Synthesis of 1-(2-Thienyl)-2-alkanones

James D. Belcher, Jr., David S. Hunter, Donald G. Hutson, Robert L. McBroom, and Eldon H. Sund[1]
Department of Chemistry, Midwestern University, Wichita Falls, Tex. 76308

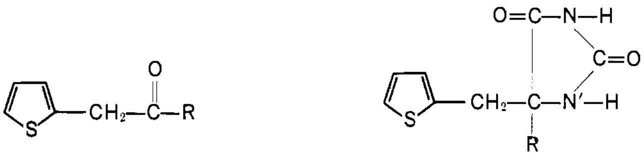
Eight 1-(2-thienyl)-2-alkanones were prepared by the Darzens glycidic ester condensation of 2-thiophenecarboxaldehyde and the requisite ethyl 2-bromoester with subsequent saponification and decarboxylation. Physical properties were determined, and hydantoin derivatives of these ketones were prepared.

Recently, we had need of some 1-(2-thienyl)-2-alkanones. A careful perusal of the literature revealed that only one of the required ketones had been prepared; therefore, physical properties as well as derivatives of these ketones were lacking. Consequently, as the ketones were prepared, some of their physical constants were determined, and a hydantoin derivative was prepared.

The ketones were prepared by the Darzens glycidic ester condensation of 2-thiophenecarboxaldehyde and the requisite ethyl 2-bromoester similar to that described by Ruzicka and Ehmann (*3*), with subsequent saponification and decarboxylation. Hydantoin derivatives were prepared by the method of Henze and Speer (*2*).

Table I lists the yields of the 1-(2-thienyl)-2-alkanone ketones, as well as some of their physical constants and mp of the hydantoin derivatives.

Table I. 1-(2-Thienyl)-2-alkanones[a] and 5-Alkyl-5-(2-thenyl)hydantoins[b]



R	Yield, %	Bp, °C/mm	$n^{20}D$	d^{20}_4	Mp, °C
CH_3	71	66/1.3[c]	1.5347[d]	1.129[e]	198–9
C_2H_5	61	58/0.2	1.5270	1.099	228.5–9.5
n-C_3H_7	69	83/0.9	1.5198	1.075	217–8
iso-C_3H_7	60	90/2.2	1.5187	1.081	238.5–40.5
n-C_4H_9	41	74/0.3	1.5143	1.046	191.5–3.5
iso-C_4H_9	58	80/0.4	1.5118	1.047	228.5–30.5
sec-C_4H_9	82	76/0.3	1.5111	1.074	219.5–20.5
n-C_5H_{11}	66	84/0.2	1.5094	1.029	182.5–4.5

[a] Elemental analyses (C, H, and N) in agreement with theoretical values have been obtained and submitted for review. [b] Elemental analyses (N) in agreement with theoretical values have been obtained and submitted for review. [c] Reported by 105–6/12 mm (*1*). [d] Reported $n^{13.5}D$ 1.5366 (*1*). [e] Reported d^{19}_4 1.130 (*1*).

Experimental

Reactants were obtained commercially and used without further purification except in the case of some of the ethyl 2-bromoesters which were prepared by the method of Schwenk and Papa (*4*). Elemental analyses were performed by Huffman Microanalytical Laboratories, Wheatridge, Colo. Melting points were determined on a Thomas-Hoover melting-point apparatus and were corrected. Density determinations were determined with a pycnometer which held 1.5291 grams of water at 4.0°C (*5*). Samples utilized for density and refractive index determinations were further purified by preparative column chromatography with a 10-ft × ⅜-in. column with 20% FFAP on 45/60 chromsorb W. The following examples illustrate the synthesis of the 1-(2-thienyl)-2-alkanones and the 5-alkyl-5-(2-thenyl) hydantoins. Repeated attempts to condense ethyl 2-bromo-3,3-dimethylbutanoate with 2-thiophenecarboxaldehyde were unsuccessful, and an essentially quantitative yield of 2-bromo-3,3-dimethylbutanoic acid was recovered.

1-(2-Thienyl)-3-methyl-2-pentanone. A mixture of 67.2 grams (0.30 mole) of ethyl 2-bromo-3-methylpentanoate and 36.0 grams (0.32 mole) of thiophenecarboxaldehyde was cooled to 5–10°C. While maintaining this temperature and with stirring, a solution of sodium ethoxide prepared from 13 grams (0.56 mole) sodium and 150 ml of ethanol was slowly added to the ester–aldehyde mixture. The reaction mixture was stirred an additional 30 min at this temperature and then allowed to warm to room temperature with an additional 3 hr of stirring. Approximately 30 ml of water were added, and the mixture was stirred in a steam bath for 3 hr.

The reaction mixture was cooled to room temperature, and a sufficient quantity of dilute phosphoric acid was added to the solution to bring the pH to 3. As the acid was added, a large quantity of carbon dioxide was evolved. The ketone was extracted with ether and washed with 5% sodium bicarbonate solution, water, and dried over anhydrous sodium sulfate. After removal of the ether by flash distillation, the ketone was distilled through a Nester-Faust annular Teflon spinning-band column under reduced pressure. There were obtained 44.9 grams (82%) of 1-(2-thienyl)-3-methyl-2-pentonone, bp, 76/(0.3 mm), $n^{20}D$ 1.5111, d^{20}_4 1.074.

5-sec-Butyl-5-(2-thenyl)hydantoin. A mixture of 4.5 grams of ammonium carbonate, 1.3 grams of potassium cyanide, and 1.0 gram of 1-(2-thienyl)-3-methyl-2-pentanone in 50 ml of a 50% water–ethanol mixture was placed in a flask fitted with an air condenser. The flask was placed in a 70°C water bath overnight, carefully acidified with concentrated hydrochloric acid to pH 6–7, evaporated to one half volume, and cooled. The hydantoin precipitate was removed by filtration and recrystallized from the water–ethanol mixture, mp 219.5–20.5°C.

Literature Cited

(1) Cagniant, M. P., *Bull. Soc. Chim. Fr.*, **16** (5), 847 (1949).
(2) Henze, H. R., Speer, R. J., *J. Amer. Chem. Soc.*, **64**, 522 (1942).
(3) Ruzicka, T., Ehmann, T., *Helv. Chim. Acta*, **15**, 160 (1932).
(4) Schwenk, E., Papa, D., *J. Amer. Chem. Soc.*, **70**, 3626 (1948).
(5) Shriner, R. T., Fuson, R. C., Curten, D. Y., "The Systematic Identification of Organic Compounds," 4th ed., p 40, Wiley, New York, N.Y.

Received for review June 17, 1974. Accepted September 18, 1974. Financial support by the Robert A. Welch Foundation (Grant No. AO-413).

---

[1] To whom correspondence should be addressed.