g) to remove a colored impurity. Elution with ether gave the ester **20** (8.26 g, 86%) as an oil which crystallized on seeding. After trituration with hexane the solid was recrystallized from ether–hexane to give material with the following: mp 96–96.5 °C; UV (MeOH) 256, 315 nm (ε 9550, 14800); IR ($CHCl_3$) 1756, 1740, 1636, 1603, 1582 cm^{-1}; NMR ($CDCl_3$) δ 2.39 (q, 2 H, J = 7.3 Hz, CH_2), 3.50 (t, 1 H, J = 7.3 Hz, CH), 3.73 (s, 6 H, OCH_3), 4.54 (t, 2 H, J = 7.3 Hz, NCH_2), 7.59 (m, 5 H, C_6H_5).

Anal. Calcd for $C_{18}H_{17}Br_2NO_5$: C, 44.38; H, 3.52; Br, 32.81; N, 2.88. Found: C, 44.63; H, 3.54; Br, 32.95; N, 2.87.

Methyl 5-Benzoyl-7-bromo-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]pyrrole-1-carboxylate (21a) and Dimethyl 5-Benzoyl-7-bromo-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]pyrrole-1,1-dicarboxylate (21b). Sodium hydride in mineral oil (50%, 0.030 g, 0.0006 mol) was added all at once to a stirred solution of the diester **20** (0.0005 mol) in anhydrous DMF (2 mL) maintained in a nitrogen atmosphere. After 20 min the solution was slowly heated in an oil bath to 75 °C, and after 1.5 h at this temperature, the solution was cooled and poured into ether. The ethereal solution was washed with water, dried, and evaporated in vacuo, leaving an oil (0.235 g) which was filtered through a short column of Florisil, using ether as the solvent. The material obtained in this way was subjected to high-pressure liquid chromatography on a Lichrosorb column (50 cm × 9.5 mm) with ethyl acetate–hexane (15:85) as the developing solvent, at a flow rate of 8 mL/min at 1200 psig. The mono- and diesters were collected at retention times of 17.5 and 20 min, respectively. The monoester **21a** (0.025 g, 14%) was obtained as an oil which crystallized on standing. After crystallization from methanol, **21a** had the following: mp 88–89 °C; UV (MeOH) 249, 315 nm (ε 7600, 15200); IR (KBr) 1730, 1625, 1575 cm^{-1}; NMR ($CDCl_3$) δ 2.81 (m, 2 H, 2-CH_2), 3.77 (s, 3 H, OCH_3), 3.98 (dd, 1 H, J_{AX} = J_{BX} = 7 Hz, H-1), 4.48 (m, 2 H, 3-CH_2), 6.73 (s, 1 H, H-6), 7.48 (m, 3 H, H-3′,4′,5′), 7.74 (m, 2 H, H-2′,6′).

Anal. Calcd for $C_{16}H_{14}BrNO_3$: C, 55.19; H, 4.05; Br, 22.95; N, 4.02. Found: C, 55.13; H, 4.10; Br, 22.71; N, 3.92.

The diester **21b** was also obtained as an oil (0.164 g, 81%) which crystallized on trituration with ethyl acetate. Recrystallization of this solid from hexane gave material with the following: mp 109–109.5 °C; UV (MeOH) 254, 314 nm (ε 8120, 15500); IR ($CHCl_3$) 1743, 1631, 1604, 1581 cm^{-1}; NMR ($CDCl_3$) δ 3.16 (t, 2 H, J = 6.6 Hz, 2-CH_2), 3.82 (s, 6 H, OCH_3), 4.52 (t, 2 H, J = 6.6 Hz, 3-CH_2), 6.82 (s, 1 H, H-6), 7.48 (m, 3 H, H-3′,4′,5′), 7.78 (m, 2 H, H-2′,6′).

Anal. Calcd for $C_{18}H_{16}BrNO_5$: C, 53.22; H, 2.97; Br, 19.69; N, 3.45. Found: C, 53.32; H, 3.93; Br, 19.43; N, 3.41.

Synthesis of 5-Benzoyl-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]-pyrrole-1-carboxylic Acid (15a) from Dibromo Diester 20 without Purification of Intermediates. Sodium hydride in mineral oil (0.275 g, 0.0055 mol) was added to a stirred solution of compound **20** (2.44 g, 0.005 mol) in dry DMF (20 mL) maintained in an argon atmosphere. After 25 min the solution was placed in an oil bath at 74 °C where the reaction was maintained for 2.75 h. The reaction was worked up in the manner described above to give a mixture (2.04 g) of **21a** and **21b**. A solution of this mixture, in methanol (100 mL) and water (10 mL) containing sodium hydroxide (0.40 g, 0.010 mol), was heated at reflux temperature in an argon atmosphere for 2 h. The solvent was removed in vacuo and the residue was taken up in 50% aqueous methanol (125 mL) to which magnesium oxide (1.0 g) and 5% palladium on charcoal (0.40 g) were added. The mixture was hydrogenated for 2 h at room temperature and atmospheric pressure, the mixture was filtered through Celite, and the filter cake was washed with methanol and water. The filtrate was then worked up as described previously to give a solid (1.19 g) which was homogeneous by TLC. Recrystallization of this material from dichloromethane–hexane gave the product in two crops, mp 154–154.5 °C (0.699 g) and 149–151.5 °C (0.170 g). Evaporation of the mother liquor, solution of the residue in ethyl acetate, treatment of the solution with charcoal, removal of the solvent, and crystallization of the residue from methanol water gave a further quantity (0.038 g) of the carboxylic acid, mp 148–150 °C. The total yield was 71% (0.907 g) on the basis of the starting uncyclized diester **20**. The carboxylic acid prepared in this manner was spectroscopically indistinguishable from material prepared by the sulfinate displacement route.

Acknowledgment. We thank Mr. H. Carpio for providing us with an authentic sample of compound **21a** as well as the analytical and spectroscopic data corresponding thereto.

Registry No. **4**, 5617-70-9; **7**, 39095-38-0; **8a**, 80964-97-2; **8b**, 80964-98-3; **9a**, 53391-61-0; **9b**, 80964-99-4; **10a**, 80965-00-0; **10b**, 80965-01-1; **10c**, 80965-02-2; **11**, 80965-03-3; **12**, 80965-04-4; **13a**, 80965-05-5; **13b**, 80965-06-6; **13c**, 80965-07-7; **14a**, 80965-08-8; **14b**, 80965-09-9; **14c**, 80965-10-2; **14e**, 80965-11-3; **15a**, 66635-83-4; **15b**, 66635-90-3; **15c**, 80965-12-4; **16a**, 80965-13-5; **16b**, 80965-14-6; **16c**,-Na, 80965-15-7; **17a**, 80965-16-8; **17b**, 80975-60-6; **18a**, 7697-46-3; **18b**, 50372-61-7; **19**, 80965-17-9; **20**, 80965-18-0; **21a**, 80965-19-1; **21b**, 80965-20-4; dimethyl sulfide, 75-18-3; *N*-chlorosuccinimide, 128-09-6; pyrrole, 109-97-7.

Synthesis of Azaspiro Ketones via Ring Contraction of Heterocyclic Enamino Esters

Pierre Duhamel* and Mitsuharu Kotera[1]

Laboratoire de Chimie Organique, Faculté des Sciences et des Techniques de Rouen, 76130 Mont Saint Aignan, France

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Upon treatment by bromine followed by water–triethylamine, six- and seven-membered heterocyclic enamino esters **4a,b** underwent easily ring contraction, giving five- and six-membered azacyclic aldehydes **5a,b**, respectively. The resulted aldehydes **5** were converted to azaspiro ketones **8a,b** in three steps. Starting 3-substituted seven-membered heterocyclic enamino ester **4a** was synthesized by desulfurization of ketene acetal **12** with Raney nickel. 3-(Methoxycarbonyl)-*N*-methylcaprolactam, prepared from *N*-methylcaprolactam [LDA, $CO(OMe)_2$, −70 °C, Et_2O], was converted to the corresponding thio lactam by treatment with P_2S_5 in CS_2, which upon reaction with CH_3I followed by deprotonation with NEt_3 afforded the ketene acetal **12**.

In a previous paper,[2] we reported a method of obtaining spiro heterocycles from bicyclic enamines. Thus the bicyclic enamine **1a** reacted with bromine and aqueous sodium hydroxide to give **2a**. However, attempts to bring

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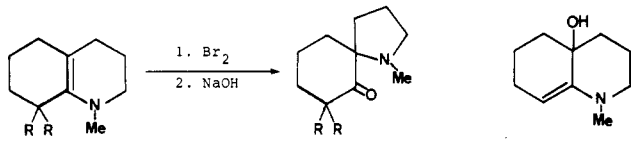


1a R = Me
1b R = H

2aR = Me
2bR = H

3

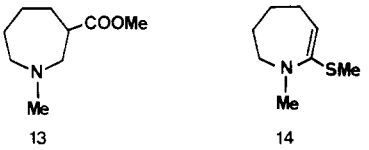
about the same reaction with the enamine **1b** were unsatisfactory, since treatment of **1b** under identical conditions provided the hydroxy enamine **3** as the major product together with minor amounts of ketone **2b**.

We have investigated an alternative synthetic route to these compounds and now present results which show that 3-functionalyzed cyclic enamines **4a,b** may be transformed into spiro heterocyclic compounds **8a,b** as shown in Scheme I.

To obtain the enamine **4a**, we have developed the route shown in Scheme II. Acylation of *N*-methylcaprolactam with LDA and $(MeO)_2CO$ provided the ester **9**. Conversion to the thio amide followed by S-alkylation, deprotonation, and desulfurization gave **4a** in an overall yield of 14% from *N*-methylcaprolactam.

In the desulfurization step, the enamino ester **4a** obtained was more than 95% pure, contaminated only by the whole reduction product **13**. This overall procedure, **9** to **4a**, represents a partial and selective reduction of an amide functional group in the presence of an ester function.[3]

Attempted condensation of **14** with ethyl chloroformate according to the described synthesis of five-membered homologues[4] resulted in a disappointingly low yield of the enamino ester.



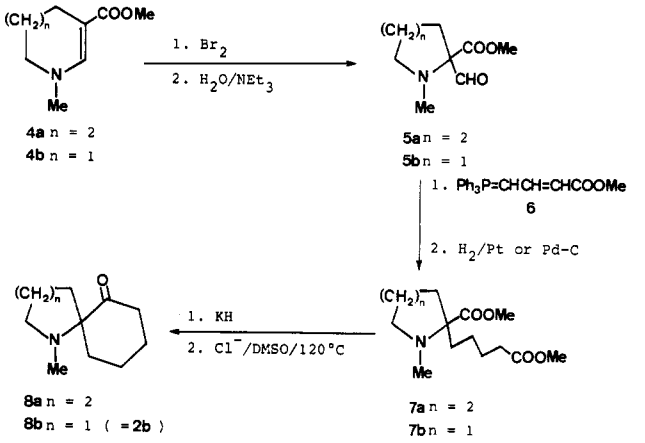
13 14

The key step of Scheme I involves the formation of aldehydes **5a,b** by ring contraction of heterocyclic enamines **4a,b**. As the heterocyclic enamines **4** can be prepared from lactam derivatives which are easily accessible from cyclanones (see Scheme II), this overall process represents formally a transformation of carbocycles to azacycles of same size.

Upon treatment by bromine followed by water–triethylamine,[5] six- and seven-membered cyclic enamines **4a,b** easily underwent ring contraction, giving the rearranged heterocyclic aldehydes **5a,b** in 89–92% yield.

The diesters **7a,b** were obtained from aldehydes **5a,b** upon treatment by the Wittig reagent **6**,[6] followed by catalytic hydrogenation.

Scheme I



4a n = 2
4b n = 1

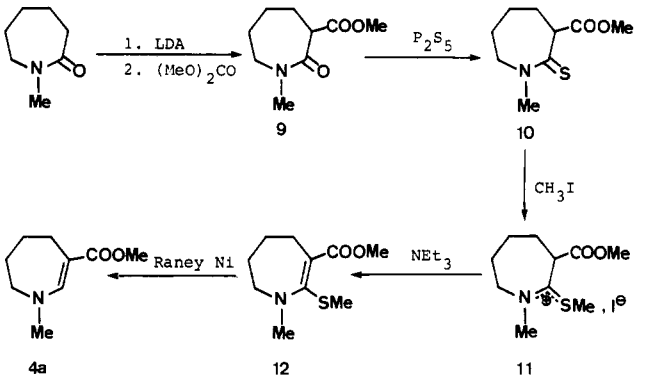
5a n = 2
5b n = 1

6

8a n = 2
8b n = 1 (=2b)

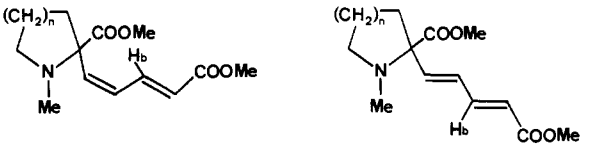
7a n = 2
7b n = 1

Scheme II



9 10 4a 12 11

The Wittig reactions with **5a,b** gave a mixture of two isomeric unsaturated diesters, **15a,b** and **16a,b**.[7]



15a n = 2
15b n = 1

16a n = 2
16b n = 1

Each of the diesters was isolated by column chromatography, and their structures were established from ^1H NMR data [for H(b): **15a**, δ 8.06; **16a**, 7.29; **15b**, 7.78; **16b**, 7.40]. The formation of isomer mixture presented no difficulty, since both yielded the same saturated diesters **7a,b** in the next step.

The spirocyclic system was completed by Dieckmann cyclization of diesters **7a,b** to ketones **8a,b** in 56–73% yield. The ketone **8b** was identified with **2b**.[2]

The structures of compounds **5a,b** and **8a,b** were established from ^1H and ^{13}C NMR data. ^{13}C NMR data are presented in Table I in the supplementary material.

(1) Taken, in part, from the third cycle thesis of M.K., University of Rouen, Oct 1980.

(2) Duhamel, L.; Poirier, J. M.; Granger, P. *J. Org. Chem.* **1979**, *44*, 3576.

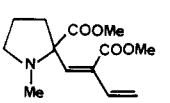
(3) After the first submission of this paper, an analogous conversion of amides to enamines by $NaBH_4$ with modest yields was reported: Sindberg, R. J.; Walters, C. P.; Bloom, J. D. *J. Org. Chem.* **1981**, *46*, 3730.

(4) (a) Gompper, R.; Elser, W. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 780. (b) Gompper, R.; Elser, W. *Justus Liebigs Ann. Chem.* **1969**, *785*, 64, 73.

(5) The rearrangement of α-bromo iminium salts by basic treatment was reported. See references cited in ref 2. For this ring contraction we used a slight excess of water in triethylamine. This improved method avoids the β rupture of the aldehyde function.

(6) The Wittig reagents must not be prepared in situ since the presence of NaOMe affords β rupture of the aldehyde function.

(7) In the case of the Wittig reaction with **5b**, the formation of another unsaturated diester, **17**, was observed. This byproduct was due to the



17

impurety of the Wittig reagent **6** and was eventually eliminated by previous purification of the reagent. An analogous rearrangement was reported: Font, J.; March, P. *Tetrahedron Lett.* **1978**, 360.

Experimental Section

General Procedure. All boiling points and melting points are uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer 337 spectrophotometer. ^1H NMR spectra were taken on a Perkin-Elmer R-12. The chemical shifts (δ values) are given in parts per million relative to Me_4Si as an internal standard in $CDCl_3$ solutions. Gas chromatography mass spectra were obtained on a JEOL D-100 instrument, with GC data determined on a Girdel 75-E 1 gas chromatograph with a 5% SE-30 column.

3-(Methoxycarbonyl)-*N*-methylcaprolactam (9). A solution of *N*-methylcaprolactam (53.0 g, 0.42 mol) in anhydrous ether (50 mL) was added to a solution of LDA (0.83 mol) in ether (500 mL) and hexane (600 mL) at −70 °C, and the reaction mixture was stirred at this temperature under N_2 for 15 min. Dimethyl carbonate (37.6 g, 0.42 mol) was added, and the mixture was allowed to warm to room temperature. The reaction mixture was added to 5 N HCl (200 mL) at 0 °C, extracted with $CHCl_3$, and dried over 4-Å molecular sieves. Removal of the solvent in vacuo gave the crude product which was recrystallized from ether: yield 45.4 g (59%); mp 66 °C; IR (Nujol) 1740, 1645 cm^{-1}; NMR δ 3.00 (s, CH_3, 3 H), 3.75 (s, CH_3, 3 H). See the paragraph at the end of the paper about supplementary material.

3-(Methoxycarbonyl)-1-methylhexahydroazepine-2-thione (10). A solution of **9** (18.5 g, 0.10 mol) was refluxed for 18 h in CS_2 (100 mL) with P_2S_5 (22.2 g, 0.10 mol) after the general procedure of Gompper and Elser.[4a] After decantation of the solvent, addition of water (300 mL) and decantation were repeated until the decomposition of residue was complete.

The combined aqueous solution was extracted several times with $CHCl_3$, and the combined extracts were washed with brine and dried over 4-Å molecular sieves. Removal of the solvent in vacuo gave a yellow viscous oil which was distilled to afford 12.1 g (60%) of **10**: bp 128 °C (0.05 mm); IR (neat) 1740 cm^{-1}; NMR δ 3.50 (s, CH_3, 3 H), 3.71 (s, CH_3, 3 H). See the paragraph at the end of the paper about supplementary material.

Methylation of Thio Lactam Ester 10. To a solution of **10** (12.1 g, 0.060 mol) in anhydrous ether (100 mL) was added methyl iodide (9.4 g, 0.066 mol) rapidly. The mixture was stirred at room temperature for 5 days, and the yellow crystalline paste was filtered and dried in vacuo (8.5 g, 41%). Recovered starting material was recycled to give 6.0 g (29%) of the iodide **11**. This product was directly used for the next step without further purification.

6-(Methoxycarbonyl)-1-methyl-7-(methylthio)-2,3,4,5-tetrahydro-1*H*-azepine (12). To a suspension of the iodide **11** (30.3 g, 0.088 mol) in anhydrous ether (50 mL) was added triethylamine (9.8 g, 0.097 mol) rapidly. The mixture was stirred at room temperature for 2 h. The resulting white precipitate was removed by filtration and washed with triethylamine. From the combined filtrate and washing was removed the solvent in vacuo to afford a yellow oil which was used for the next step without further purification. **12**: yield 16.5 g (87%); IR (neat) 1690 cm^{-1}; NMR δ 2.20 (s, CH_3, 3 H), 3.04 (s, CH_3, 3 H), 3.68 (s, CH_3, 3 H). See the paragraph at the end of the paper about supplementary material.

Desulfurization of Esters 12. To about 120 g of Raney nickel[8] previously refluxed in acetone (200 mL) for 2 h was added **12** (15.1 g, 70.2 mmol) rapidly, and the mixture was refluxed for 1 h. The catalyst was filtered, and the solvent was removed in vacuo.

The crude product was chromatographed over SiO_2 gel, and elution with ether–petroleum ether (1:4) yielded **4a**: 8.0 g (67%); IR (neat) 1685, 1620 cm^{-1}; NMR δ 1.63–1.88 (m, CH_2, 4 H), 2.35–2.65 (m, CH_2, 2 H), 2.97 (s, CH_3, 3 H), 3.08–3.33 (m, CH_2, 2 H), 3.62 (s, CH_3, 3 H), 7.40 (s, vinylic H, 1 H). Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.28. Found: C, 63.60; H, 9.01; N, 8.10. See the paragraph at the end of the paper about supplementary material.

Ring Contraction of the Heterocyclic Enamines 4a,b.[5] To a solution of enamine **4a** (7.75 g, 45.9 mmol) in dry ether (180 mL) was added at −70 °C 7.36 g (46.0 mmol) of bromine in 100 mL of dry cold (about −60 °C) ether. After the addition was complete, the resulting yellow suspension of iminium salt was stirred at this temperature for 30 min, and water (1.62 g, 90.0 mmol) was added with the excess quantity (18.0 g, 0.18 mol) of triethylamine. The reaction mixture was allowed to warm to room temperature, stirred for 2 h, and filtered. The triethylamine hydrobromide was washed with 20 mL of triethylamine, and the filtrate and the washing were combined and evaporated at 40 °C to give **5a**: 7.81 g (92%); bp 114 °C (13 mmHg); IR (neat) 1747, 1730 cm^{-1}; NMR δ 1.4–2.0 (m, CH_2, 6 H), 2.51 (s, CH_3, 3 H), 2.8 (m, CH_2, 2 H), 3.77 (s, CH_3, 3 H), 9.56 (s, CHO, 1 H).

The same procedure was followed with enamine **4b**[9] (22.3 g, 0.144 mol), bromine (25.3 g, 0.158 mol), water (3.9 g, 0.217 mol), and triethylamine (58.2 g, 0.576 mol) to afford **5b**: 22.0 g (89%); bp 100 °C (21 mmHg); IR (neat) 1730 cm^{-1}; NMR δ 1.7–2.5 (m, CH_2, 4 H), 2.52 (s, CH_3, 3 H), 2.8–3.2 (m, CH_2, 2 H), 3.74 (s, CH_3, 3 H), 9.35 (s, CHO, 1 H). See the paragraph at the end of the paper about supplementary material.

Witting Reaction of Aldehydes 5a,b. Wittig reagent **6** was prepared according to Howe[10] and recrystallized from ethyl acetate.

A mixture of aldehyde **5a** (6.76 g, 36.5 mmol), ylide **6** (15.0 g, 41.6 mmol), and toluene (150 mL) was heated to reflux for 20 h. The toluene was evaporated at 40 °C, and the residue was dissolved in 20 mL of benzene. Hexane (200 mL) was added to this solution, and the solution was decanted. The decantation was repeated five times, and the combined decanted solution was evaporated at 40 °C. The resulting oil was chromatographed over SiO_2 gel, and elution with ether-petroleum ether (1:4) furnished **15a** and **16a** (2:7), 8.2 g (74%).

A mixture of aldehyde **5b** (3.4 g, 20 mmol), ylide **6** (8.0 g, 22 mmol), and benzene (100 mL) was heated to reflux for 3 h. The reaction mixture was treated by the above procedure to afford **15b** and **16b** (1:2), 3.4 g (67%). See the paragraph at the end of the paper about supplementary material.

Hydrogenation of Unsaturated Diesters 15a,b and 16a,b. A mixture of 0.4 g of PtO_2 in 100 mL of methanol was saturated with hydrogen. A solution of diesters **15a** and **16a** (7.81 g, 29.3 mmol) in 40 mL of methanol was added and the mixture hydrogenated at room temperature and atmospheric pressure. Upon cessation of hydrogen uptake (about 2.5 h), the catalyst was filtered and washed with methanol. The combined filtrate and washing were evaporated at 40 °C. The residue was chromatographed over SiO_2 gel, and elution with ether–pentane (1:2) furnished **7a**: 5.64 g (71%); IR (neat) 1740 cm^{-1}; NMR δ 2.40 (s, CH_3, 3 H), 3.67 (s, CH_3, 3 H), 3.69 (s, CH_3, 3 H); mass spectrum, m/e 271 (M^+). Anal. Calcd for $C_{14}H_{25}NO_4$: C, 61.97; H, 9.29; N, 5.16. Found: C, 61.67; H, 9.15; N, 5.21.

Hydrogenation of 10.2 g (40.3 mmol) of **15b** and **16b** with 2 g of 10% palladium/charcoal in methanol (200 mL) under the above conditions and workup yielded **7b**: 8.1 g, 79%); bp 120 °C (0.01 mmHg); IR (neat) 1740, 1730 cm^{-1}; NMR δ 2.26 (s, CH_3, 3 H), 3.64 (s, CH_3, 6 H); mass spectrum, m/e 257 (M^+). Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.50; H, 8.97; N, 5.56. See the paragraph at the end of the paper about supplementary material.

Dieckmann Cyclization of Diesters 7a,b. To a suspension of 1.3 g (8.6 mmol) of potassium hydride (23% oil dispersion) in dioxane (50 mL), which has been distilled from benzophenone ketyl, was added to a solution of 1.1 g (4.06 mmol) of diester **7a** in dioxane (5 mL) at room temperature rather rapidly. The mixture was heated to reflux for 6 h and treated with 0.5 N HCl (50 mL) at 15 °C. This aqueous solution was extracted with ether to eliminate the oil and evaporated at 40 °C. The resulting wet residue was dissolved in Me_2SO (40 mL) and the solution heated at 115–120 °C for 3 h.[11] The reaction mixture was treated with 30% NaOH (100 mL) and extracted with ether (6 × 30 mL). The combined extracts were washed with 20% NaOH (5 × 10 mL), dried over molecular sieves (4 Å), and evaporated. The residue was once more treated with 20% NaOH (50 mL) extracted with ether (8 × 30 mL) dried, and evaporated to afford **8a**: 0.41 g (56%); bp 130 °C (13 mmHg); IR (neat) 1717 cm^{-1}; NMR δ 1.3–2.0

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(9) Wenkert, E.; Dave, K. G.; Haglid, F.; Lewis, R. G.; Oishi, T.; Stevens, R. V.; Terashima, M. *J. Org. Chem.* **1968**, *33*, 747.

(10) Howe, R. K. *J. Am. Chem. Soc.* **1971**, *93*, 3457.

(11) Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, 957.

(m, CH_2, 12 H), 2.3 (m, CH_2, 2 H), 2.33 (s, CH_3, 3 H), 2.7 (m, CH_2, 2 H); mass spectrum, m/e 181 (M^+). Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.84; H, 10.48; N, 7.60.

The analogous procedure was followed for the preparation of **8b**. To a suspension of 0.45 g (2.5 mmol) of potassium hydride (23% oil dispersion) in THF (5 mL) was added a solution of 0.26 g (1.0 mmol) of diester **7b** in THF (2 mL) at room temperature. The mixture was refluxed for 20 h and treated with 1.5 N HCl (3.5 mL). The aqueous solution was extracted with ether to eliminate the oil, 0.7 g (4.08 mmol) of baryum hydroxide was added to the aqueous solution, and the mixture was heated to reflux for 20 h, filtered, extracted with $CHCl_3$ (5 × 10 mL), dried over molecular sieves (4 Å), and evaporated to afford **8b**: yield 122 mg (73%); bp 110 °C (13 mmHg); IR (neat) 1710 cm^{-1}; NMR δ 1.6–2.2 (m, CH_2, 10 H), 2.4 (m, CH_2, 2 H), 2.45 (s, CH_3, 3 H), 3.0 (m, CH_2, 2 H); mass spectrum, m/e 167 (M^+).[2] Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.95; H, 10.10; N, 8.29. See the paragraph at the end of the paper about supplementary material.

Registry No. **4a**, 80754-31-0; **4b**, 3284-32-0; **5a**, 80754-32-1; **5b**, 80754-33-2; **7a**, 80754-34-3; **7b**, 80754-35-4; **8a**, 80754-36-5; **8b**, 71032-69-4; **9**, 80754-37-6; **10**, 80754-38-7; **11**, 80754-39-8; **12**, 80754-40-1; **15a**, 80754-41-2; **15b**, 80754-42-3; **16a**, 80754-43-4; **16b**, 80754-44-5; *N*-methyl caprolactam, 2556-73-2.

Supplementary Material Available: IR data for **4a**, **5**, **7–10**, **12**, **15**, and **16**, ^1H NMR data for **7**, **9**, **10**, **12**, **15**, and **16**, and ^{13}C NMR data for **5** and **8** (Table I) (5 pages). Ordering information is given on any current masthead page.

New Rearrangements of Arylhydrazones in Polyphosphoric Acid: Extension to the Thiophene and Indole Series. 5

Raffaello Fusco and Franco Sannicolò*

Centro CNR per lo Studio sulla Sintesi e Stereochimica di Speciali Sistemi Organici, Università degli Studi di Milano, Istituto di Chimica Industriale, 20133 Milano, Italy

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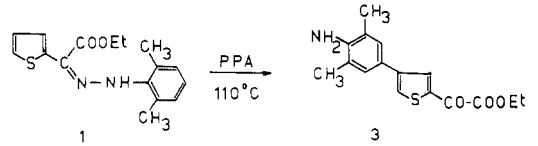
The behavior toward polyphosphoric acid of arylhydrazones of a few heterocyclic carbonyl compounds of the thiophene and indole series is described. The phenylhydrazone and 2,6-dimethylphenylhydrazone of ethyl α-thienylglyoxylate gave ethyl 4- and 5-(4-aminoaryl)-α-thienylglyoxylate, arising from two different sigmatropic rearrangements. The *N*,3,5-trimethylphenylhydrazone of 2-methylindole-3-carboxaldehyde afforded the 4-[4-(methylamino)-2,6-dimethylphenyl]-2-methylindole-3-carboxaldehyde resulting from a [5,5] sigmatropic rearrangement, while the 2,6-dimethylphenylhydrazone of the same carbonyl compound unexpectedly gave the 3-(4-amino-3,5-dimethylphenyl)-2-methylindole-3-carboxaldehyde generated through a [3,5] sigmatropic reaction. Chemical evidences are given for the assigned structures.

This report extends to some thiophene and indole substrates the previously studied polyphosphoric acid (PPA) induced rearrangements of arylhydrazones of aromatic carbonyl compounds.[1]

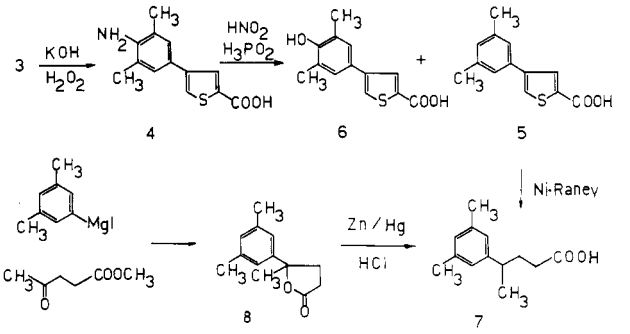
The thiophene derivatives, the 2,6-dimethylphenylhydrazone (**1**), and the phenylhydrazone (**2**) of ethyl α-thienylglyoxylate were treated with PPA under the experimental conditions usually employed for this type of reaction.

The workup of the reaction mixture for the former compound **1** gave an approximately 40% yield of a product assigned the structure of ethyl 4-(4-amino-3,5-dimethylphenyl)-2-thienylglyoxylate (**3**),[2] based on analytical and spectroscopic data. This structure assignment was confirmed chemically as shown in Scheme I.

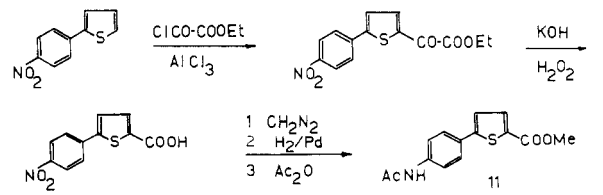


1 3

Scheme I



Scheme II



Treatment of the phenylhydrazone of α-thienylglyoxylic ester **2** with PPA gave an approximately 35% yield of a mixture of two isomeric rearrangement products, in an approximately 7:3 ratio. While these could not be separated by column chromatography, they were easily seen in HPLC and in the NMR spectrum.

(1) (a) Fusco, R.; Sannicolò, F. *Tetrahedron Lett.* **1977**, 3163. (b) *Ibid.* **1978**, 1233. (c) Fusco, R.; Sannicolò, F. *Tetrahedron Rep.* **1980**, *No. 72* 161. (d) Fusco, R.; Sannicolò, F. *J. Org. Chem.* **1981**, *46*, 83. (e) *Ibid.* **1981**, *46*, 90.

(2) The NMR spectrum showed the presence of a small percentage of an isomeric compound, which, however, did not appear in thin-layer chromatography and which could not be separated by column chromatography. This isomer was lost in the successive chemical reactions. The compound was probably the 2,5-disubstituted thiophene derivative (see discussion for compound **2**).

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