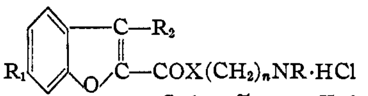
TABLE I

DERIVATIVES OF COUMARILIC ACIDS



R₁	R₂	X	n	R	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
H	H	O	2	$(CH_3)_2$	187.5–188.8	$C_{13}H_{16}ClNO_3$	57.89	58.08	5.98	5.96	13.11	13.22
H	H	O	2	C_7H_{14}[a]	207.6–208.8	$C_{18}H_{24}ClNO_3$	63.99	64.04	7.16	7.24	10.50	10.42
H	H	O	3	C_6H_{12}[b]	180.0–181.2	$C_{18}H_{24}ClNO_3$	63.99	64.12	7.16	7.07	10.50	10.34
H	H	S	2	$(C_2H_5)_2$	209.5–210.5	$C_{15}H_{20}ClNO_2S$	[c]	[c]	..	..	11.30	11.10
H	H	S	4	$(C_2H_5)_2$	153.1–153.9	$C_{17}H_{24}ClNO_2S$	[d]	[d]	..	..	10.37	10.10
H	H	NH	3	$(C_2H_5)_2$	81.0– 84.0	$C_{16}H_{23}ClN_2O_2$	...	...	..	..	11.41	11.26
CH_3	CH_3	O	2	$(CH_3)_2$	187.4–188.8	$C_{15}H_{20}ClNO_3$	60.50	60.34	6.77	6.73	11.91	11.76
CH_3	CH_3	O	3	C_6H_{12}[b]	184.0–185.2	$C_{20}H_{28}ClNO_3$	65.65	65.94	7.71	7.63	9.69	9.38
C_4H_9O	CH_3	O	2	$(CH_3)_2$	158.0–160.0	$C_{18}H_{26}ClNO_4$	60.75	60.85	7.37	7.25	9.96	9.77
C_4H_9O	CH_3	O	3	C_6H_{12}[b]	168.7–169.9	$C_{23}H_{34}ClNO_4$	65.15	65.08	8.08	7.83	8.36	8.10

[a] 2,6-Dimethyl-1-piperidyl. [b] 2-Methyl-1-piperidyl. [c] Calcd.: S, 10.22. Found: S, 10.30. [d] Calcd.: S, 9.38. Found: S, 9.48.

7-hydroxy-4-methylcoumarin, *n*-butyl benzenesulfonate and anhydrous potassium carbonate in *m*-xylene solution gave a 61% yield of 7-butoxy-4-methylcoumarin, m.p. 51–52° (lit.[5] m.p. 51°). From this was obtained a 44% yield of **6-butoxy-3-methylcoumarilic acid**, m.p. 130.2–131.2°.

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.72; H, 6.42. Found: C, 67.50; H, 6.46.

Derivatives.—The coumarilic acids were converted to the acid chlorides by means of thionyl chloride. The crude crystalline acid chlorides then reacted directly, in benzene solution, with an alcohol, thiol or amine. The compounds prepared are listed in the accompanying Table I.

---

(5) Bose, Sen and Chakravarti, *Ann. Biochem. Exptl. Med.*, **5**, 1 (1945).

STERLING-WINTHROP RESEARCH INSTITUTE
RENSSELAER, N. Y.
RECEIVED DECEMBER 22, 1950

Synthesis of β-(6-Methoxy-1-naphthoyl)-propionic Acid

BY WILLIAM G. DAUBEN AND KLAUS A. SAEGEBARTH

The preparation of β-(6-methoxy-1-naphthoyl)-propionic acid is a continuation of an earlier investigation in this Laboratory[1] on the use of organocadmium reagents for the preparation of substituted β-aroylpropionic acids. It has been previously reported[1,2,3] that poor yields of the diaryl cadmium derivative were obtained when the latter was prepared from the aryl iodide, whereas the corresponding bromide gave good results. These results suggested the need for a suitable method of synthesis of 1-bromo-6-methoxynaphthalene. This latter compound has been previously prepared[4] in the standard fashion in 4% yield. The bromide has now been prepared in a 34% yield employing the mercuric bromide double salt method of Schwechten.[5,6] Conversion of the 1-bromo-6-methoxynaphthalene to its cadmium derivative and subsequent reaction with β-carbomethoxypropionyl chloride[7] resulted in a 44% yield of the β-(6-methoxy-1-naphthoyl)-propionic acid.

Subsequently, it has been found that the keto acid can be prepared in 41% yield by the addition of 6-methoxy-1-naphthylmagnesium iodide to a suspension of succinic anhydride[8] in an ether–benzene solution. Although the yield of product is slightly higher employing the cadmium reaction, the more efficient preparation of the iodide[9] (65% compared with 34%) makes the inverse Grignard the more preferable method.

Reduction of the carbonyl by either the modified Wolff–Kishner[10] method or by hydrogenolysis[11] gave γ-(6-methoxy-1-naphthyl)-butyric acid in yields of 83 and 53%, respectively.

Experimental[12]

1-Bromo-6-methoxynaphthalene.—To an orange-colored solution of 6-methoxy-1-naphthyldiazonium chloride, prepared according to the procedure of Wilds and Close,[9] from 50 g. (0.238 mole) of 6-methoxy-1-naphthylamine hydrochloride, was added with stirring a cold suspension of mercuric bromide[6] formed by treating 80.0 g. (0.246 mole) of mercuric nitrate with 113.6 g. (1.226 moles) of sodium bromide in 240 ml. of water. The product was processed according to the method of Newman and Wise.[6] The yield of air-dried complex varied from 96–112 g. (90–115% calculated on the basis of $(C_{11}H_9ON_2Br)_2HgBr_2$).

For the decomposition, the mercuric bromide double salt was finely ground and added in several portions through a wide rubber tube[13] to a flask fitted with a reflux condenser and containing 200 ml. of dimethylaniline heated to 110–120°. After each addition of complex, a vigorous nitrogen evolution occurred; heating was continued until no further reaction was noticed. The time for the decomposition varied between two and three hours, depending upon the amount of double salt employed. The reaction mixture was digested with benzene, the benzene extract washed with dilute acid and alkali and the benzene removed. The residue of 1-bromo-6-methoxynaphthalene was purified by vacuum distillation, b.p. 124.5–126.0° (0.8 mm.), $n^{26}D$ 1.6481, yield 18.0–19.2 g. (32–34%).

Anal. Calcd. for $C_{11}H_9OBr$: Br, 33.71. Found: Br, 33.83. The picrate melts at 104.8–105.5° (alc.). Cohen, *et al.*[4] report 105–106°.

β-(6-Methoxy-1-naphthoyl)-propionic Acid. A. By the Cadmium Reaction.—The procedure of Dauben and Tilles[1] was followed for the preparation of the diaryl cadmium de-

---

(1) W. G. Dauben and H. Tilles, *J. Org. Chem.*, **15**, 785 (1950).

(2) J. Cason, THIS JOURNAL, **68**, 2070 (1946); *Chem. Revs.*, **40**, 15 (1947).

(3) H. Gilman and J. F. Nelson, *Rec. trav. chim.*, **55**, 518 (1936).

(4) A. Cohen, J. W. Cook, C. L. Hewett and A. Girard, *J. Chem. Soc.*, 653 (1934).

(5) H. W. Schwechten, *Ber.*, **65**, 1605 (1932).

(6) M. S. Newman and P. H. Wise, THIS JOURNAL, **63**, 2847 (1941).

(7) J. Cason, "Org. Syntheses," Vol. 25, John Wiley and Sons, Inc., New York, N. Y., p. 19.

(8) M. S. Newman, R. B. Taylor, T. Hodgson and A. B. Garrett, THIS JOURNAL, **69**, 1784 (1947).

(9) A. L. Wilds and W. J. Close, *ibid.*, **69**, 3079 (1947).

(10) Huang-Minlon, *ibid.*, **68**, 2487 (1946).

(11) E. C. Horning and D. B. Reisner, *ibid.*, **71**, 1036 (1949).

(12) Microanalyses by the Microanalytical Laboratory of the Department of Chemistry, University of California. All melting points are corrected; all boiling points are uncorrected.

(13) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 287.

rivative from 20 g. (0.085 mole) of 1-bromo-6-methoxynaphthalene which was allowed to react with an equimolar amount of β-carbomethoxypropionyl chloride[7] and the synthesis was conducted in the usual fashion. The crude keto ester was saponified with alcoholic potassium hydroxide and the resulting β-(6-methoxy-1-naphthoyl)-propionic acid recrystallized from methanol; m.p. 153.7–154.6°, yield 9.6 g. (44%).

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 69.55; H, 5.34.

B. **By the Inverse Grignard Reaction.**—1-Iodo-6-methoxynaphthalene was prepared in 65% yield by the method of Wilds and Close,[9] purified by vacuum distillation (b.p. 145–155° at 0.5 mm.) and subsequently recrystallized from methanol, m.p. 34–35°.[4,14]

A solution of 28.5 g. (0.1 mole) of the iodide and 10.5 g. (7.3 ml., 0.096 mole) of ethyl bromide in 75 ml. of dry thiophene-free benzene was added dropwise over the period of 80 minutes to 4.9 g. (0.2 mole) of magnesium turnings and 50 ml. of dry ether in a nitrogen atmosphere. Refluxing was continued for one hour after all the reagent had been added. The Grignard reagent was diluted with 100 ml. of dry benzene and added during 15 minutes to a vigorously stirred suspension of 20 g. (0.2 mole) of succinic anhydride[8] in 120 ml. of 1:2 ether–benzene. The mixture was refluxed for two hours and the yellow complex that formed was decomposed with ice and acidified to congo red with 6 *N* hydrochloric acid. The keto acid produced was extracted with 10% sodium carbonate solution. The crude brown colored acid obtained upon acidification was collected by filtration, washed with water to remove any acidic material produced by the Grignard carrier, dried over potassium hydroxide and weighed; 13.4 g. (52%), m.p. 135–138°. After two recrystallizations from methanol 10.7 g. (41%) of the white crystalline acid was obtained, m.p. 153.5–154.3°.

---

[14] A. Butenandt and G. Schramm, *Ber.*, **68**, 2083 (1935).

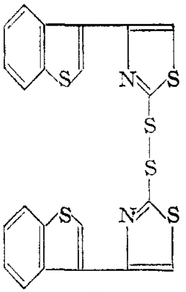
CHEMICAL LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY 4, CALIF.

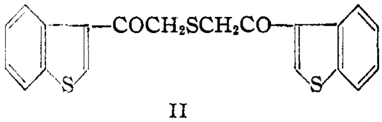
RECEIVED OCTOBER 31, 1950

4-(3'-Thianaphthyl)-2-mercaptothiazole

BY WILLIAM S. EMERSON

When 3-chloroacetylthianaphthene was treated with ammonium dithiocarbamate in ethanol suspension, according to the procedure used for the preparation of 4-(2'-thienyl)-2-mercaptothiazole,[1] the product isolated was 69% of 4-(3'-thianaphthyl)-2-thiazolyl disulfide (I). Only 2% of the desired 4-(3'-thianaphthyl)-2-mercaptothiazole was obtained. However, treatment with zinc and acetic acid converted the disulfide to the mercaptan quantitatively.


I


II

In a preparation in which the ammonium dithiocarbamate was of poor quality, the principal product isolated was bis-(3-thianaphthacyl) sulfide (II). The identity of this compound was shown by a separate preparation from 3-chloroacetylthianaphthene and sodium sulfide and by oxidation to the corresponding sulfone.

Experimental

3-Chloroacetylthianaphthene.—A stream of chlorine was introduced into a vigorously stirred solution of 50 g. of 3-acetylthianaphthene (Jefferson Chemical Co.) in 100 cc. of chloroform and 100 cc. of carbon tetrachloride initially at room temperature. No cooling bath was used. After 20 minutes the chlorine flow was stopped and the reaction mixture was cooled in ice. The white crystals were separated by filtration, washed with hexane and dried to give 40 g. (67% yield) of 3-chloroacetylthianaphthene, m.p. 137–140°.[2] An analytical sample was recrystallized twice from a mixture of benzene and hexane, m.p. 139.5–140.5°.

Anal.[3] Calcd. for $C_{10}H_7OSCl$: C, 57.0; H, 3.32. Found: C, 57.4; H, 3.46.

4-(3'-Thianaphthyl)-2-thiazolyl Disulfide.—A suspension of 21 g. of 3-chloroacetylthianaphthene and 77 g. of ammonium dithiocarbamate in 325 cc. of ethanol was allowed to stand with occasional shaking for eight days. Then the mixture was cooled in ice, diluted with 325 cc. of water and filtered. The precipitate was washed three times with water and sucked as dry as possible. It then was suspended in benzene which was boiled for 13 hours while the evolved water was collected in a Dean and Stark trap. The resulting suspension was heated to boiling and filtered hot. When the filtrate was chilled, crystals appeared. These were separated by filtration, washed with benzene and dried to give 0.5 g. (2%) of crude 4-(3'-thianaphthyl)-2-mercaptothiazole, m.p. 212–214°. One recrystallization from a mixture of benzene and ethanol raised the melting point to 221–223°. Dilution of the original filtrate with hexane precipitated 4.5 g. of crude 4-(3'-thianaphthyl)-2-thiazolyl disulfide, m.p. 109–117°. The solid which had been filtered from the original hot benzene suspension was crystallized from a mixture of ethanol and dioxane. Two crops were collected: I, 10.5 g., m.p. 126–127° and II, 2.0 g., m.p. 116–120°. The total yield of crude 4-(3'-thianaphthyl)-2-thiazolyl disulfide was 17 g. (69%). When a sample of fraction I was crystallized successively from benzene, ethanol and dioxane, and benzene and ethanol, the melting point remained the same.

Anal. Calcd. for $C_{22}H_{12}N_2S_6$: C, 53.2; H, 2.42. Found: C, 53.5; H, 2.24.

4-(3'-Thianaphthyl)-2-mercaptothiazole.—Excess powdered zinc was added to a solution of 6 g. of 4-(3'-thianaphthyl)-2-thiazolyl disulfide in 200 cc. of glacial acetic acid. After boiling for one hour, the solution was filtered hot and the funnel was washed with boiling acetic acid. The filtrate was diluted to 1 l. with water containing 25 cc. of concd. hydrochloric acid. The precipitate was separated by filtration, washed four times with water and crystallized from a mixture of ethanol and benzene. The essentially quantitative yield of 4-(3'-thianaphthyl)-2-mercaptothiazole was collected in two crops: I, 5 g., m.p. 221–223°, and II, 1 g., m.p. 220–222°.

Anal. Calcd. for $C_{11}H_7NS_3$: C, 53.0; H, 2.81. Found: C, 52.9; H, 2.82.

Bis-(3-thianaphthacyl) Sulfide.—A suspension of 21 g. of 3-chloroacetylthianaphthene and 12 g. of sodium sulfide nonahydrate in 200 cc. of ethanol was shaken occasionally and allowed to stand overnight. The mixture, now dark brown, was cooled in ice and diluted with 200 cc. of water. The crude product was separated by filtration and crystallized from a mixture of benzene and ethanol (Norit) to yield 10.5 g. (55%) of bis-(3-thianaphthacyl) sulfide in three crops, m.p. 149.5–150.5°, 149–150° and 149.0–149.5°.

Bis-(3-thianaphthacyl) sulfide also was isolated from a 3-chloroacetylthianaphthene–ammonium dithiocarbamate reaction in which the carbamate was of poor quality. The product was leached five times with boiling ethanol, crystallized from a benzene–hexane mixture and then from a benzene–ethanol mixture, m.p. 149–150°. An analytical sample was recrystallized from benzene–hexane, m.p. 150–151°.

---

[1] Emerson and Patrick, *J. Org. Chem.*, **13**, 722 (1948).

[2] All of the melting points are uncorrected.

[3] Microanalyses by Mr. P. J. Adams and Mr. Donald Stoltz of this Laboratory and by the Micro-Tech Laboratories, 8000 Lincoln Avenue, Skokie, Illinois.