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mL of saturated aqueous NaCl. The solution was dried ($MgSO_4$), and the solvent was distilled at reduced pressure to give 137 mg (0.5 mmol, 74%) of carbamate **20** as a residue that solidified on standing to give an off-white solid. Mp: 124–125 °C. IR ($CDCl_3$): 3424, 1768, 1600 cm^{-1}. ^1H NMR: δ 6.23 (s, 1 H), 5.50 (br d, 1 H, $J \sim 6$ Hz), 3.50–3.77 (m, 1 H), 2.22 (s, 3 H), 1.1–2.1 (m, 10 H). ^{13}C NMR: δ 181.4, 150.6, 138.1, 102.0, 51.3, 32.5, 24.9, 24.3, 13.0. Anal. Calcd for $C_{11}H_{16}N_2O_2S_2$: C, 48.51; H, 5.92. Found: C, 49.20, 49.34; H, 6.14, 6.15. We note the high value for carbon in the analysis.

3-[[(4-Pentenyl)carbamoyl]oxy]-4-methylthiazole-2-(3*H*)-thione (7b). To a stirred solution of 2.14 g (21.6 mmol) of 5-hexenoic acid[11] in 250 mL of benzene were added 2.34 mL (32.1 mmol) of thionyl chloride and 0.1 mL of DMF. The solution was stirred at 25 °C for 18 h. Most of the benzene was distilled to give a light brown residual oil. The residue was dissolved in 250 mL of THF, and 1.11 g (20.4 mmol) of LiN_3 was added to the solution. The mixture was stirred at 25 °C for 18 h and then heated at reflux for 0.5 h. To the cooled solution was added 3.00 g (20.4 mmol) of thione **5** and 25 mg of DMAP. Stirring was continued for 18 h; the solution developed a faint blue color. Solvent was distilled at reduced pressure, and the residue was dissolved in 100 mL of CH_2Cl_2. The solution was extracted with 70 mL of 10% aqueous $KHSO_4$, 50 mL of saturated aqueous $NaHCO_3$, and 50 mL of saturated aqueous NaCl. The solution was dried ($MgSO_4$), and the solvent was distilled at reduced pressure to give a light blue oil as a residue. Pentane (25 mL) and ether (5 mL) were added to the residual oil, and the mixture was stirred vigorously; carbamate **7b** precipitated. Filtration gave 3.30 g (12.8 mmol, 67%) of **7b** as a light blue solid. Mp: 62–63 °C. IR ($CDCl_3$): 3439, 1768, 1644, 1598 cm^{-1}. ^1H NMR: δ 6.26 (s, 1 H), 5.7–6.0 (m, 2 H), 5.04 (m, 2 H), 3.33 and 3.30 (2 overlapping t, 2 H, $J \sim 6$ Hz), 2.22 (s, 3 H), 2.17 and 2.13 (2 overlapping t, 2 H, $J \sim 7$ Hz), 1.70 (m, 2 H). ^{13}C NMR: δ 181.3, 151.5, 138.1, 137.4, 115.6, 102.3, 41.5, 30.7, 28.6, 13.5. Anal. Calcd for $C_{10}H_{14}N_2O_2S_2$: C, 46.49; H, 5.46. Found: C, 47.05, 47.03; H, 5.38, 5.53. We note the high value for carbon in the analysis.

Reactions of TTOC Carbamate 7a. Carbamate **7a** (314 mg, 1.0 mmol), malonic acid (320 mg, 3 mmol), and the appropriate amount of Ph_2Se_2 (if desired) were placed in a quartz tube. The tube was sealed with a septum and flushed with N_2, and 10 mL of CH_3CN and the appropriate amount of *t*-BuSH (if desired) were added. The resulting solution was irradiated with a 6-W UV lamp (thiol reactions) or a 450-W high-pressure Hg lamp (Ph_2Se_2 reaction) at a distance of ca. 12 cm for 48 h (thiol) or 3.5 h (Ph_2Se_2). The resulting mixture was diluted with 10 mL of THF. Solid KOH (ca. 25 mg) and 0.3 mL of 50% aqueous NaOH were added, and the mixture was stirred for ca. 0.2 h. $MgSO_4$ was added, and the mixture was filtered through a 25 × 10 mm column containing basic alumina (THF elution). Hexadecane (75 μL) was added, and the yields of products in the resulting solution were determined by quantitative GC. The identities of **6a**, **11a**, and **12a** were determined by co-injection with authentic samples.[3b,d]

***N*-Butyl-2-[[(4-methylthiazol-2-yl)thio]methyl]pyrrolidine (13a)** was obtained in 80% yield from a reaction as a described above with 0.1 equiv of *t*-BuSH. The product mixture was subjected to high vacuum to remove **11a**; product **13a** remained as a light brown oil. ^1H NMR: δ 6.72 (s, 1 H), 3.48 (dd, 1 H, J = 3, 13 Hz), 3.14 (dd, 2 H, J = 8, 13 Hz), 2.40 (s, 3 H), 2.20 (m, 2 H), 1.74 (m, 4 H), 1.42 (m, 4 H), 0.93 (t, 3 H, J = 7 Hz). ^{13}C NMR: δ 164.7, 152.9, 112.8, 63.1, 54.5, 54.3, 39.3, 31.0, 30.3, 22.7, 20.8, 17.2, 14.1. Exact mass: calcd for $C_{13}H_{22}N_2S_2$ m/e 270.1224, found m/e 270.1201.

Reactions of TTOC Carbamates 7b and 20. The reactions were run by the same methods as described above for reactions of **7a** to the point of product isolation. The reaction was extracted with 25 mL of 10% aqueous $KHSO_4$. Excess 50% aqueous NaOH was added to the crude reaction mixtures in CH_2Cl_2. The mixtures were cooled to 0 °C, and benzoyl chloride (1.1–1.5 equiv) was added. After 12 h, the phases were separated, and the solvent was distilled from the organic phase. The residual oil was analyzed by quantitative GC; product yields were calculated from predetermined response factors or, for **13b**, with an estimated response factor. *N*-cyclohexylbenzamide (from **20**) was identified by comparison to an authentic sample.

***N*-Benzoyl-2-methylpyrrolidine (11b).** The residual product mixture from the reaction of **7b** in the presence of *t*-BuSH was purified by preparative TLC on silica gel with a 6:1 (v:v) mixture of CCl_4 and ethyl acetate as developing solvent. Amide **11b** was obtained as an oil in 78% yield. The identity of the product was confirmed by comparison to an authentic sample prepared from commercial 5-methyl-2-pyrrolidinone by $LiAlH_4$ reduction and treatment of the crude amine product with benzoyl chloride. ^1H NMR: δ 7.44 (m, 5 H), 3.9–4.4 (complex m, 1 H), 1.5–2.2 (complex m, 4 H), 1.37 (d, 3 H, J = 7 Hz). ^{13}C NMR: δ 169.9, 129.7, 128.3, 128.2, 127.2, 53.0, 49.7, 32.6, 24.7, 19.6.

***N*-Benzoyl-2-[(phenylseleno)methyl]pyrrolidine (12b).** The residual product mixture from the reaction of **7b** in the presence of Ph_2Se_2 was purified by chromatography as above. Product **12b** was obtained in 25% yield as an oil. ^{13}C NMR: δ 170.4, 137.1, 131.6, 130.2, 129.3, 128.3, 127.5, 126.6, 57.3, 50.9, 30.6, 30.5, 25.0. Exact mass: calcd for $C_{18}H_{19}NOSe$ m/e 345.0632, found m/e 345.0636.

2-[[(4-Methylthiazol-2-yl)thio]methyl]pyrrolidine. A pure sample of the benzamide **13b** was not obtained, but the product identity was confirmed for the benzyloxycarbonyl (CBZ) derivative. A reaction of TTOC **7b** conducted in the presence of 0.1 equiv of *t*-BuSH was worked up as described above. The crude product mixture was treated with benzyl chloroformate in a reaction similar to that described above for benzoyl chloride functionalization. Preparative TLC (silica gel, 10:1 hexanes–ethyl acetate development) gave the CBZ derivative in 20% yield. ^1H NMR: δ 7.35 (m, 5 H), 6.7 and 6.8 (2 br s, 1 H), 5.14 (s, 2 H), 4.19 (m, 1 H), 3.1–3.7 (complex m, 4 H), 2.37 (d, 3 H, J = 5 Hz), 1.91 (complex m, 4 H). ^{13}C NMR: δ 154.8, 153.0, 136.7, 130.9, 128.8, 128.5, 128.2, 128.0, 127.8, 113.7, 67.0, 66.8, 57.4, 56.6, 47.2, 38.0, 37.4, 30.3, 29.6, 23.8, 22.9, 17.2. Exact mass: calcd for $C_{17}H_{20}N_2OS_2$: m/e 348.0966. Found: m/e 348.0952.

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Supplementary Material Available: ^1H and ^{13}C NMR spectra of compounds **12b**, **13a**, and the CBZ derivative of 2-[[(4-methylthiazolyl-2-yl)thio]methyl]pyrrolidine (6 pages). Ordering information is given on any current masthead page.

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The Influence of Microwaves on the Rate of Reaction of Propan-1-ol with Ethanoic Acid

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Recent reports have suggested that the rates of some chemical reactions are accelerated by microwave irradiation. Rate enhancement factors between five and over one thousand, in comparison to classical methods of heating, have been recorded.[1-4] The majority of the reactions where rate enhancement has been observed were carried out in sealed polytetrafluoroethylene vessels. From the information published, it is not possible to separate the

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rate enhancement caused by the more rapid and uniform heating, and the consequent high pressures, from the claimed intrinsic effects of the microwave radiation, such as specific bond activation.

In a recent paper, in which accurate temperature measurement within the microwave-heated sample was carried out, Jahngen et al.[5] have shown that the increased rates of hydrolysis of adenosine triphosphate reported by Sun et al.[4] are due solely to enhanced temperature and are not in any way related to an intrinsic effect of the microwave irradiation. We have addressed the question of microwave rate enhancement by a different approach and have undertaken a detailed comparison of the rates of the acid-catalyzed esterification of propan-1-ol with ethanoic acid both in the presence and absence of microwaves, all other parameters being maintained the same. The reaction was chosen at it has been reported that esterifications are greatly accelerated by microwave irradiation at a frequency of 2.45 GHz.[6] Reactants were selected such that they, and the products of reaction, all had similar boiling points. Mole ratios of reactants were selected so as to give pseudo-first-order kinetics. Our conclusions are in agreement with those of Jahngen et al.[5] We have shown that, in a carefully controlled system, the rates of esterification of propan-1-ol with ethanoic acid are identical in the presence and absence of microwave radiation.

In order to achieve identical temperatures and pressures in both the thermally heated and microwave-irradiated systems, the reactions were performed at reflux temperature at atmospheric pressure. Because of the inherent difficulties in determining temperatures in the presence of strong microwave fields, the reflux temperature was not measured. In separate experiments, it was confirmed that both *reactants* absorbed microwaves. Propan-1-ol and ethanoic acid were found to be heated more rapidly than water by factors of 1.61 and 1.35, respectively. The experiments in the absence of microwaves were carried out using conventional reflux apparatus. The reactions in the presence of microwaves were carried out in a modified domestic 2.45 GHz, 650-W microwave oven.

The extent of reaction was monitored using gas–liquid chromatography to analyze samples withdrawn periodically from the reaction vessels. As is common practice for esterification, it was found necessary to add a catalyst to the reaction systems in order to attain reasonable rates of reaction. Two series of experiments were carried out using sulfuric acid for one and silica (Cab-O-Sil M-5) for the other.

Figure 1 shows the plot of conversion against time for both the sulfuric acid and Cab-O-Sil catalyzed systems using conventional thermal heating and using microwave irradiation. The results clearly show that, for this reaction, microwave radiation has no effect on the rate of reaction different from that of conventional heating.

The present reaction system was such that reactants and products were all strong absorbers of microwave radiation. Further experiments will be carried out in which not all chemical species present absorb microwave radiation and where activation of specific molecules might be more likely.

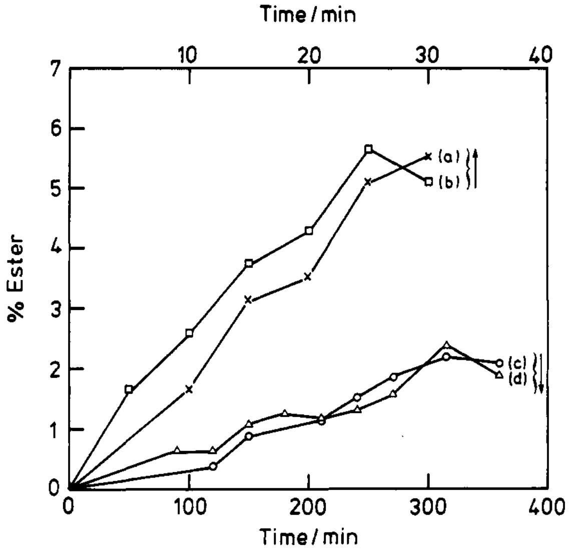

Figure 1. Concentration of ester as a function of time during heating under reflux at atmospheric pressure. (a) H_2SO_4 catalyst, conventional heating; (b) H_2SO_4 catalyst, microwave irradiation; (c) silica catalyst, conventional heating; (d) silica catalyst, microwave irradiation.

Experimental Section

Chemicals. Propan-1-ol and ethanoic acid were both AR grade reagents supplied by Koch-Light Ltd.

Sample Preparation. Propan-1-ol (0.4 mol, 24 g) and ethanoic acid (0.04 mol, 2.4 g) were mixed in a 50-mL conical flask. Reactions were catalyzed by the addition of either 5 μL of concentrated sulfuric acid or 0.2 g of silica (Cab-O-Sil M-5).

Microwave Heating. The mean power of the oven, a Toshiba Model ER-7720E/EW operating at a frequency of 2.45 GHz ± 10 MHz with a maximum power output of 650 W, could be varied over a range of eight preset levels by alteration of the duration of the microwave pulses. The reactants were contained in a Pyrex conical flask, situated in the oven, connected by a polytetrafluoroethylene tube which passed through a 10-mm hole in the back of the oven wall to an externally mounted reflux condenser. To avoid damage to the oven, which would result from prolonged operation under conditions of low load, a beaker containing 500 mL of water was also placed in the oven. The oven was operated at a power level sufficient to maintain a reasonable rate of reflux. From the difference betwen the heating rates of the 500-mL sample of water in the absence and presence of the reactants, it was estimated that microwave energy was absorbed by the reactants at a rate of 28 W.

Because of the nonhomogeneous nature of the power distribution within microwave ovens, care was taken to ensure that the flask containing the reactants and the beaker of water were always placed in the same position.

Since carrying out this work, it has come to our attention that the experimental arrangement used is similar to that which has been reported as being beneficial in the synthesis of organometallic compounds.[7]

Analysis. The extent of esterification was monitored by analyzing samples, withdrawn by means of a narrow bore polytetrafluoroethylene tube inserted into the reaction vessel through the external reflux condenser, by gas chromatography. Propan-1-ol, ethanoic acid, and propyl ethanoate were readily separated on a 1-m column of 8% FFAP (free fatty acid phase) supported on HCl-washed Chromosorb W. The column was operated at an initial temperature of 35 °C; it was then ramped at 2 °C per minute to 60 °C, and then at 10 °C per minute to 150 °C before being held at the final temperature for 5 min.

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