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(14) Fellow of the Alfred P. Sloan Foundation, 1978–1980.

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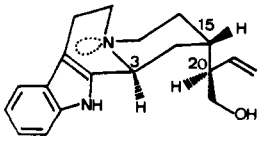
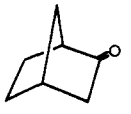
Synthesis of (±)-Antirhine from (±)-Norcamphor

Sir:

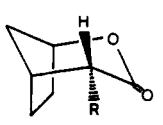
Antirhine (**1**),[1] the major alkaloid of *Antirhea putaminosa*, is an unique yohimbonoid variant with cis C/D ring juncture and only two congeners, hunterburnine α- and β-methochlorides[2] (10-hydroxyantirhine α- and β-methochloride), have been isolated so far. Although a structurally simple compound, **1** has not previously been synthesized, probably owing to difficulty in the stereocontrolled construction of the three chiral centers, the centers at C_3 and C_{15} with the less stable anti relationship, and the center at C_{20} bearing vinyl and hydroxymethyl moieties.[3] We describe here the first stereoselective synthesis of (±)-antirhine (**1**), starting from (±)-norcamphor[4] (**2**).



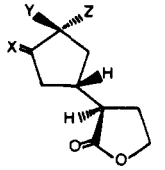
1



2



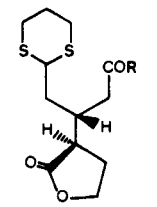
3: R=H
4: R=$CH_2CH{=}CH_2$
5: R=CH_2CH_2OH

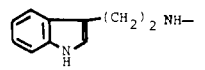


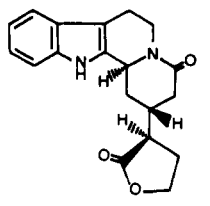
6: X=H_2, Y=H, Z=OH
7: X=H_2, Y=Z=-O-
8: X=-S$(CH_2)_3$S-, Y=Z=-O-

Ozonization of the bicyclic δ-lactone **4** [prepared stereoselectively from (±)-norcamphor (**2**) via **3** (75.4% overall yield)[4c]] in methanol (−78 °C), followed by direct reduction with sodium borohydride in the same flask (−78 °C to room temperature) furnished the oily γ-lactone **6**[5] [79.9% yield; IR (neat) 3400, 1755 cm^{-1}; mass spectrum *m/e* 171 ($M^+ + 1$) 153 (100%)] spontaneously through the δ-lactone **5**. Oxidation of **6** with Jones reagent gave the keto lactone **7**, mp 78–80 °C, in 79.8% yield: IR (Nujol) 1750, 1725 cm^{-1}; mass spectrum *m/e* 168 (M^+), 140 (100%). Regioselective thioketalization was achieved by treatment of the pyrrolidine enamine derived from keto lactone **7** with trimethylene dithiotosylate[6] in the presence of triethylamine, affording the α-diketone monothioketal **8**, mp 142–144 °C, in 51.8% yield: IR (Nujol) 1755, 1720 cm^{-1}; mass spectrum *m/e* 272 (M^+), 272 (100%).

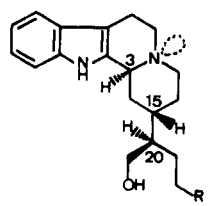
Base cleavage[7] of **8** (KOH-*t*-BuOH, 60 °C, 1 h) and acid workup produced the carboxylic acid **9**, amorphous foam, in quantitative yield: IR (Nujol) 3400–2400, 1758, 1710 cm^{-1}; NMR ($CDCl_3$) δ 3.94–4.55 (3 H, m), 10.36 (1 H, s, disappeared with D_2O); mass spectrum *m/e* 290 (M^+), 119 (100%). Treatment of **9** with ethyl chloroformate in the presence of triethylamine[8] (CH_2Cl_2, room temperature, 4 h) gave the crude mixed anhydride, which on condensation with tryptamine (CH_2Cl_2, room temperature) afforded the secondary amide **10**, amorphous foam, in 76.8% overall yield: IR (Nujol) 3250, 1752, 1640 cm^{-1}; NMR ($CDCl_3$) δ 3.57 (2 H, br t), 4.13 (3 H, m), 6.05–6.50 (1 H, br q, disappeared with D_2O), 6.96–7.90 (5 H, m), 8.88 (1 H, s, disappeared with D_2O); mass spectrum *m/e* 432 (M^+), 143 (100%).

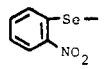


9: R=OH
10: R=  $(CH_2)_2$ NH–



11



12: R=OH
13: R=  Se–

On hydrolysis of the dithiane group, by treatment of **10** with methyl iodide in aqueous acetonitrile at room temperature[9,10] (~48 h), cyclization occurred to furnish the lactam **11**, mp 214–217 °C, in 36.8% yield: IR (Nujol) 3140, 1759, 1608 cm^{-1}; NMR ($CDCl_3$ + CF_3CO_2H) δ 4.00–4.46 (2 H, m), 4.78–5.28 (2 H, m), 7.05–7.70 (4 H, m), 8.72 (1 H, br s); mass spectrum *m/e* 324 (M^+), 184 (100%). Reduction ($LiAlH_4$, boiling THF, 3.5 h) of the lactam **11** gave the aminodiol **12** with the anti C_3–C_{15} relationship, mp 215–218 °C, in 92.5% yield: IR (Nujol) 3170 cm^{-1}; NMR ($CDCl_3$) δ 3.40–3.98 (4 H, m), 4.15 (3 H, br s, 2 H, disappeared with D_2O), 6.90–7.60 (4 H, m), 9.02 (1 H, br s, disappeared with D_2O); mass spectrum *m/e* 314 (M^+), 225 (100%). Support for the assignment of the stereochemistry at C_3 and C_{15} was obtained from spectral examination. As expected, the IR spectrum did not exhibit Bohlmann bands, while the NMR spectrum exhibited the C_3 H as a multiplet centered at δ 4.15, both indicating the cis B/C configuration owing to the anti C_3–C_{15} relationship.[3b,11,12]

Treatment of the diol **12** with 1 molar equiv of *o*-nitrophenyl selenocyanate and tri-*n*-butylphosphine[13] (THF, room temperature, 2 h) allowed selective selenylation at the desired position to give the monoselenide **13**, mp 175–177 °C, in 39.2% yield (64.3% yield based on recovered **12**): IR ($CHCl_3$) 3470, 3280, 1590, 1330 cm^{-1}; NMR ($CDCl_3$) δ 4.21 (1 H, br s), 6.95–7.70 (7 H, m), 8.27 (1 H, d, J = 7.6 Hz), 8.73 (1 H, br s, disappeared with D_2O); mass spectrum *m/e* 498 (M^+), 225 (100%). The selenide **13**, upon oxidation with *m*-chloroperbenzoic acid (1.3 equiv, CH_2Cl_2, −20 °C to room temperature) afforded (±)-antirhine (**1**), mp 100–102 °C (lit.,[1] 112–114 °C), in 71.7% yield, which had R_f values and IR, NMR, and mass spectra identical with those of the natural product.[14] Since chiral norcamphor has been obtained,[15] the present method is potentially useful for a chiral synthesis of antirhine (**1**).

Acknowledgment. We thank the Ministry of Education, Japan, for supporting this work.

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(5) All new compounds reported in this work gave satisfactory spectral and analytical analyses.
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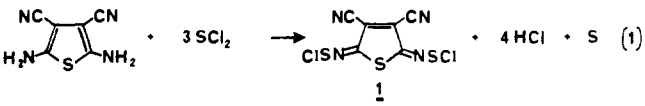
2,5-Di-*N*-chlorothioimino-3,4-dicyanothiophene: A Novel Monomer of Unusual Molecular and Solid-State Structure

Sir:

The title compound (**1**) was a molecule we sought as a possible monomer for the preparation of polymers of unsaturated sulfur-nitrogen-carbon backbone.[1] These polymers are of interest because they are expected to exhibit high electronic conductivity in the solid state in analogy[2] to $(SN)_x$. Here we describe the preparation and some properties of this heterocycle and its unique solid-state structure.

The *S*-chlorosulfurimino functional group is rare[3,4] and was isolated only in the case of highly electronegatively substituted small molecules.[5] It was, therefore, uncertain whether the title compound could be prepared and isolated for complete characterization. Fortunately, the mild conditions shown in eq[6] 1



(1)

1

afforded **1** in good yield as red crystals: IR (KBr) 2230 (vw), 1530 (s), 1500 (s), 1345 (s), 1240 (w), 892 (s), 841 (s), 820 (m) cm^{-1}; MS (*m/e*) 296 (P + 2), 294 (P), 259 (P − Cl), 224 (P − Cl_2), 192 (P − SCl_2), 146 (P − $NSCl_2$), etc. Anal. Calcd for $C_6Cl_2N_2S_3$: C, 24.41; Cl, 24.07; N, 18.98; S, 32.54. Found: C, 24.21; Cl, 23.93; N, 18.66; S, 32.83. Since attempts to determine its ^{13}C NMR spectrum failed owing to low solubility in most appropriate solvents and molecular weight determinations in solution again failed because of the instability of the compound in suitable solvents, we had to resort to X-ray structure determination.[7]

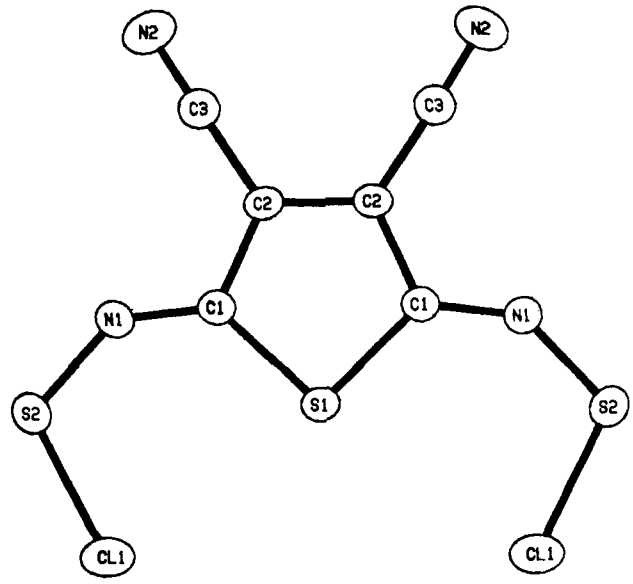


Figure 1. Molecular structure of 2,5-di-*N*-chlorothioimino-3,4-dicyanothiophene.

Data were collected on a 0.2 × 0.2 × 0.2 mm crystal mounted on a glass fiber. The orthorhombic *C*-centered (space group *Cmcm*) solid with extinctions *hkl* ($h + k \neq 2n$); *h0l* ($h = 2n$, $l \neq 2n$) had the following cell constants: $a = 6.327$ (3), $b = 9.678$ (8), $c = 17.337$ (17) Å; $\alpha = \beta = \gamma = 90°$; $V = 1061.7$ Å^3; $\lambda = 0.710730$ Å (based on computer centering of 25 reflections followed by least-squares refinement of the setting angles). Calculated density was 1.847 g/cm^3 for four molecules per unit cell of above dimensions.[8]

Intramolecular bond angles and bond distances are shown in Table I; molecular and solid-state structures are shown in Figures 1 and 2. The most striking features of the molecular structure are planarity and the inward folding of the S–Cl bonds such that the S-1 to Cl-1 distance (cf. Table I and Figure 1) of 3.29 Å is 0.26 Å shorter than the sum of Van der Waals radii for S and Cl.[9]

The solid-state structure reveals uniform stacks along the *a* axis and sheets along the *b*–*c* plane. The closest intermolecular contact (3.110 Å) is between Cl-1 and N-2 of two molecules within a sheet in the *b* direction (cf. Figure 2).

Although compound **1** could be considered an acid chloride

Table I[a]

Bond Distances in Ångstroms

atom 1	atom 2	distance	atom 1	atom 2	distance	atom 1	atom 2	distance
S-1	Cl-1	3.290 (1)	N-1	C-1	1.283 (2)	C-2	C-2	1.363 (3)
S-1	C-1	1.775 (1)	N-2	C-3	1.136 (2)			
S-2	Cl-1	2.049 (1)	C-1	C-2	1.439 (2)			
S-2	N-1	1.583 (1)	C-2	C-3	1.431 (2)			

Bond Angles in Degrees

atom 1	atom 2	atom 3	angle	atom 1	atom 2	atom 3	angle	atom 1	atom 2	atom 3	angle
C-1	S-1	C-1	91.3 (1)	S-1	C-1	C-2	110.2 (1)	C-2	C-2	C-3	123.39 (9)
Cl-1	S-2	N-1	111.29	N-1	C-1	C-2	120.8 (1)	N-2	C-3	C-2	178.5 (2)
S-2	N-1	C-1	138.5 (1)	C-1	C-2	C-2	114.13 (8)				
S-1	C-1	N-1	129.0 (1)	C-1	C-2	C-3	122.5 (1)				

[a] Numbers in parentheses are estimated standard deviations in the least significant digits.

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