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FACILE CONVERSION OF THIOAMIDES INTO AMIDES

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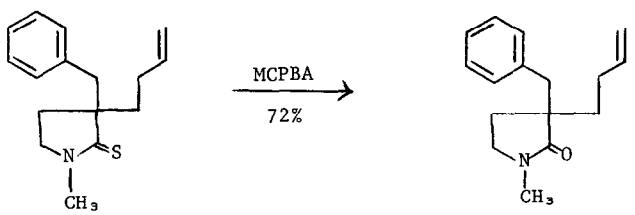
ABSTRACT Thioamides react with m-chloroperoxybenzoic acid (MCPBA) to give good yields of the corresponding amides.

Amides have been prepared from thioamides by using basic hydrogen peroxide,[2] nitrous acid,[3] ozone,[2a] potassium ferricyanide[2a] and selenium dioxide[4] although the last three reagents give poor conversions.[2a,4] Two-step procedures for this process include the use of thiophosgene[5] or trimethyloxonium tetrafluoroborate[6] followed by hydrolysis. In addition, thiopyridones yield pyridones when alkylated and then exposed to base.[7] Direct hydrolysis of thioamides gives amides among other products.[8]

In connection with a total synthesis of alkaloids, a new method for the conversion of thiolactams into lactams has been discovered (eq 1). This reaction is particularly rapid and

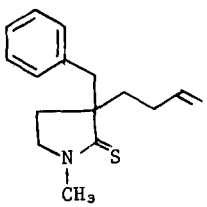
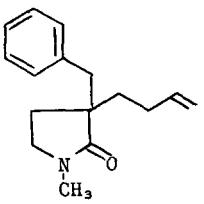
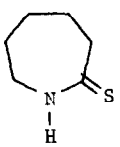
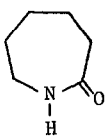
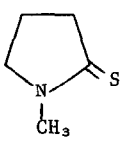
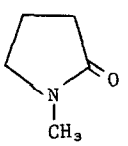
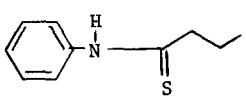
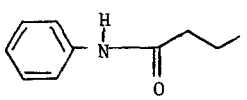
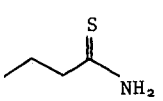
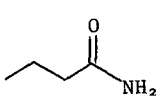
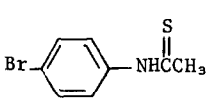
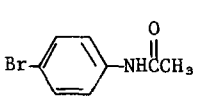
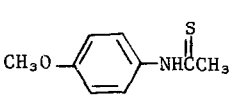
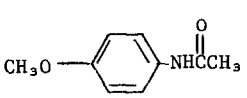


(1)

occurs to the total exclusion of olefin epoxidation as shown in eq 1. Furthermore, this reaction applies to thioamides as well as thiolactams and proceeds in high yields (see Table I). Primary, secondary and tertiary thioamides undergo this reaction with equal efficiency. For example, butyramide is produced in 76% yield, caprolactam in 89% yield and N-methylpyrrolidone in 82% yield. The reaction can be conducted at room temperature by very slow addition of MCPBA (exothermic) or at 0°C where less than 2 hr is needed for complete reaction.

The mechanism of this new reaction is not well understood. Nevertheless, it is clear that sulfur is produced as a by-product.[12] In fact, N-phenylthiobutyramide gives a 79% isolated yield of sulfur (small scale reaction) so that essentially one equivalent of sulfur is produced. The oxidation of thioketones with peroxyacids usually gives sulfines (e.g. eq 2).[13-17] An analogous intermediate may be involved here.[18]

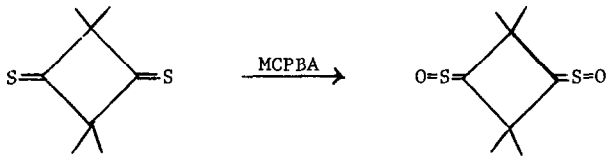
TABLE I. Amides from Thioamides[a]

THIOAMIDE	AMIDE	% YIELD[b]
		72
		89
		82 (85)[c]
		90
		76
		95
		98

[a]All reactions were conducted using 1.2-1.3 equivalents of MCPBA at room temperature except as indicated.

[b]Pure by GC/MS and NMR. All compounds are known except the first two.[19]

[c]Run for 2 hr at 0°C.



(2)

A typical experimental procedure is as follows:

N-Methylthiopyrrolidone (1.00 g, 8.69 mmol) was dissolved in 15 ml of dry methylene chloride under nitrogen[20] and 2.24 g (10.4 mmol) of MCPBA[21] was added in small portions over a 4 min period. The reaction is exothermic and becomes cloudy with the deposition of an off-white solid.[12] After 2 hr,[22] the reaction mixture was concentrated and the residue was dissolved in 30 ml of anhydrous ether. Ammonia was introduced for 5 min and the white precipitate which formed (presumably ammonium benzoate) was removed by filtration. The filtrate was concentrated to give 0.76 g (82%) of liquid (BP 93-100°C (2 mm)) pure by GC/MS and identical in all respects to authentic material.

Acknowledgement

We wish to acknowledge with great appreciation the assistance of Jim Spriggle with the Finnigan 4021-C GC/MS and the generous support provided for KSK by Bucknell University.

References and Notes

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11. K. A. Petrov and L. N. Andreev, Russ. Chem. Rev., 40, 505 (1971).
12. Sulfur identity was confirmed by mass spectral analysis.

13. Several non-enolizable thiones are converted cleanly into sulfines: B. Zwanenburg, A. Wagenaar, L. Thijs and J. Stratling, J. Chem. Soc., Perkin I, 73 (1973).

14. The same products can be obtained by ozonolysis of hindered thiones. Unhindered thioketones give ketones: B. Zwanenburg and W. A. J. Janssen, Synthesis, 617 (1973). Singlet oxygen converts di-tert-butyl thione into a mixture of the sulfine and the parent ketone: S. Tamagaki, R. Akatsuka, M. Nakamura and S. Kozuka, Tetrahedron Lett., 3665 (1979).

15. (a) The thiocarbonyl of hindered thiones, thionoesters and trithiocarbonates is converted into a carbonyl by 1,2-dibromo-1,1,2,2-tetrachloroethane in the presence of an organotellurium catalyst: S. V. Levy, C. A. Meerholz and D. H. R. Barton, Tetrahedron Lett., 1785 (1980).

(b) Carbohydrate trithiocarbonates are converted to the carbonyl analogues by either chlorine or potassium permanganate although the yields are low: B. S. Shasha, W. M. Doane, C. R. Russell and C. E. Rist, J. Org. Chem., 34, 1642 (1969).

16. MCPBA converts dithioesters into the corresponding S-oxides: G. E. Veenstra and B. Zwanenburg, Recueil, 95, 202 (1976).

17. Selenoketones are oxidized to ketones with MCPBA: T. G. Back, D. H. R. Barton, M. R. Britten-Kelly and F. S. Guziec, Jr., J. Chem. Soc., Chem. Comm., 539 (1975).

18. The sulfine may close to an oxathiirane which should lose sulfur. (The oxathiirane may be formed in a concerted reaction as well (our thanks to a referee for this suggestion).) Alternatively, sulfine could react with m-chlorobenzoic acid to give, after transfer of the benzoyl group, the observed amide plus a thioperoxyacid anion ($^{\ominus}$S-O-$\overset{O}{\overset{\|}{C}}$Ar) which should yield sulfur upon decomposition (our thanks to Professor F. A. Casey for this suggestion).

19. Spectral data for the new compounds are as follows: 2-benzyl-2-(3-butenyl)-1-methyl-2-pyrrolidone: IR (NaCl) cm^{-1} 3050, 2900, 1680, 1640, 1600, 1500, 1450, 1400, 1300, 1265, 1100, 1030, 990, 910, 745, 700; ^{1}H NMR ($CDCl_3$) δ 1.5-2.6 (m, 8H), 2.65 (s, 3H, NCH_3), 2.67-3.05 (m, 2H), 4.8-5.9, (m, 3H, $CH{=}CH_2$), 7.19 (s, 5H); GC/MS m/e (rel. abund.) 243(P, 13), 228(2), 214(1), 189(100), 152(13), 112(29), 98(12), 91(70), 77(4), 65(14), 55(12), 42(40); ^{13}C NMR ($CDCl_3$) δ 26.870, 28.766, 29.525, 37.380, 43.502, 46.373, 49.136, 114.524, 126.551, 127.960, 129.910, 137.711, 138.361, 177.313; 2-benzyl-2-(3-butenyl)-1-methyl-2-thiopyrrolidone: IR (NaCl) cm^{-1} 2870, 1640, 1600, 1580, 1530, 1500, 1450, 1400, 1300, 1250, 1175, 1020, 1005, 900, 850, 820, 700; ^{1}H NMR ($CDCl_3$) δ 1.4-2.7 (m, 8H), 3.05 (s, 3H, $N{-}CH_3$), 3.2 (m, 2H), 4.8-5.9 (m, 3H, $CH{=}CH_2$), 7.2 (s, 5H); GC/MS m/e (rel. abund.) 259(P, 10), 218(3), 205(80), 168(100), 128(45), 114(53), 91(67), 85(5), 77(6), 65(18), 55(18), 47(30).

20. Other systems were run in flasks open to the air with no effect on the yield of the conversion.

21. The MCPBA was obtained from the Aldrich Chemical Company. The purity was assumed to be 80%.

22. Other systems were allowed to react for 2-12 hours for convenience.

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