

## Synthesis, structure and properties of 2-(acenaphthen-5-yl)-3-methylbutanoic acid and its derivatives

W. Kowalewska and W. Podkościelny  
*Department of Organic Chemistry and Technology,  
Maria Curie-Skłodowska University,  
ul. Gliniana 33, 20-614 Lublin, Poland*

Synthesis, structure and fundamental chemical and physical properties as well as biological activity of 2-(acenaphthen-5-yl)-3-methylbutanoic acid and its some derivatives were described. The chemical structure of the newly obtained compounds was confirmed by elementary analysis and FTIR and  $^1\text{H-NMR}$  spectroscopies. 2-(Acenaphthen-5-yl)-3-methylbutanoic acid and its amide and ester derivatives were investigated at the Institute of Organic Chemistry in Warsaw in view their biological activity. It was found that the high fungicidal activity characterized the acid chloride and amide of 2-(acenaphthen-5-yl)-3-methylbutanoic acid.

### 1. INTRODUCTION

The purpose of this article, which is a continuation of investigation on finding new compounds exhibiting potential biological activity [1-3], is the synthesis, structure and properties of 2-(acenaphthen-5-yl)-3-methylbutanoic acid and some of its derivatives. It is well known that an essential requirement in effective research on new pesticide compounds is to recognize the dependence between the structure of compounds and their biological activity. This dependence was unconditionally described by O'Brien and Yamamoto [4] on the basis of synthetic pyrethroids. (Figure 1):

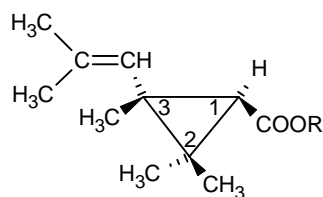


Fig. 1.

It was pointed out by the authors that a significant in the high biological activity was accomplished by a dimethyl group of carbon atom attached in 2-position, whereas groups in 3-position have secondary importance. What is more, taking into consideration the influence of three-dimensional groups of chiral carbon atom in 1-cyclopropane, it was pointed out that molecules with 1R configuration reveal very high biological activity, while those with 1S isomers do not reveal this property at all. According to Barteau and co-workers [5], cyclopropane ring displays little importance in the biological activity of pyrethroids. This fact is caused by very active insecticide fenvalerate with two methyl groups in isopropyl structure. (Figure 2):

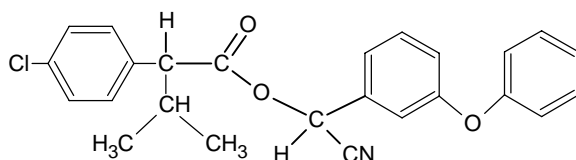
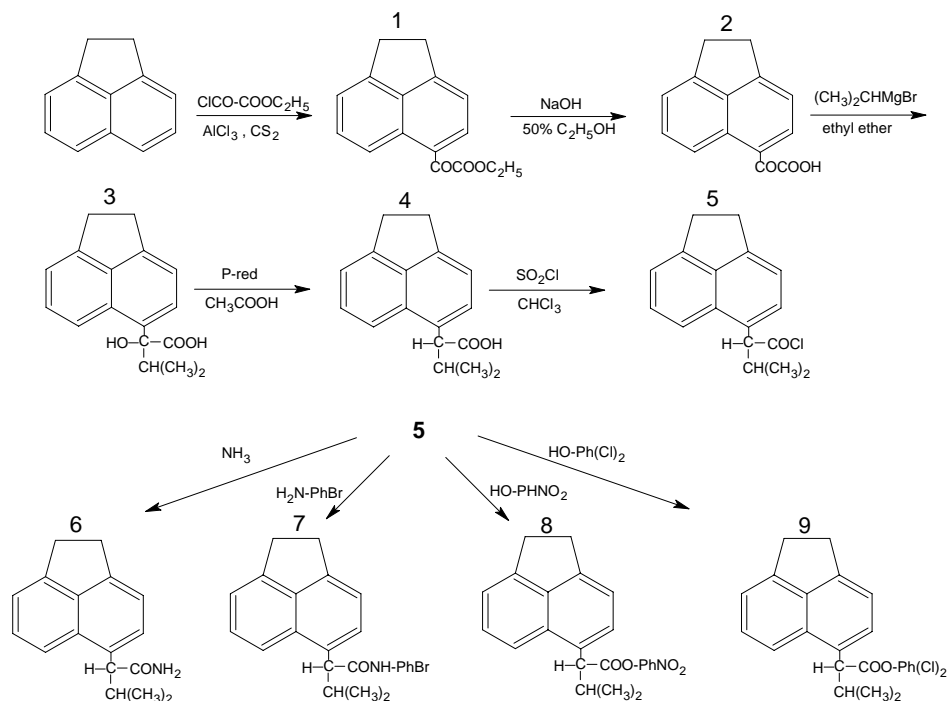


Fig. 2.

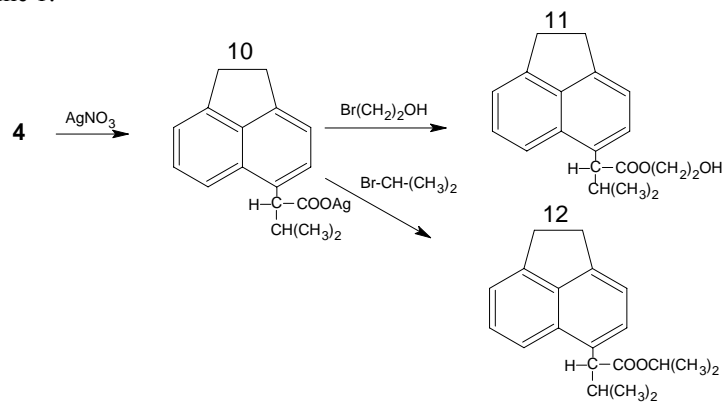
Following the above information, we undertook investigation on synthesis and the biological activity of the new compounds containing isopropyl group in its structure, e.g. 5-acenaphthyl- $\alpha$ -isopropylacetic acid and some of its ester or amide derivatives. As a starting material, ethyl ester of 5-acenaphthylglyoxylic acid was used, which was obtained according to the Friedel-Craft reaction from acenaphthene and chloride of mono ethyl ester of oxalic acid in the solution of  $\text{CS}_2$  with  $\text{AlCl}_3$ . The obtained ester [6] underwent ethanolic alkalic hydrolysis in the presence of  $\text{NaOH}$ . Next this compound according to Grignard reaction with isopropyl bromide in dry dimethyl ether, gave 2-(acenaphten-5-yl)-2-hydroxy-3-methylbutanoic acid, which after reduction with red phosphorous in glacial acetic acid gave 2-(acenaphthen-5-yl)-3-methylbutanoic acid.

The obtained compound in reaction with thionyl chloride in dry chloroforme converted into acid chloride, which in reaction with ammonia and p-bromoaniline gave a suitable amides, whereas in reaction with o-nitrophenol and 3,5-dichlorophenol was changed into its esters (Scheme 1). 2-(Acenaphthen-5-yl)-3-methylbutanoic acid in reaction with silver nitrate in neutral medium gave its silver salt which in reaction with bromoethanol and isopropyl bromide exchanged into a suitable esters (Scheme 2). The structures of the newly obtained compounds were confirmed by elemental analysis (Table 1), FTIR and  $^1\text{H-NMR}$  spectroscopies (Table 2). 2-(Acenaphthyl-5-yl)-3-methylbutanoic acid and all its amide and ester derivatives were investigated at the Institute of Organic Industry in Warsaw in view of their biological activity. The physiological activity of the compounds mentioned above was studied against the insects, the *Tetranychus urticae* Koch, some plants and fungi.[7] The investigated compounds did not show any insecticide activity, neither the

*Tetranychus urticae* Koch nor phytocidal. One of them (11 and 12) turned out to have a good *Erysiphe graminis* reaction while compounds (4, 6 and 9) were characterized by middle and weak one.



Scheme 1.



Scheme 2.

Tab. 1. Melting points, yields and results of the elementary analyses of newly obtained compounds

Compound Nr	M.p. [°C]	Yield [%]	Analysis C, H and N [%]	
			Calcd.	Fund.
4	96-97	60	80,28 %C 7,13 %	80,60 %C H 7,28 %H
6	180-181	90	5,52 %	N 5,36 %N
7	oil	85	67,65 %C 5,45 %	67,38 %C H 5,68 %H
8	oil	80	73,58 %C 5,63 %	73,29 %C H 6,00 %H
9	oil	82	69,18 %C 5,04 %H	69,41 %C 5,30 %H
11	oil	84	76,48 %C 7,43 %H	76,64 %C 7,66 %H
12	oil	81	81,04 %C 8,16 %	81,25 %C H 8,29 %H

Tab. 2. Results of IR and <sup>1</sup>H-NMR analysis

Compound	IR (KBr, cm <sup>-1</sup> )	<sup>1</sup> H-NMR (ppm) (CDCl <sub>3</sub> )
4	2918-3032 (OH, v <sub>s</sub> ); 1663 (C=O, v <sub>s</sub> )	1,20-1,27 (6H -CH <sub>3</sub> ), 2,18-2,41 (1H -CH(CH <sub>3</sub> ) <sub>2</sub> ), 3,67 (1H -CH-CO), 3,42 (4H -CH <sub>2</sub> -CH <sub>2</sub> ), 8,37-8,76 (5 H -aryl) 10,15 (1H -COOH)
6	1598, 1667 (CONH <sub>2</sub> , v <sub>s</sub> )	1,098-1,20 (6H -CH <sub>3</sub> ), 2,15-2,26 (1H -CH(CH <sub>3</sub> ) <sub>2</sub> ), 3,64 (1H -CH), 3,38 (4H -CH <sub>2</sub> -CH <sub>2</sub> ), 7,23-8,43 (5H aryl), 10,46 (2H -NH <sub>2</sub> )
7	3377-3470 (CONH, v <sub>s</sub> ); 1598 (C=O, v <sub>as</sub> )	0,97-1,01 (6H -CH <sub>3</sub> ), 1,45-2,15 (1H -CH(CH <sub>3</sub> ) <sub>2</sub> ), 3,19 (4H -CH <sub>2</sub> -CH <sub>2</sub> ), 3,98 (1H -CH), 6,36 (1H -NH), 7,12-8,18 (9H aryl)

Compound	IR (KBr, cm <sup>-1</sup> )	<sup>1</sup> H-NMR (ppm) (CDCl <sub>3</sub> )
8	1709 (C=O, ν <sub>s</sub> ); 1228 (C=O, ν <sub>as</sub> )	1,03-1,10 (6H -CH <sub>3</sub> ), 1,57-2,26 (1H - CH(CH <sub>3</sub> ) <sub>2</sub> ), 3,36 (4H -CH <sub>2</sub> -CH <sub>2</sub> ), 4,41-4,48 (1H -CH), 6,92-8,22 (9H aryl)
9	1675 (C=O, ν <sub>s</sub> ); 1580 (C=O, ν <sub>as</sub> )	0,69-0,75 (6H -CH <sub>3</sub> ), 1,48-1,60 (1H - CH(CH <sub>3</sub> ) <sub>2</sub> ), 3,38 (4H -CH <sub>2</sub> -CH <sub>2</sub> ), 4,45-4,52 (1H -CH), 6,67-8,30 (8H aryl)
11	1735, 1580 (C=O, ν <sub>s</sub> ); 3439 (OH, ν); 1345-1442 (OH, δ)	0,67-0,74 (6H -CH <sub>3</sub> ), 2,05-2,36 (1H - CH(CH <sub>3</sub> ) <sub>2</sub> ), 3,31 (4H -CH <sub>2</sub> -CH <sub>2</sub> ), 3,51-3,68 (2H -CH <sub>2</sub> -OH), 3,88-4,03 (2H -COOCH <sub>2</sub> -), 4,85 (1H -OH), 7,19-7,86 (5H aryl)
12	1705-1729 (COO, ν <sub>s</sub> ); 1272 (C=O, ν <sub>as</sub> ); 2932-2979 (CH-, ν <sub>s</sub> )	1,07-1,11 (6H -(CH <sub>3</sub> ) <sub>2</sub> -CHCOO), 1,13-1,17 (6H -(CH <sub>3</sub> ) <sub>2</sub> ), 1,38-1,46 (1H -CH), 3,35 (4H - CH <sub>2</sub> -CH <sub>2</sub> ), 3,93-3,97 (1H -CH-COO), 7,20- 8,21 (5H aryl)

## 2. EXPERIMENTAL

**Ethyl (acenaphthen-5-yl)oxoacetate.** In a round-bottomed flask fitted with a condenser, mechanical stirrer, dropper-ended tube with CaCl<sub>2</sub>, 61,6g acenaphthene, 400 mL of dry CS<sub>2</sub> and 56g AlCl<sub>3</sub> was placed. The mixture was cooled to 0-5° C and 57,4 g of chloride mono ethyl oxalic acid was dropped during 1h. The resulting solution was then heated at 40-60°C in water bath until the HCl was removed (about 6h). Next, the layer with CS<sub>2</sub> was decanted and the resulting dark-brown complex was decomposed by ice-cold hydrochloride acid diluted 1:1. The resulting brown oil, after extraction with CS<sub>2</sub>, was washed with water and finally dried over dry magnesium sulfate. The solvent was distilled off and the compound obtained was crystallized from 200 mL of 96% ethanol, giving glistening plates with m.p. 74-76°C and after recrystallization from this alcohol the product with m.p. 80-81°C was obtained.

**Acenaphthen-5-yl(oxo)acetic acid.** In a round-bottomed flask fitted with mechanical stirrer and condenser 28g ethyl ester of 5-acenaphthyloxalic acid and 5,2g NaOH in 300 mL of 50% ethanol was placed. The reaction mixture was mixed with active coal and heated in a water bath for 30 min., then acidified with 1:1 hydrochloride acid.

The resulting precipitate was extracted with dimethyl ether, washed with water and dried over anhydrous magnesium sulfate. Then the ether was distilled off and the resulting precipitate was crystallized from benzene, giving yellow needles with m.p. 103-105° C. (lit. 13).

**2-(Acenaphthen-5-yl)-2-hydroxy-3-methylbutanoic acid.** Using the same apparatus as described above, 80 mL of dry dimethyl ether with magnesium shavings was taken and 23 mL of isopropylbromide dissolved in 50 mL of dry dimethyl ether after cooling (0-5°C) was gradually added and the resulting isopropylmagnesium bromide after cooling (0-5°C) was added during vigorous mixing to keto acid dissolved in 40 mL dry dimethyl ether. During the addition of magnesium-organic compound the orange precipitate was converted into a yellow soluble product which after adding 1:1 diluted hydrochloride acid with ice was extracted with dimethyl ether. When removing the solvent, a dark oil compound was obtained.

**2-(Acenaphthen-5-yl)-3-methylbutanoic acid.** In a round-bottomed flask fitted with condenser, 0,5g iodine, 1,4g red phosphorus and 30 mL of glacial acetic acid was placed. The whole was heated in an oil bath under reflux for 3h, and was then allowed to stand at room temperature. After filtration 60 mL of water was added and the obtained filtrate was extracted with dimethyl ether, washed with water and dried over anhydrous magnesium sulfate. After removing the solvent, the oily residue solidified. A crude compound was crystallized from acetic acid giving dark needles with m.p. 96-97°C. Yield 60%.

#### Analysis

For C<sub>17</sub>H<sub>18</sub>O<sub>2</sub> (254,33)

Calcd 80,28%C; 7,13%H;

Found 80,60%C; 7,28%H

**2-(Acenaphthen-5-yl)-3-methylbutanoyl chloride.** In a round-bottomed flask fitted with condenser-ended with CaCl<sub>2</sub>, 50g of 5-acenaphthyl- $\alpha$ -isopropylacetic acid, 100 mL dry chloroforme and 25 mL thionyl chloride was placed. The mixture was allowed to stand at room temperature for 24h, and was warmed in the water bath at 80°C for 30 min. The solvent and unreacted thionyl chloride were distilled off, and the residue was distilled under reduced pressure giving oil.

## Analysis

For  $C_{17}H_{17}ClO$  (272,77)

Calcd. 12,99%CL;

Found 12,66% CL

**2-(Acenaphthen-5-yl)-3-methylbutanamide.** Using the apparatus described above, 5,6g chloride of 5-acenaphthyl- $\alpha$ -isopropylacetic acid and 100 mL of 25% ammonia was placed. The whole was warmed in the water bath at 60°C for 1h. After cooling the mixture was poured into cold water. The resulting amide was extracted with dimethyl ether and then, after washing with water, dried over anhydrous sodium sulfate. When the solvent was distilled off, the residue was crystallized from ethanol giving colorless powder with m.p. 180-181°C.

## Analysis

For  $C_{17}H_{19}NO$ 

Calcd. 5,52%N;

Found 5,36%N

**4-Bromophenyl-2-(acenaphthen-5-yl)-3-methylbutanamide.** In a three-necked round-bottomed flask fitted with a mechanical stirrer, dropper and condenser, 5,6g chloride of 5-acenaphthyl- $\alpha$ -isopropylacetic acid and 50 mL dioxane was placed and 5,1g bromoaniline in 50 mL of dioxane was dropwise added. The whole was vigorously stirred at room temperature for 2h, than it was poured into 200 mL of water, acidified with 10 mL of hydrochloride acid. The oily residue after extracting with benzene, was washed several times with water, 1M HCl, water, 5% of NaOH and finally with water, and dried over anhydrous sodium sulfite. When the solvent was removed, the oily residue was obtained with yield 90%.

**2-Nitrophenyl-2(acenaphthen-5-yl)-3-methylbutanoate.** Using the apparatus described above, 2,8g o-nitrophenol, 0,8g of NaOH, 0,1g Triethylbenzylammonium chloride (TEBA) and 70 mL of water were placed. The whole was vigorously stirred for 20 min., then 5,4 g chloride of 5-acenaphthyl- $\alpha$ -isopropylacetic acid in 50 mL methylene chloride was added dropwise. The content was stirred at room temperature for 30 min, then at 40°C for 10 min. After cooling the organic layer was separated, washed with water and dried over anhydrous magnesium sulfate. After removing the solvent a dark oily residue was obtained with yield 80%.

## Analysis

For  $C_{23}H_{21}O_4N$  (375,42)

Calcd. 73,58%C; 5,45%H; 3,73%N;

Found 73,29%C; 5,08%H; 3,73%N

**3,5-Dichlorophenyl-2-(acenaphthen-5-yl)-3-methylbutanoate.** Using the apparatus described above, 3,2g 3,5-dinitrophenol, 0,8g NaOH, 0,1g Triethylbenzylammonium chloride (TEBA) and 70 mL of water was taken. The whole was vigorously stirred for 10 min, then 5,4g chloride of 5-acenaphthyl- $\alpha$ -isopropylacetic acid in 70 mL of methylene chloride was added dropwise. Mixing was continued at room temperature for 30 min, and at 40°C for 10 min. The resulting organic layer was separated, washed with water and dried over magnesium sulfite. When solvent was distilled off, an oily residue was obtained with 82%.

## Analysis

For  $C_{23}H_{20}O_2Cl_2$  (399,32)

Calcd. 69,18%C; 5,04%H;

Found 69,41%C; 5,30%H

**Silver salt of 2-(acenaphthen-5-yl)-3-methylbutanoic acid.** A sample of 9g 5-acenaphthyl- $\alpha$ -isopropylacetic acid was suspended in 80 mL water and neutralized with 5% solution of NaOH (pH=9). To this solution 8g silver nitrate was added in 60 mL of water. The white caseous precipitate immediately formed was filtered and, after washing with water, was consequently dried.

**2-Hydroxyethyl-2-(acenaphthen-5-yl)-3-methylbutanoate.** In a round-bottomed flask fitted with a reflux condenser, 5,4g of corresponding silver salt and 100 mL of benzene was placed and 3g chloroethanol in 50 mL of dry benzene was added dropwise. The whole was warmed in a boiling water bath for 4h and the resulting silver chloride was filtered, and benzene was distilled off under reduced pressure. The oily residue was dissolved in 96% ethanol and after adding active coal, filtered. When ethanol was removed, the oily product was obtained with 84% yield.

## Analysis

For  $C_{19}H_{22}O_3$  (298,39)

Calcd 76,48%C; 7,45%H;

Found 76,64%C; 7,66%H

**Isopropyl 2-(acenaphthen-5-yl)-3-methylbutanoate.** To 5,4g of corresponding silver salt in 100 mL of dry benzene 4g isopropylbromide in 50 mL dry



benzene was added dropwise. The resulting silver bromide was filtered and the solvent, was distilled off under reduced pressure. The compound obtained was dissolved in ethanol and, after adding active coal, filtered. After removing the solvent, the oily residue was obtained with 81% yield.

#### Analysis

For  $C_{20}H_{24}O_2$  (296,41)

Calcd 81,04%C; 9,16%H;

Found 81,25%C; 8,29%H

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#### CURRICULA VITAE



**Wanda Kowalewska.** M. Sc. 1970, Ph. D. 1978. Research areas: organic chemistry, polymer chemistry, chemistry of compounds of potential biological activity, synthesis and properties of polymers containing sulfur in the main chain, particularly of polythioesters, polysulfonates and segmented polyuretanes, synthesis, structure and properties of new compounds of potential biological activity.



**Wawrzyniec Podkościelny.** Assistant Professor. M. Sc. 1955; Ph. D. 1964, Habilitation 1994. Postdoc: University of Wisconsin, McArdle Laboratory for Cancer Research, USA (1966–1967), Vice-Director of the Institute of Chemistry, UMCS (1970–1978); (1981–1984). Director of Institute of Chemistry (1988–1989), Head of the Department of Organic Synthesis (1970–1976), Head of Department of Organic Chemistry and Technology (1979–). Research areas: organic chemistry – polymer chemistry, chemistry of compounds of potential biological activity, synthesis, structure and properties of polymers containing sulfur in the main chain, particularly of polythioesters, polysulfonates,

thioetherglycidyl resins and recently nonsegmented and segmented polyurethanes, synthesis, structure and properties of new compounds of potential biological activity, synthesis, structure and properties of monomers, oligomers and polymers as well as UV cured compositions for optical fibre coatings. Results of the investigations from these various areas were presented in over 100 scientific national and foreign journals, 60 patents and 50 communications. In 1958 he became a member of the Polish Chemical Society and, up to now he promoted 8 doctoral dissertations and over 200 M. Sc. degrees.