaldehyde, 100-52-7; propylhydrazine, 5039-61-2.

Supplementary Material Available: X-ray data consisting of tables of temperature factors, bond distances, and bond angles (3 pages). Ordering information is given on any current masthead page.

Preparation of Thiopyrano- and Pyrano[4,3-*c*]pyrazoles. Structure Elucidation of Dehydro Coproducts

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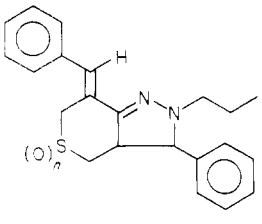
Reaction of *n*-propylhydrazine with tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one gives 2-propylhexahydrothiopyrano[4,3-*c*]pyrazole (**1**) as the major product. However, this reaction provides a dehydro coproduct whose structure has been shown to be the 1-substituted isomer B rather than the 2-substituted isomer A. Analogous reactions give varying amounts of the 1-substituted dehydro coproducts, the proportion being determined, probably, by both steric and electronic effects. Structure determination of the dehydro coproducts was aided by ^{1}H NMR spectroscopy, by X-ray crystallography of one of the 1-substituted dehydro coproducts (**14**), and by synthesis of the isomeric 2-substituted dehydro product **23** by dehydrogenation of **13**.

In a previous paper[1] we described a method for preparing 2,3,3a,4,6,7-hexahydrothiopyrano[4,3-*c*]pyrazoles (**1–3**) and discussed our studies using ^{1}H NMR and ^{13}C

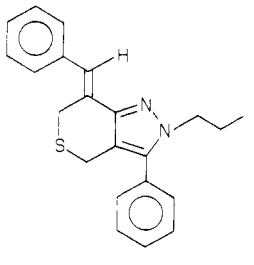


1, n = 0
2, n = 1 (two sulfoxide isomers)
3, n = 2

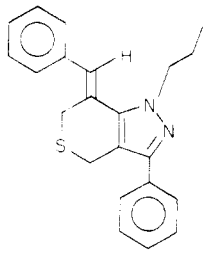
NMR in which shift reagents were utilized in making conformational assignments in this bicyclic system. The utility of the S→O bond in making assignments in a relatively complex rigid system was demonstrated, the conformational assignment being confirmed in one case by X-ray crystallographic data. We mentioned but did not elaborate therein on the finding of dehydro coproducts during the isolation of the major products **1** and **3**. This paper describes our studies on the elucidation of the structure of these pyrazole coproducts.

Chemistry and Discussion

When tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one[2] is treated with *n*-propylhydrazine in refluxing methanol for 3 h and the mixture cooled, **1** deposits as the major product; several recrystallizations are required to obtain the product pure. The TLC of the mother liquor revealed the presence of a slightly more polar coproduct. Concentration of the mother liquor afforded a low yield of the minor product, which was further purified by several recrystallizations. This product possessed m/e 346 (M^+), indicating a loss of two hydrogens relative to **1**, while the ^{1}H NMR ($CDCl_3$) spectrum showed the presence of an *n*-propyl group at δ = 1.1 (t, J = 7.0 Hz, CH_3), 2.1 (m, CH_2), and 4.35 (t, J = 7.0 Hz, NCH_2); the position of the NCH_2 signal was shifted downfield 1.5 ppm relative to the NCH_2 signal of **1** (δ = 2.8), consistent with attachment of the propyl group to an aromatic pyrazole nitrogen. We were, thus, afforded the option that the dehydro coproduct was one of two possible pyrazole structures (A or B), indistinguishable on the basis of spectral data alone.



A



B

Our initial observations led us to favor structure B; for example, prolonged heating or the addition of excess *n*-propylhydrazine to the reaction mixture failed to increase the amount of pyrazole coproduct formed, making it unlikely that the observed dehydro coproduct was derived by dehydrogenation of **1**. Likewise, compound **1** remained unchanged when heated in methanol in the presence of *n*-propylhydrazine. In fact, we found compound **1** to be quite stable to various dehydrogenating conditions, such as *p*-chloranil in either refluxing *tert*-butyl alcohol or xylene solution, DDQ in refluxing dioxane, or 5% palladium/charcoal or sulfur in refluxing DMF solution. Extended reaction times led in some cases only to

(1) M. Puar, G. Rovnyak, A. I. Cohen, B. Toeplitz, and J. Z. Gougoutas, *J. Org. Chem.*, preceding paper in this issue.
(2) N. J. Leonard and D. Choudhury, *J. Am. Chem. Soc.*, **79**, 156 (1957).

0022-3263/79/1944-2518$01.00/0

darkening and decomposition; no pyrazole formation was evident. A dihydro product corresponding to B (i.e., imine double bond reduced and having a labile N–H) would be expected to undergo dehydrogenation more readily than the dihydropyrazole product **1**, where both hydrogens to be removed are attached to carbon. The failure of **1** to dehydrogenate under various conditions, thus, led us to speculate that pyrazole product formation resulted from *n*-propylhydrazine addition to the bis(benzylidene) adduct (see Scheme I for analogous reaction) in the opposite sense from that leading to **1**.

Our synthetic program led us to prepare a large number of analogues related to **1** for a structure–activity study.[3] In many cases, nine in all, we were able to isolate a pyrazole coproduct; the product pairs are listed in Table I. Table II lists the tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one derivatives employed in the hydrazine cyclization reactions.

When compound **13** was treated with *o*-chloranil[5] in $CHCl_3/CCl_4$ solution at ambient temperature, the major product was the benzodioxane adduct **22**; however, we were able to isolate a second product, albeit in low yield, which was shown to be the desired pyrazole product **23** [mass spectrum *m/e* 406 (M^+); NMR ($CDCl_3$) NCH_2 of the *n*-propyl side chain shifted downfield from δ 2.86 for **13** to δ 4.02 for **23**]. The melting point and spectral data for **23** were different from those of the pyrazole coproduct **14**, formed during the preparation of the dihydropyrazole product **13**. Since the structure assignment of the dihydropyrazole **13** is based on previous[1] work, we can assign pyrazole **23** as the 2-isomer, thereby establishing the pyrazole coproduct **14** as the 1-isomer. Pyrazole coproduct **14** was partially analyzed by X-ray diffraction to a degree sufficient to confirm the location of the *n*-propyl side chain at position 1 (analogous to pyrazole structure B).[4]

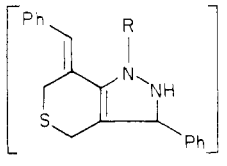
Further treatment of the benzodioxane adduct **22** with *o*-chloranil gave the pyrazole–*o*-chloranil adduct **24**. Scheme I summarizes these reactions.

Although our work with *o*-chloranil was limited to **13**, similar results could be expected with the other dihydropyrazole compounds (Table I), including **1**, for which dehydrogenation with *p*-chloranil failed.

The chemical shift of the benzylidene proton of **13** is δ 7.46 and is shifted downfield to δ 7.70 upon conversion to the pyrazole **23**, whereas the chemical shift of the benzylidene proton of the isomeric pyrazole **14**, formed as coproduct of **13**, is shifted upfield relative to **13** to δ 7.1. These chemical shift differences can be reasonably explained by the shielding effect of the propyl group, being greater for the 1-isomer **14** than for the 2-isomer **23**. In addition, the lone pair of electrons of N-1 may operate on the benzylidene hydrogen through a peri effect[6] consistent with the observed chemical shifts: a maximum effect for the 2-propyl planar aromatic **23**, an intermediate effect for the 2-propyl dihydropyrazole **13**, and a minimum effect for the 1-propyl aromatic **14** (planar but the nitrogen lone pair is now orthogonal to the benzylidene hydrogen.

Table I lists the benzylidene chemical shift values for all of the dihydropyrazole/pyrazole product pairs obtained. With the exception of compound **7**,[7] the chemical shift of the benzylidene proton of all of the pyrazole coproducts is shifted upfield (shielded) relative to the corresponding 2-alkyl dihydropyrazole products. This chemical shift correlation permits the reasonable deduction that the pyrazole coproducts formed are, in every case, the 1-alkyl isomers.

Pyrazoline formation from monoalkyl hydrazines and α,β-unsubstituted carbonyl substrates often proceeds via hydrazone formation, followed by ring closure.[8] If, for either electronic or steric reasons, the initial hydrazine attack occurs at the carbonyl carbon by the secondary NH or at the β carbon in a Michael sense by the primary NH_2, the resulting 3-pyrazoline C, a probable intermediate, must be sufficiently unstable to spontaneously lose hydrogen[9] to give the observed pyrazole products.



C

There appears to be little effect of the enone substrate aryl substituent on the proportion of pyrazole coproduct formed; compare, for example, the first five product pairs in Table I. Generally, less pyrazole formation was observed when X = SO_2 than when X = S; compare **13/14** vs. **11/12** (in other examples where X = SO_2 or SO, not shown in Table I, no pyrazole products were isolated). The major factor determining the extent of pyrazole formation appears to be the nature of the substituted hydrazine; compare **13/14** vs. **17/18** for a dramatic increase in pyrazole formation in going from *n*-propyl to the highly electronegative but sterically similar (2,2,2-trifluoroethyl)hydrazine; likewise, the more sterically hindered isopropylhydrazine afforded considerable pyrazole (**15/16**),

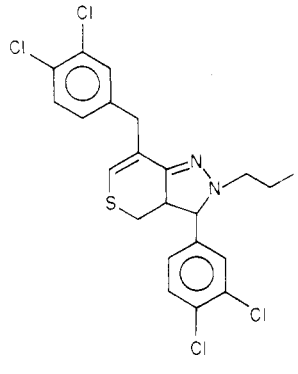
(3) Some of these compounds showed antiinflammatory activity; the biological activity of this series of compounds will be reported elsewhere.

(4) The triclinic crystal structure [a = 11.121 (2) Å, b = 10.881 (2) Å, c = 9.124 (2) Å, α = 102.8 (1)°, β = 98.6 (1)°, γ = 84.0 (1)°, Z = 2] appears to be partially disordered crystallographically and no attempt has been made to refine it. We thank Mrs. B. Toeplitz of The Squibb Institute for Medical Reseach for the X-ray data.

(5) Lalif et al. (N. Lalif, N. Meshriky, and N. S. Gerqis, *Chem. Ind. (London)*, 28 (1976)) report the ready dehydrogenation of dihydropyrazoles to pyrazoles with *o*-chloranil.

(6) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed., Pergamon Press, New York, 1969, Chapter 3-6.

(7) The unusually high field shift observed at δ 6.0 in the ^1H spectrum of **7** presents an apparent anomaly, explainable, however, by an exo- to endocyclic double bond shift to give the following probable assignment for **7**:

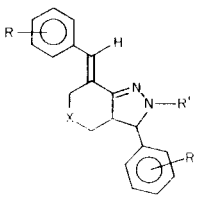
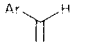
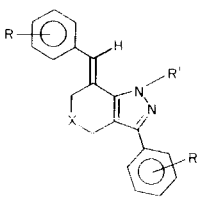
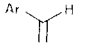


Other unusual features of the ^1H as well as the ^{13}C spectra of **7** are, thus, made consistent by the endocyclic double bond assignment. Unlike all other dihydropyrazole analogues in Table I, compound **7** exhibits a singlet at δ 3.62 (2 H, benzylic CH_2) in the ^1H spectrum. In the ^{13}C spectrum of the closely related analogue **5** (4-chloro), two SCH_2 carbon resonances are observed at 29.6 and 31.3 ppm; in **7** only one resonance appears in this region (29.2 ppm), but a new resonance appears at 37.5 ppm (benzylic CH_2). In addition, the failure of **7** to crystallize may result from the greater number of degrees of freedom afforded by the benzyl group relative to the benzylidene group.

(8) C. H. Jarboe, *Heterocycl. Compd.*, **22**, 189–90 (1967).

(9) I. L. Finar and K. E. Godfrey, *J. Chem. Soc.*, 2293 (1954).

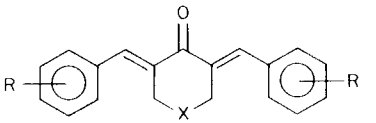
Table I. Dihydropyrazole and Pyrazole Product Pairs from Substituted Hydrazine Reactions[n]

compd	X	R	R'	mp, °C	solvent	time (reflux), h	% yield isolated	δ (CDCl$_3$)	% yield isolated	δ (CDCl$_3$)
1	S	H	n-C$_3$H$_7$	119.5–122	MeOH	3	28[a]	7.23		
4				115.5–117.5					3–4[i]	6.77
5	S	4-Cl	n-C$_3$H$_7$	118–122	ClCH$_2$CH$_2$Cl	2.5	41[b]	7.16		
6				192–194.5					9[b]	6.72
7	S	3,4-Cl$_2$	n-C$_3$H$_7$	oil	MeOH/CHCl$_3$	12	34[c]	6.0[7]		
8				161–162.5					8[j]	6.61
9	S	4-OCH$_3$	n-C$_3$H$_7$	149.5–151.5	MeOH	3.5	35[e]	7.44		
10				131.5–133.5					10[e]	7.15–7.35 (buried)
11	S	4-CH$_3$	n-C$_3$H$_7$	89–91.5	MeOH	5	45[f]	7.1–7.35 (buried)		
12				140–143					9[d]	6.77
13	SO$_2$	4-CH$_3$	n-C$_3$H$_7$	221–224	MeOH	1.5	65[e]	7.46		
14				235–238					2.8[m]	7.1
15	SO$_2$	3-CF$_3$	i-C$_3$H$_7$	196–198.5	MeOH	3	38[g]	7.35–7.72 (buried)		
16				170–172					21[f]	7.13
17	SO$_2$	4-CH$_3$	CH$_2$CF$_3$	211–213	MeOH	5	19[h]	7.52		
18				190–192					26[l]	7.18
19	O	H	n-C$_3$H$_7$	113.5–115	MeOH	3	35[d]	7.2–7.4 (buried)		
20				126.5–128.5					10[k]	6.91

[a] Recrystallized from methanol and then acetonitrile. [b] Recrystallized from acetone–acetonitrile. [c] Obtained as an oil. [d] Recrystallized from ether–hexane. [e] Recrystallized from acetone–hexane. [f] Recrystallized from methanol–water. [g] Recrystallized from ethyl acetate–hexane. [h] Recrystallized from carbon tetrachloride and then acetone–hexane. [i] Recrystallized from methanol. [j] Recrystallized from methanol and then chloroform. [k] Recrystallized from ether–hexane and then cyclohexane. [l] Recrystallized from chloroform–carbon tetrachloride and then acetone–hexane. [m] Recrystallized from chloroform–methanol, then carbon tetrachloride–hexane, and then acetone–hexane. [n] Satisfactory analyses (±0.4 for C, H, N, and S (except for **19** and **20**)) were reported.

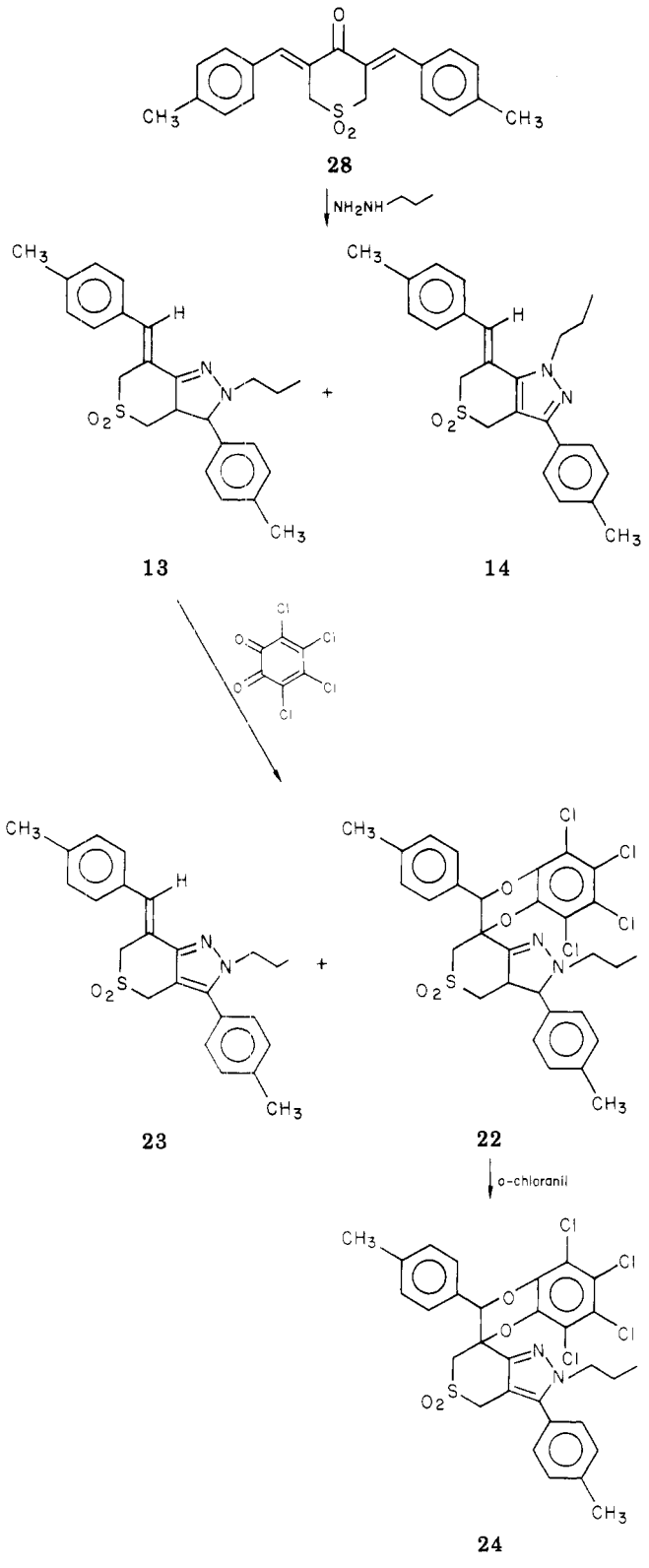
Table II. Tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one Derivatives 25–32



	X	R	mp, °C	yield, %	solv of recrystn	ref	formula[a]
25	S	H	150–151	93	EtOH	2	
26	S	4-OCH$_3$	182.5–184.5	66	EtOH	2	
27	S	4-CH$_3$	197.5–200.5	75	CHCl$_3$/EtOH	2	
28	SO$_2$	4-CH$_3$	198–200	82	EtOH	2	
29	O	H	185–187	52	CHCl$_3$/EtOH	2	
30	S	4-Cl	163–165	64	CHCl$_3$/EtOH		C$_{19}$H$_{14}$Cl$_2$SO
31	S	3,4-Cl$_2$	151–152.5	68	CHCl$_3$/MeOH		C$_{19}$H$_{12}$Cl$_4$SO
32	SO$_2$	3-CF$_3$	154.5–155.5	55	CHCl$_3$/hexane		C$_{21}$H$_{14}$F$_6$SO$_3$

[a] New compounds gave elemental analyses within 0.3% of theoretical.

Scheme I



whereas *n*-propylhydrazine gave no isolated pyrazole (all other substituents were the same; not shown in Table I).

Experimental Section

Melting points were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected. Proton NMR spectra were obtained on a Perkin-Elmer PE R12B spectrometer operating at 60 MHz and on a Varian T-60 spectrometer, using Me_4Si as an internal standard; chemical shifts are reported on the δ scale. Mass spectra were obtained on an AEI-MS-902 spectrometer. Infrared spectra were obtained on a Perkin-Elmer Model 621 or Infracord spectrometer. New compounds gave elemental analyses that were within 0.3% of the calculated values unless otherwise noted.

Preparation of Tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one Derivatives (25-32, Table II). A. Compounds 25-29 have been described[2] although our method of preparation employed concentrated HCl in ethanol (except for **29** where the method of ref 2 was used); for example, a typical procedure is described in ref 1 for preparation of **25**. Compounds **30–32** are new and are described below.

B. Tetrahydro-3,5-bis[(4-chlorophenyl)methylene]-4*H*-thiopyran-4-one (30). To a solution of tetrahydro-4*H*-thiopyran-4-one (10 g, 0.086 mol) and 4-chlorobenzaldehyde (24 g, 0.172 mol) in 60 mL of EtOH was added 6 mL of concentrated HCl. The mixture was heated on a steam bath for 2 h and then cooled to 25 °C. The product (10 g) was collected and washed well with fresh EtOH. The combined filtrate and washings were concentrated to the original volume, 4 mL of concentrated HCl was added, and the solution was heated on a steam bath for another 2 h. After the solution was cooled, 8 g of product was collected. Repeating this procedure once more provided another 4 g of product. The combined product was recrystallized from $CHCl_3$/EtOH to give 20 g; mp 163–165 °C.

C. Tetrahydro-3,5-bis[(3,4-dichlorophenyl)methylene]-4*H*-thiopyran-4-one (31). Procedure B was employed. Thus from tetrahydro-4*H*-thiopyran-4-one (10 g, 0.086 mol) and 3,4-dichlorobenzaldehyde (30 g, 0.172 mol) was obtained 26 g of crude product. Recrystallization from $CHCl_3$/MeOH afforded 20 g of product; mp 151–152.5 °C.

D. Tetrahydro-3,5-bis[[3-(trifluoromethyl)phenyl]-methylene]-4*H*-thiopyran-4-one 1,1-Dioxide (32). 1. Procedure B was employed. Thus, from tetrahydro-4*H*-thiopyran-4-one 1,1-dioxide (3.0 g, 0.02 mol) and 3-(trifluoromethyl)benzaldehyde (7.4 g, 0.042 mol) was obtained 3.7 g of product; mp 148–151 °C.

2. An alternate procedure was found to provide **32** in higher yield. Following procedure B, tetrahydro-4*H*-thiopyran-4-one (23.2 g, 0.2 mol) and 3-(trifluoromethyl)benzaldehyde (76.6 g, 0.44 mol) provided 75 g of crude condensation product. Recrystallization from $CHCl_3$/EtOH afforded 53.9 g (63%) of tetrahydro-3,5-bis[[3-(trifluoromethyl)phenyl]methylene]-4*H*-thiopyran-4-one; mp 113.5–116 °C. Anal. Calcd for $C_{21}H_{14}SOF_6$: C, 58.87; H, 3.29; S, 7.49; F, 26.21. Found: C, 58.94; H, 3.32; S, 7.78; F, 26.41.

A mixture of tetrahydro-3,5-bis[[3-(trifluoromethyl)phenyl]-methylene]-4*H*-thiopyran-4-one (18 g, 0.042 mol) in 300 mL of glacial HOAc containing 27 mL of 30% H_2O_2 was heated on a steam bath for 0.5 h. A small amount of H_2O was added to cloud point and the mixture was allowed to cool to 0 °C. The product was collected and recrystallized from $CHCl_3$/hexane to give **32** (75%); mp 154.5–155.5 °C.

General Procedure for Hydrazine Cyclization Reaction Compounds (1, 4–20). The products listed in Table I were obtained by reacting an equimolar amount of the tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one derivative (Table II) with the appropriate substituted hydrazine[10] in a solvent (usually methanol) at reflux temperature. The method of separation and purification for each product pair is addressed individually; reaction conditions and solvents of crystallization are noted in Table I.

A. 1 and 4. Compound **1** precipitated from the cooled reaction mixture and was recrystallized. Compound **4** was obtained by concentrating the reaction mother liquor, after removal of **1**, and then recrystallized.

B. 5 and 6. The reaction mixture was washed with dilute HCl and H_2O, dried ($CaCl_2$), and concentrated in vacuo. The residue was chromatographed on Al_2O_3 (neutral, activity I). Elution with 0–5% EtOAc/hexane gave **5** which was recrystallized; further elution with EtOAc and then $CHCl_3$ afforded **6**, which was further purified by recrystallization.

C. 7 and 8. Unreacted starting material precipitated from the cooled reaction mixture and was removed. The remainder was concentrated in vacuo, redissolved in $CHCl_3$ and washed with

(10) The substituted hydrazines were either prepared (*Chem. Abstr.*, 59, 8742*f* (1963), *n*-C_3HNHNH_2 and *i*-$C_3H_7NHNH_2$) or purchased (Aldrich Chemicals, $CF_3CH_2NHNH_2$ as 70% aqueous solution).

dilute HCl and H_2O, dried (anhydrous $MgSO_4$), and concentrated in vacuo. This was chromatographed on Al_2O_3 (neutral, activity I). Compound **7** was obtained as an oil upon elution with 10–40% Et_2O/hexane; continued elution with 50–80% Et_2O/hexane gave **8**, which was recrystallized.

D. 9 and 10. A product mixture which precipitated from the cooled reaction was chromatographed on Al_2O_3 (neutral, activity I). Elution with 10–20% EtOAc/hexane afforded **9**, which was recrystallized; further elution with 10–60% $CHCl_3$/hexane gave **10**, which was purified by recrystallization.

E. 11 and 12. A product mixture which precipitated from the cooled reaction was chromatographed on Al_2O_3 (neutral, activity I). Compound **11** was eluted first with 10–20% Et_2O/hexane and was recrystallized; elution with 40–60% Et_2O/hexane provided **12**, which was further purified by recrystallization.

F. 13 and 14. The cooled reaction mixture provided a mixture of crystalline **13** and **14**. Crystals of **14** are large cubes and dissolve quite slowly in cold $CHCl_3$, whereas crystals of **13** are light, fluffy needles which rapidly dissolve in $CHCl_3$. A rapid wash of the mixture of **13** and **14** with cold $CHCl_3$ leaves the latter behind, which can then be further purified by recrystallization. The filtrate, containing mainly **13**, was concentrated in vacuo and purified by recrystallization.

G. 15 and 16. The cooled reaction gave a mixture of **15** and **16**; several recrystallizations afforded **15**. The combined mother liquors were concentrated in vacuo and the residue was recrystallized to give **16**.

H. 17 and 18. The cooled reaction gave a mixture of **17** and **18**; two recrystallizations afforded **18**. The combined mother liquors were concentrated in vacuo and chromatographed on silica gel; elution with 10% EtOAc/hexane gave **17**, which was further purified by crystallization.

I. 19 and 20. Solvent was removed in vacuo and the residue dissolved in $CHCl_3$ and washed with dilute HCl and H_2O. The organic layer was dried (anhydrous $MgSO_4$) and concentrated in vacuo and the residue was chromatographed on Al_2O_3 (neutral, activity I). Elution with hexane gave **19**, which was further purified by recrystallization. Et_2O elution afforded **20**, which was then recrystallized.

Reaction of 13 with *o*-Chloranil. Preparation of 22–24. To a suspension of **13** (2.0 g, 4.9 mmol) in 100 mL of CCl_4 at ambient temperature was added a solution of *o*-chloranil (1.25 g, 5.1 mmol) in 100 mL of CCl_4 over a period of 2.5 h. The reaction mixture, which became homogeneous near the end of the *o*-chloranil addition, was allowed to stir for another 0.5 h before washing with dilute NaOH and H_2O. The organic layer was dried ($CaCl_2$) and concentrated in vacuo and the residue was chromatographed on Al_2O_3 (neutral, activity I). Elution with CCl_4/$CHCl_3$ (100/0 to 65/35) gave two major fractions as followed by TLC.

The first product to elute was **22** (1.4 g) which was recrystallized from CCl_4/hexane to give 1.1 g: mp 152–154 °C dec; IR (Nujol) 1520, 1570 (C=N), 1130, 1310 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 7.10–7.22 (m, 8 H, ArH), 5.73 (s, 1 H, OCH), 2.78 (t, 2 H, J = 7 Hz, NCH_2). Anal. Calcd for $C_{30}H_{28}N_2Cl_4SO_4$: C, 55.05; H, 4.31; N, 4.28; S, 4.90; Cl, 21.67. Found: C, 55.34; H, 4.09; N, 4.11; S, 4.84; Cl, 21.43.

The second product to elute was **23** (0.4 g), which was purified by recrystallization from CCl_4/hexane and then from acetone/hexane to give 0.2 g: mp 161–163 °C; m/e 406 (M^+); IR (Nujol) 1450, 1500 (PhCH=CC=N), 1125, 1315 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 7.68 (br s, 1 H, =CH), 7.18 (s, 8 H, ArH), 4.02 (t, 2 H, J = 7 Hz, NCH_2), 2.43, 2.37 (two s, 6 H, $ArCH_3$). Anal. Calcd for $C_{24}H_{26}N_2O_2S$: C, 70.70; H, 6.45; N, 6.89; S, 7.89. Found: C, 71.03; H, 6.68; N, 6.93; S, 8.00.

When **22** (325 mg, 0.5 mmol) in 15 mL of CCl_4 containing *o*-chloranil (130 mg, 0.5 mol) was heated at reflux temperature for 2 h, the initial red dissipated and a solid separated. After the mixture had cooled overnight, there was collected a small amount of **24**: mp 275.5–277°C dec; m/e 650 (M^+); NMR ($CDCl_3$) δ 7.00–7.38 (m, 8 H, ArH), 5.92 (s, 1 H, OCH_2), 4.13 (t, 2 H, J = 7 Hz, NCH_2), 2.43, 2.35 (two s, 6 H, $ArCH_3$). Anal. Calcd for $C_{30}H_{26}N_2Cl_4SO_4$: C, 55.22; H, 4.02; N, 4.29; S, 4.92; Cl, 21.74. Found: C, 55.35; H, 4.32; N, 4.37; S, 4.70; Cl, 21.53.

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Synthesis and Nuclear Magnetic Resonance Spectra of *N*-Carboethoxy-4-spiro-1,4-dihydropyridines

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A series of *N*-carboethoxy-4-spiro-1,4-dihydropyridines (**11**) has been prepared via condensation reactions of glutaraldehydes with ammonia or ethyl carbamate. While ammonia gives substantial amounts of 2-amino-1,2,3,4-tetrahydropyridines as well as some 1,4-dihydropyridines, ethyl carbamate condenses in benzene solution in the presence of catalytic amounts of *p*-toluenesulfonic acid to give **11** exclusively. The latter reaction, run as a one-pot synthesis from diol to *N*-carboethoxy-1,4-dihydropyridine, gives yields of 70–80%. NMR data, both ^1H and ^{13}C, show that in the ground state the rings in these spirourethanes do not interact. NMR investigation of glutaraldehyde isolated from water solution shows it to consist in Me_2SO of a 1:1 mixture of free dialdehyde and polymeric cyclic acetal. In contrast, periodate cleavage of 3,3-tetramethine-1,2-cyclopentanediol gives the monomeric cyclic acetal.

Dihydropyridines occupy a central position in metabolism (NAD–NADH oxidation–reduction system), and their analogues have been therapeutically useful in a variety of physiological disorders.[1,2] Also, these com-

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