-113.95°, 123-124 °C, 2.5 g. 8th P:L (5:2), -113.95°, 123-124 °C, 1.5 g. A = acetone, E = ethyl ether, PE = petroleum ether (50-60 °C), P = pentane, L = ligroin.

The mother liquor from the first recrystallization yielded 27 g of ester, $[\alpha]_D$ -11.32°, which was recrystallized from 25 mL of ether to yield 8 g of ester, $[\alpha]_D$ -29.85°. The mother liquor yielded 19 g of ester, $[\alpha]_D$ -2.52°, mp 80-82 °C. This was recrystallized 5 times to yield 0.3 g of *R* ester: $[\alpha]_D$ +77.35°; mp 115.5-116.5 °C. The IR and NMR spectra were identical with those of the (-)-(*S*) diastereomer. Anal. Calcd for $C_{28}H_{48}O_2$: C, 74.94; H, 10.78; S, 7.14. Found: C, 74.65; H, 10.58; S, 7.09. These five recrystallizations proceeded as follows. 1st, A, -0.70°, 81-91 °C, 15.2 g, 2nd, A:E (6:5), +10.23°, 85-95 °C, 8 g. 3rd, A:E (1:1), +38.50°, 98-105 °C, 2 g. 4th, A:E (2:1), +70.45°, 112.5-113.5 °C, 1.2 g, 5th, A:E (1:1), +77.35°, 115.5-116.5 °C, 0.3 g. 6th, A:E (1:1), +76.85°, 116.0-116.5 °C, 0.2 g.

Synthesis of Optically Active Sulfoxides: General Procedure. A solution of *O*-cholesteryl methanesulfinate (1 equiv) in ether (25.0 mL/mmol of sulfinate) was added dropwise to an ethereal solution of the appropriate Grignard reagent (3 equiv) at room temperature. After completion of the addition, the reaction mixture was stirred for 2 h at room temperature. Then, the reaction mixture was quenched with 50 mL of a saturated aqueous solution of ammonium chloride. After being stirred the layers were separated and the ether phase was extracted twice with water (20 mL). The combined water solution after saturation with sodium chloride was extracted with chloroform (5 × 20 mL). The chloroform solution was dried over magnesium sulfate. Rotoevaporation of the solvent left the crude sulfoxide which was purified by column chromatography on aluminum oxide using methylene chloride as eluent. IR spectra were the same as those of authentic samples of the racemic sulfoxides. The yield and optical rotation of sulfoxides obtained in this way are collected in Table I.

Acknowledgment. The work at Durham was supported in part by grants from the National Science Foundation CHE-8308245, GP8136, and GP5283.

Registry No. MeS(O)Cl, 676-85-7; (*R*)-MeS(O)Pr, 37177-70-1; (*S*)-MeS(O)Bu, 763-95-1; (*S*)-MeS(O)-*i*-Bu, 26451-17-2; (*R*)-MeS(O)-*p*-C_6H_4Me, 1519-39-7; (*S*)-MeS(O)CH_2Ph, 14090-81-4; (-)-cholesterol, 57-88-5; (-)-cholesteryl (-)-(*S*)-methanesulfinate, 63520-69-4; (-)-cholesteryl (+)-(*R*)-methanesulfinate, 63520-66-1.

A Novel Reaction of Cyanamide with 1,3-Diketones

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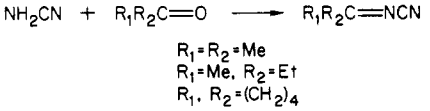
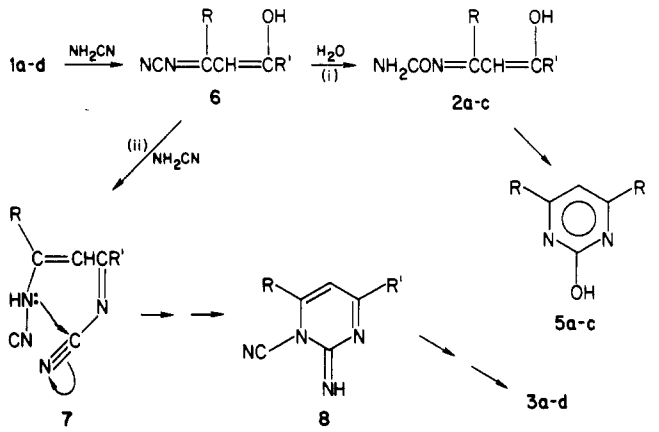
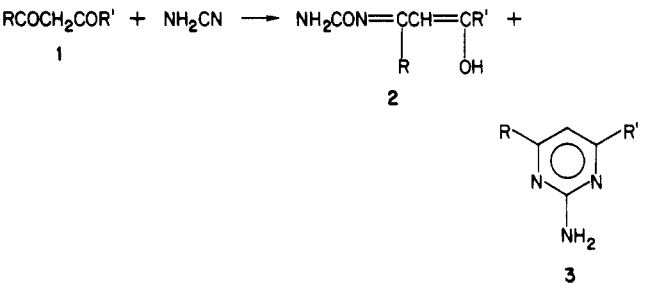
Only a few reactions of cyanamide with ketones have been reported in the literature. Typical examples are the reactions of simple aliphatic ketones with cyanamide at 60 °C for 6 h to give the corresponding cyanoimino compound in moderate yield[1] and the reaction of sodium cyanamide with ethyl acetoacetate to give the same derivative of the keto group.[2]



Scheme I



We have found that cyanamide and 2,4-pentanedione (**1a**) react in water without added acid or base to give after 8 h, a 23% yield of 4-[(aminocarbonyl)imino]-2-penten-2-ol (**2a**) and a 38% yield[3] of 2-amino-4,6-dimethylpyrimidine (**3a**). The same reaction in methanol gave much lower



a, R = R' = Me
b, R = CF_3; R' = Me
c, R = CF_3; R' = *i*-Pr
d, R = Me; R' = Ph

yields of **2a** and **3a**. The reaction in aqueous carbonate gave a 43% yield[3] of **3a** and 3% of 4-amino-3-penten-2-one (**4**).

The reaction of cyanamide with four other 1,3-diketones has also been explored. Most of these reactions were run for several days at room temperature and only the major products were isolated. (1) When a 1.25 M aqueous solution of 1,1,1-trifluoropentane-2,4-dione (**1b**) was treated with a 1 molar excess of cyanamide, a 68% yield[3] of 2-amino-4-(trifluoromethyl)-6-methylpyrimidine (**3b**) was obtained. Under similar conditions a 1:1 molar ratio of **1b** and cyanamide gave a good yield of a mixture of **3b** and 4-(trifluoromethyl)-2-hydroxy-6-methylpyrimidine (**5b**). No intermediates for this reaction could be detected by TLC. (2) With water, in which it was not very soluble, 1,1,1-trifluoro-5-methylhexane-2,4-dione (**1c**) gave only a very low yield of 4-(trifluoromethyl)-2-hydroxy-6-isopropylpyrimidine (**5c**) with cyanamide. In homogeneous media, methanol or 50/50 methanol/water, a 25% yield of **5c** was isolated. (3) From benzoylacetone and 3 equiv of cyanamide, a 13% yield[3] of 2-amino-4-methyl-6-phenylpyrimidine (**3d**) was isolated. (4) With 1,3-cyclohexanedione there was little or no reaction.

Information about the reaction mechanism was obtained from control experiments. Thus, urea, a possible hydrolysis product of cyanamide,[4] did not react with **1a** under the reaction conditions. Furthermore, cyanoguanidine, the dimerization product of cyanamide,[4] did not react with **1a**

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(2) (a) Brigl, P. *Chem. Ber.* **1912**, *45*, 1557-63. (b) Sonn, A. *Chem. Ber.* **1912**, *45*, 1958-60.
(3) All yields reported for **3** are based upon a stoichiometry of 2 mol of cyanamide to 1 mol of ketone 1.
(4) American Cyanamide Company, "Cyanamide", New York, 1958.

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to form any **3a**. Finally, **3a** was not formed by reaction of either **2a**, **4**, or **5a** with cyanamide. Literature precedent precludes ammonia as a significant reactant.[4]

While an unequivocal mechanism cannot be written for the formation of products **2**, **3**, and **5**,[5] one possible pathway is shown in Scheme I. The first step is the usual reaction of cyanamide with a carbonyl group to give the cyanoimino compound **6**.[6] That there is a competition for an intermediate by water and cyanamide is illustrated by the results in the reactions of **1b** with differing amounts of cyanamide (see above). In Scheme I this competition is illustrated by the reactions of **6**. The ready hydrolysis of **6** has ample precedent.[7] That **6** reacts with cyanamide to give **7** and not a derivative of the cyanoimino group is strongly suggested by the fact that the condensation of cyanoguanidine with **1a**, a reaction which requires base, gives only 2-(cyanoamino)-4,6-dimethylpyrimidine and no **3**. Finally compound **7** can undergo an intramolecular nucleophilic reaction of a type typical for cyanamides[4] to give **8**. Compound **8** either undergoes hydrolysis or attack by cyanamide followed by loss of dicyanamide to give **3**.

The reaction of cyanamide with ketones is clearly suppressed in compounds where there is steric hindrance around or resonance interaction with the carbonyl group as in ketones **1c** and **1d**. Thus, in **6c**, the carbonyl group would be too sterically hindered for attack of another molecule of cyanamide to compete with hydrolysis to **2**.

Experimental Section

The proton NMR spectra were recorded on a Varian EM-360 NMR spectrometer at 60 MHz. The mass spectral molecular weights were determined on an AEI MS-9 mass spectrometer. Infrared spectra were taken on a Perkin-Elmer IR-283 spectrometer. Melting points were taken on a Meltemp apparatus and are uncorrected.

Cyanamide and 1a. To 15 g (0.11 mol) of potassium carbonate in 50 mL of water was added 2.157 g (0.051 mol) of cyanamide (Aldrich) and after swirling, 5.014 g (0.050 mol) of **1a**. After an hour some needles had precipitated out of the reaction mixture. After 8 h the reaction mixture was filtered and the crystals washed with water to give 0.901 g of 2-amino-4,6-dimethylpyrimidine (**3a**), mp 156–158 °C. The filtrate was extracted with three 75-mL portions of chloroform, washed once with water, dried ($MgSO_4$), and filtered, and the filtrate was removed under reduced pressure to give an oily solid which smelled like starting material. (This procedure is hereafter referred to as the usual workup.) Thick-layer chromatography on silica gel GF, developed with ethyl acetate, gave an additional 0.698 g of **3a**, mp 150–155 °C; total yield, 1.499 g (43%),[3] identified by IR comparison and mixture melting point (no depression) with an authentic sample synthesized by the method of Benary.[8] Also from the thick layer was obtained 0.167 g (3%) of 4-amino-3-penten-2-one, identified on the basis of an IR spectrum, identical with that of an authentic sample (see below) and identical R_f on the same TLC plate.

Under neutral conditions 4.5 g (0.11 mol) of cyanamide and 10.0 g (0.10 mol) of **1a** in 70 mL of water were allowed to stand for 22 h. The lustrous crystals which had formed were filtered off to give 3.0 g, mp 177–180 °C dec; second crop, 0.2 g, mp 166–169 °C. The total yield was 3.2 g (23%) of 4-[(aminocarbonyl)imino]-2-penten-2-ol (**2a**). The usual workup of the water layer gave 2.9 g (38%)[3] of crude 2-amino-4,6-dimethylpyrimidine. After the water layer had been allowed to stand for a week, 0.8 g of needles, mp 190–201 °C, were collected. Recrystallization from methanol gave straw-colored needles, mp 197.5–199.5 °C, which were identical (IR, mmp) with an authentic sample of the 1:1 complex of urea and 2-hydroxy-4,6-dimethylpyrimidine (**5a**) prepared by the method of Birtwell.[9]

Compound **2a** was recrystallized to analytical purity from methanol, mp 172.5–174.5 °C, with bubbling; ^1H NMR (Me_2SO-d_6) 2.1 (s, 3, CH_3) 2.3 (s, 3, CH_3), 5.3 (s, 1, CH), 6.8 (br s, 2, NH_2), 11.5 ppm (br s, 1, OH); IR (KBr) 2850–3500 (br, OH, NH_2), 1710 (C=O), 1580 (br, enol) 1260 cm^{-1}; MS calcd M_r 142.0743, found 142.0741. Anal. Calcd for $C_6H_{10}N_2O_2$: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.68; H, 6.92; N, 19.68.

Compound **2a** (1.01 g) in 20 mL of 6 N HCl was heated on the steam bath for 2 min. The usual workup of the aqueous layer gave 0.490 g (29%) of **6a**; IR identical with authentic sample, same R_f on TLC. The remaining aqueous layer was basified with potassium carbonate and the water was removed in vacuo. Subsequent treatment with methanol, filtering off the inorganic material, and removal of the methanol was repeated 6 or 7 times, leaving 0.420 g (98%) of a yellow solid, mp 115–118 °C, identified as urea by comparison with an authentic sample (mmp, IR).

Compound **2a** was pyrolyzed at 195 °C under nitrogen until bubbling ceased, about 10 min. Both 4-amino-3-penten-2-one and **5a** were isolated and identified by comparison (IR, mmp) with authentic samples. Compound **5a** was synthesized by the method of Kosolapoff and Roy.[10]

A reaction was run for 6 days with 4.345 g (0.10 mol) of cyanamide and 5.013 g (0.05 mol) of **1a** in 35 mL of methanol. Methanol and unreacted **1a** were removed under reduced pressure, and the remaining oil was thick-layer chromatographed. Along with a good deal of recovered cyanamide, 1.056 g (15%)[3] of **3a** was obtained.

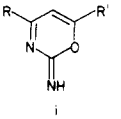
Synthesis of 4-Amino-3-penten-2-one (4). The preparation is a modification of the method of Combes.[11] When 250 mL of concentrated ammonium hydroxide was added to 55 g of **1a**, a solid immediately formed in a mildly exothermic reaction. The reaction mixture was allowed to stand for 2 days and then dissolved in chloroform and washed twice with water. The chloroform was dried ($MgSO_4$), filtered, and removed under reduced pressure to give 59 g of a yellow oily solid. Distillation under reduced pressure (10 mm; bath temperature, 170 °C) gave 39 g (71%) of a pale yellow solid.

Cyanamide and Benzoylacetone. A mixture of 2.000 g (0.0123 mol) of benzoylacetone (Aldrich) and 1.555 g (0.0369 mol) of cyanamide in 15 mL of methanol was allowed to stand for 7 days at room temperature. TLC showed no significant changes over the last 2 days of the reaction. Thick-layer chromatography gave unreacted ketone, cyanamide, and its decomposition products and 0.306 g (13%) of yellow solid, mp 163–176 °C, identified as 2-amino-4-methyl-6-phenylpyrimidine by comparison (IR, mmp) with an authentic sample prepared by the method of Falco et al.[12]

Cyanamide and 1,3-Cyclohexanedione. A mixture of 2.8 g (0.025 g) of the diketone and 1.1 g (0.026 mol) of cyanamide in 17 mL of water was allowed to stand for 4 days. TLC showed only starting material.

Cyanamide and 1,1,1-Trifluoro-2,4-pentanedione, (1b). A solution of 3.9 g (0.025 mol) of **1b** and 1.1 g (0.026 mol) of cyanamide in 17 mL of methanol was allowed to stand for 4 days at room temperature. The reaction mixture was poured into 100 mL of water and the usual workup gave an oil. After 1 day, 0.853 g (19%) of yellow crystals of 4-(trifluoromethyl)-2-hydroxy-6-methylpyrimidine (**5b**), mp 181–183 °C, were formed and recrystallized to analytic purity from ethyl acetate: mp 188–190 °C; ^1H NMR ($CDCl_3$) 2.5 (s, 3, CH_3), 6.6 ppm (s, 1, CH); IR 2500–3500 (br, OH), 1500–1800 cm^{-1} (br); MS, M_r calcd for

(5) For example, a referee has suggested another scheme consistent with the results which includes compound **i** as a key intermediate which can undergo nucleophilic attack by water or cyanamide and lead by a variety of reasonable processes to **2**, **3**, and **5**.



i

(6) This is probably the major tautomer.

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$C_6H_5F_3N_2O$ 178.0355, found 178.0352. Anal. Calcd for $C_6H_5F_3N_2O$: C, 40.46; H, 2.83; N, 15.73. Found: C, 40.62; H, 2.79; N, 15.98.

A solution of 3.927 g (0.0255 mol) of **1b** and 2.256 g (0.0537 mol) cyanamide in 20 mL of water was allowed to stand at room temperature for 7 days. The crystals which had formed were filtered, giving 3.049 g (68%)[3] of **3b**: mp 119–123 °C (lit.[13] mp 128 °C); NMR ($CDCl_3$) 2.4 (s, 3, CH_3), 5.3–6.0 (s, 2, NH_2), 6.6 ppm (s, 1, CH); IR 3320–3400 (br, NH_2), 3220 (NH_2), 1640 cm^{-1}; MS, M_r calcd for $C_6H_6F_3N_3$ 177.0515, found 177.0514. A 2% yield of **5b**, mp 189–191 °C, was also obtained from this run.

When the same reaction was run with 7.852 g (0.051 mol) of **1b** and 2.250 g (0.0536 mol) of cyanamide in 20 mL of water, 4.892 g of very sticky yellow solid, mp 89–140 °C, was obtained; a second crop of pale yellow crystals, 0.730 g, mp 176–186 °C, was obtained. Several recrystallizations of these solids from ethyl acetate gave 0.749 g of shiny needles, mp 187–191 °C, which were identical (IR, mmp) with **5b** described above. TLC's of the original solid and the residues from recrystallization showed the only major components of the mixture to be **3b** and **5b**.

Cyanamide and 1,1,1-Trifluoro-5-methyl-2,4-hexanedione (1c). A solution of 4.604 g (0.025 mol) of **1c** and 1.145 g (0.027 mol) of cyanamide in 17 mL of methanol was allowed to stand for 8 days at room temperature. The methanol was removed under reduced pressure and, after 1 day, a solid formed. Filtration gave 1.382 g (25%) of 4-(trifluoromethyl)-2-hydroxy-6-isopropylpyrimidine: mp 180–192 °C; recrystallized to analytic purity from methanol, mp 191–191.5 °C; NMR (Me_2SO-d_6) 1.2 (d (J = 7 Hz), 6, CH_3), 2.9 (equintet (J = 7 Hz), 1, CH); IR (KBr) 2500–3300 (br, OH), 1640 cm^{-1}; MS, M_r calcd for $C_8H_9F_3N_2O$: 206.0668, found 206.0656. Anal. Calcd for $C_8H_9F_3N_2O$: C, 46.60; H, 4.40; N, 13.59. Found: C, 46.59; H, 4.17; N, 13.74.

Registry No. **1a**, 123-54-6; **1b**, 367-57-7; **1c**, 30984-28-2; **1d**, 93-91-4; **2a**, 91606-59-6; **3a**, 767-15-7; **3b**, 5734-63-4; **3d**, 15755-15-4; **4**, 1118-66-7; **5a**, 108-79-2; **5b**, 91606-60-9; **5c**, 91606-61-0; **6a**, 91606-62-1; $NCNH_2$, 420-04-2; NH_4OH, 1336-21-6; 1,3-cyclohexanedione, 504-02-9.

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X-ray Crystallographic Structure Determination and Carbon-13 Nuclear Magnetic Resonance Spectrum of 2,2,3,4,5,6,6-Heptachloro-3-(2,3,4,5,6-pentachlorophenoxy)-4-cyclohexenone. An Intermediate in the Synthesis of Nonachloro-3-phenoxyphenol

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Analysis of technical pentachlorophenol (PCP) shows the presence of numerous chlorinated byproducts which arise in the manufacturing process.[1] The potential health hazards from exposure to these chemicals is of some concern. It has been shown, for example, that nonachloro-3-phenoxyphenol, a manufacturing byproduct of PCP,[2] has a hemolytic potency at least a hundred times greater than

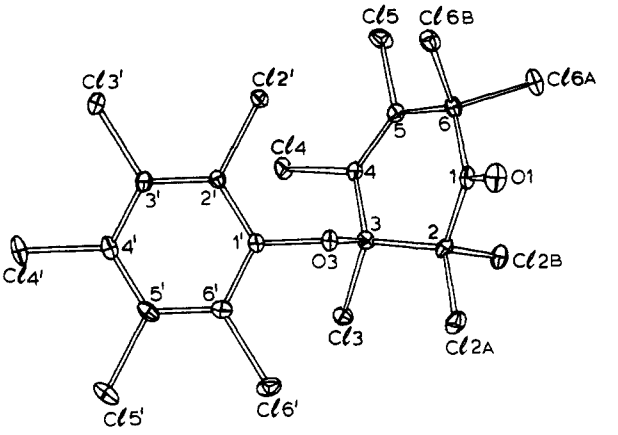

Figure 1. Conformational representation of 2,2,3,4,5,6,6-heptachloro-3-(2,3,4,5,6-pentachlorophenoxy)-4-cyclohexenone (I).

that of PCP.[3] In the synthesis of this contaminant[4] polychlorinated dienone and enone intermediates are produced which subsequently are reduced with sodium iodide to nonachloro-3-phenoxyphenol. Efforts to identify these intermediates depended chiefly on the use of ^{13}C NMR spectroscopy.[4] One of these intermediates, the title compound (I), (V in ref 4) whose structure was not reported, has since been determined by ^{13}C NMR and confirmed by X-ray crystallographic analysis. The results from these studies serve to support the assignments[4] made for the synthetic intermediates reported previously, as well as to provide the spectroscopic information to identify I, another potential contaminant in technical PCP.

Compound I has a molecular ion in the mass spectrum of m/z 596. It also has IR absorptions at 1771 cm^{-1} (carbonyl) and 1582 cm^{-1} (olefin) and a broad absorption around 1350 cm^{-1}. X-ray crystallographic analysis shows that like the crystal structure of the two independent rings of 2,3,4,5,6-pentachloro-4-(pentachlorophenoxy)-2,5-cyclohexadienone,[5] the phenoxy ring of I is planar with a root mean square deviation of the atoms from the plane of only 0.03 Å. The 4-cyclohexenone ring, however, has an envelope conformation with C2 displaced 0.68 Å from the plane formed by the remaining five atoms in the ring. The relative orientation of the two rings about the bonds linking them together is much different from that observed in cyclohexadienone structures. This is a consequence of having a puckered cyclohexenone ring in I rather than the planar cyclohexadienone ring (Figure 1). In the crystal structure of I the O3–C1′ bond is oriented transoid to the C3–Cl3 bond forming a torsion angle, Cl3–C3–O3–C1′, of −172.7°, while the corresponding angles, Cl1–C1–O1–C1′, in the two cyclohexadienone structures are −122.2° and 126.9°. Similarly, the C3–O3 bond is directed nearly perpendicular to the planar phenoxy ring forming torsion angles C3–O3–C1′–C2′ and C3–O3–C1′–C6′ or −92.4 and 94.6°. The corresponding cyclohexadienone torsion angles are C1–O1–C1′–C2 and C1–O1–C1′–C6′. In these two structures, the angles are −166.4° and −122.1° and 73.2° and 77.9°, showing the skewing away from the perpendicular orientation. These crystallographic results also confirm the spectroscopically assigned structure.

The carbon-13 NMR spectrum was obtained by dissolving I in deuteriochloroform. Unlike the enones re-

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