

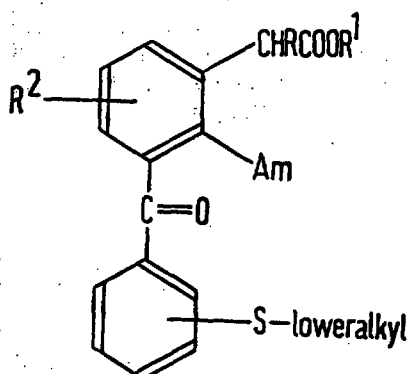
SPECIFICATION

2-Amino-3-(alkylthiobenzoyl)-phenylacetic acids

5 The present invention relates to certain novel 2-amino-3-benzoylphenylacetic acids having alkylthio substitution on the benzoyl moiety, their alkylesters and metal salts, and pharmaceutical compositions incorporating such compounds.

Certain 2-amino-3-(5 and 6) benzoylphenylacetic acids having the benzoyl moiety substituted by lower alkyl, halogen, nitro and trifluoromethyl groups and methods of preparing and using the same are disclosed in U.S. Patent 4,045,576. The compounds of the present invention cannot be prepared by the procedures disclosed therein.

The invention is more specifically concerned with 2-amino-3-(alkylthiobenzoyl)phenylacetic acids, alkylesters and metal salts having the formula:



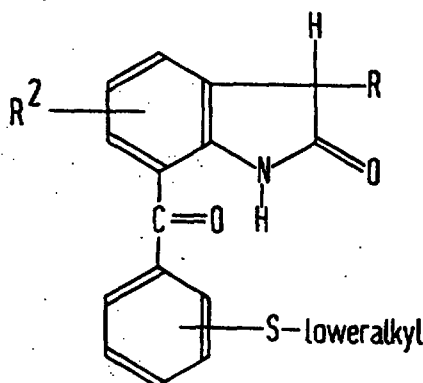
Formula I

wherein:

30 R represents a hydrogen atom or a lower alkyl group,
 R¹ represents a hydrogen atom or a lower alkyl group or a pharmaceutically acceptable metal cation,
 R² represents a hydrogen or a halogen atom or a lower alkyl or lower alkoxy group, and
 Am represents a primary amino (-NH₂), methylamino or dimethylamino group, and pharmaceutically acceptable esters and salts thereof.

35 The novel compounds of Formula I possess valuable pharmacological properties and are useful as pharmaceutical agents. The compounds exhibit anti-inflammatory and analgesic activity and inhibit blood platelet aggregation in warm-blooded animals.

United Kingdom Patent Application No. 82.14848 Serial No. which is a divisional from this application describes and claims certain novel intermediates, the 7-(S-loweralkylthiobenzoyl)-indolin-2-ones, which may be represented by Formula II:



Formula II

55 wherein R and R² are as hereinabove defined.

The anti-inflammatory activity has been demonstrated in laboratory animals using a modification of the Evans Blue Carrageenan Pleural Effusion Assay of Sancilio, L.F., J. Pharmacol. Exp. Ther. 168, 199-204 (1969).

60 The compounds of Formula I have been demonstrated to be inhibitors of blood platelet aggregation by use of the test of reduction of platelet aggregation as described by Born, J. of Phys. 162, 67-68 p. (1962) and Evans et al, J. of Expt. Med. 128, 877-894 (1968). Rats were orally administered test drugs and after 2 hrs the rats were bled and platelet rich plasma obtained. Collagen was added to the platelet rich plasma to induce platelet aggregation and comparisons were made between control and treated samples.

65 The present invention encompasses the compounds of Formula I set forth above with accompanying

definitions as composition of matter and the utilization of these novel compounds in living animals for their pharmacological effects as set forth herein.

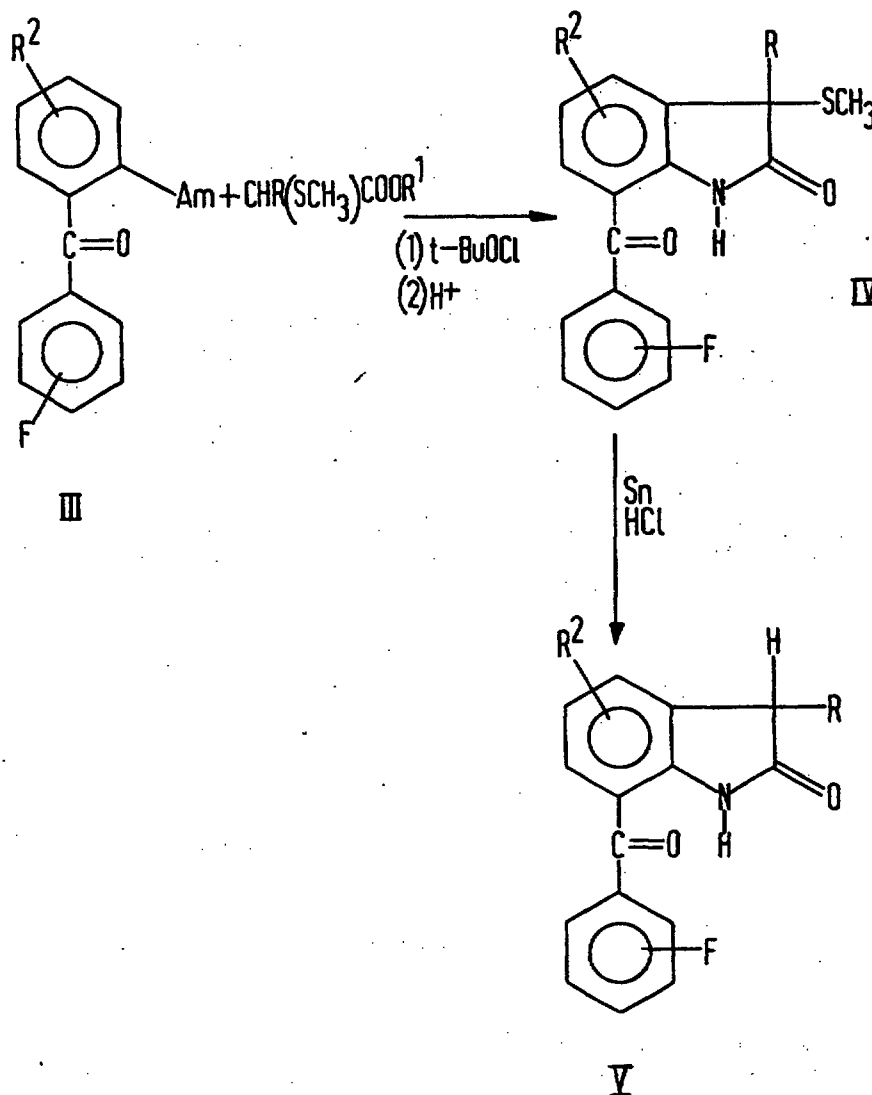
In the definition of the symbols of the formulae hereof and where they appear elsewhere throughout this specification, the terms have the following significance.

- 5 The term "lower alkyl" as used herein includes straight and branched chain groups of up to six carbons inclusive, and is exemplified by such groups as methyl, ethyl, propyl, isopropyl, butyl, secondary butyl, tertiary butyl, amyl, isoamyl and hexyl. Preferably lower alkyl groups having no more than four carbon atoms are used. The term "lower alkoxy" has the formula -O-lower alkyl.

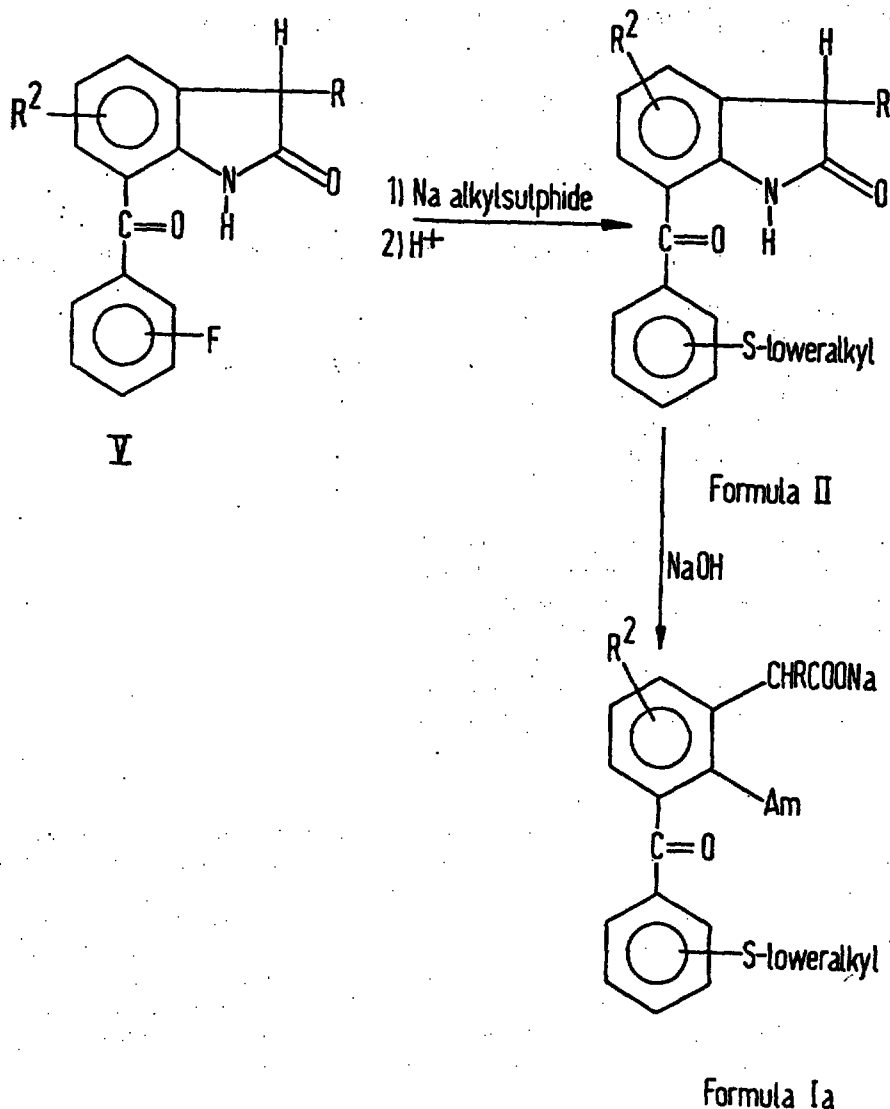
The term "halogen" when referred to herein means Cl, F, Br and I.

- 10 Illustrative of pharmaceutically acceptable metal cations are sodium, potassium, calcium, magnesium, zinc, copper and the hydrates thereof.

- The starting fluorobenzoylindolin-2-ones used to prepare the compounds of this invention may be prepared by one or more of the methods disclosed in U.S. Patent 4,045,576. One method disclosed therein begins by reacting 2-amino-4'-halobenzoylbenzophenone with ethyl methylthioacetate, t-BuOCl (tertiary butyl oxychloride) and Et₃N (triethylamine) to give 7-(halobenzoyl)-3-methylthioindolin-2-ones which are then reduced using a Raney nickel catalyst to produce the 7-(halobenzoyl)-3-indolin-2-one. A modification of this procedure was used wherein the Raney nickel was replaced by tin powder in alcohol and concentrated hydrochloric acid. The following equation is representative of the preparation of 7-(fluorobenzoyl)-indolin-2-ones used to prepare the compounds of the invention:



- 60 The preparation of the compounds of this invention is accomplished by reacting fluorobenzoyl indolin-2-ones with alkali metal alkylsulphide, followed by acid hydrolysis to obtain the 7-(alkylthiobenzoyl)indolin-2-ones and hydrolyzing with an alkali-metal base to give the alkali-metal salt of the 2-amino-3-(alkylthiobenzoyl)phenylacetic acids. The following reaction sequence illustrates the preparation of the alkali-metal salts of the compounds of Formula I:



To obtain the free acid ($R^1 = H$) from the alkali metal salt, acetic acid is carefully added to an aqueous solution of the salt which causes the free acid to precipitate. The free acid is then separated by filtration, washed with water and dried. To obtain the ester ($R^1 = \text{lower alkyl}$), the alkali metal salt is treated in a suitable solvent such as dry dimethylformamide with a lower alkyl iodide. Water is added and the ester extracted from the mixture with a suitable solvent such as diethyl ether, dried over sodium sulphate and the solvent removed by evaporation.

The compounds of Formula I wherein Am is dimethylamino are prepared by reacting a 2-aminophenylacetic acid ester of Formula I wherein Am is $-NH_2$ with formaldehyde and sodium cyanoborohydride in a solvent such as acetonitrile under mildly acidic conditions as provided by the use of glacial acetic acid.

The invention may be put into practice in various ways and a number of specific embodiments will be described to illustrate the invention with reference to the accompanying preparations 1 to 10 of some starting materials, and preparations 11 to 14 (which are the subject of our above mentioned copending application), Examples 1 to 4 of the compounds of the invention and Examples 5 to 7 of pharmaceutical compositions in accordance with the invention.

PREPARATION 1

7-(4-Fluorobenzoyl)-3-methylthioindolin-2-one.

A solution of 42.2 g (0.196 mole) of 2-amino-4'-fluorobenzophenone in 2 litres of methylene chloride was cooled to -65°C and 26.5 g (0.198 mole) of ethyl methylthioacetate was added. A solution of 23.0 g (0.21 mole) of 95% tertiary butoxychloride in 50 ml of methylene chloride was added dropwise, keeping the temperature below -65°C . One hour after the addition was complete, 22.2 g (0.22 mol) of triethylamine was added dropwise and the mixture was allowed to warm to room temperature. The solution was concentrated to 700 ml and then washed with water. The organic solution was concentrated and the residue dissolved in 400 ml of methanol containing 30 ml of concentrated hydrochloric acid. The mixture was heated at reflux for one hour followed by cooling. The mixture was allowed to stand overnight, the crystals collected and

Analysis:

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Found: C, 70.80; H, 4.12; N, 5.51

PREPARATIONS 6A to 6G

Utilizing the procedure of Preparation 5 but substituting for 7-(4-fluorobenzoyl)-3-methylthioindolin-2-one, equal molar amounts of the following:

- 5 7-(4-fluorobenzoyl)-4-methyl-3-methylthioindolin-2-one, 5
 7-(4-fluorobenzoyl)-5-methyl-3-methylthioindolin-2-one,
 7-(4-fluorobenzoyl)-6-methyl-3-methylthioindolin-2-one,
 7-(4-fluorobenzoyl)-4-chloro-3-methylthioindolin-2-one,
 7-(4-fluorobenzoyl)-5-chloro-3-methylthioindolin-2-one,
 7-(4-fluorobenzoyl)-6-chloro-3-methylthioindolin-2-one,
 10 7-(4-fluorobenzoyl)-5-methoxy-3-methylthioindolin-2-one, 10
 there are obtained:
 (6A) 7-(4-fluorobenzoyl)-4-methylindolin-2-one,
 (6B) 7-(4-fluorobenzoyl)-5-methylindolin-2-one,
 (6C) 7-(4-fluorobenzoyl)-6-methylindolin-2-one,
 15 (6D) 7-(4-fluorobenzoyl)-4-chloroindolin-2-one, 15
 (6E) 7-(4-fluorobenzoyl)-5-chloroindolin-2-one,
 (6F) 7-(4-fluorobenzoyl)-6-chloroindolin-2-one,
 (6G) 7-(4-fluorobenzoyl)-5-methoxyindolin-2-one.

20 PREPARATION 7

7-(2-Fluorobenzoyl)-indolin-2-one.

A mixture of 60 g (0.2 mole) of 7-(2-fluorobenzoyl)-3-methylthioindolin-2-one and 60 g (0.5 mol) of tin powder in one litre of 95% ethanol was heated to reflux and 150 ml of concentrated hydrochloric acid was added. Heating was continued for 18 hrs then the mixture was cooled and the precipitate was collected by
 25 decanting the slurry from the remaining tin and filtering the slurry. The filter cake was recrystallized twice from absolute ethanol to give 31 g (60%) white needles, m.p. 209-210°C.

Analysis:

30	Calculated for $C_{15}H_{10}NO_2F$:	C, 70.58; H, 3.95; N, 5.49	30
	Found:	C, 70.31; H, 4.08; N, 5.56	

PREPARATION 8.

- Utilizing the procedure of Preparation 7 but substituting for 7-(2-fluorobenzoyl)-3-methylthioindolin-2-one, equal molar amounts of the following:
 35 7-(3-fluorobenzoyl)-3-methylthioindolin-2-one, there is obtained:
 7-(3-fluorobenzoyl)-indolin-2-one.

PREPARATION 9

- 40 Utilizing the procedure of Preparation 1 but substituting equal molar amounts of ethyl α -(methylthio) propionate for ethyl methylthioacetate, there is obtained
 7-(4-fluorobenzoyl)-3-methyl-3-methylthioindolin-2-one.

PREPARATION 10

- 45 Utilizing the procedure of Preparation 5 but substituting equal molar amount of 7-(4-fluorobenzoyl)-3-methyl-3-methylthioindolin-2-one, there is obtained
 7-(4-fluorobenzoyl)-3-methylindolin-2-one.

The reaction conditions employed for preparing the novel intermediates and compounds of the invention are more fully illustrated in the examples which follow.

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PREPARATION 11

7-(4-Methylthiobenzoyl)indolin-2-one.

($R^2=R=H$; lower alkyl = CH_3)

- A solution of sodium methyl mercaptide, prepared from 400 ml of 3N sodium hydroxide and 24 g (0.5 mole) of methyl sulphide, was mixed with 25.5 g (0.1 mole) of 7-(4-fluorobenzoyl)indolin-2-one (see Preparation 5). The mixture was refluxed for 1.5 hr, cooled and acidified with caution since much methyl sulphide evolves rapidly. The resulting precipitate was collected and recrystallized twice from benzene to give 17.8 g (70%) as yellow crystals, m.p. 167.0-169.0°C.

Analysis:

60	Calculated for $C_{16}H_{13}NO_2S$:	C, 67.82; H, 4.63; N, 4.94	60
	Found:	C, 67.65; H, 4.63; N, 4.91	

PREPARATION 12A TO 12I

Utilizing the procedure of Example 1 but substituting for 7-(4-fluorobenzoyl)indolin-2-one, equal molar amounts of the following:

5	7-(4-fluorobenzoyl)-4-methylindolin-2-one, (see Preparation 6A)	5
	7-(4-fluorobenzoyl)-5-methylindolin-2-one, (see Preparation 6B)	
	7-(4-fluorobenzoyl)-6-methylindolin-2-one, (see Preparation 6C)	
	7-(4-fluorobenzoyl)-4-chloroindolin-2-one, (see Preparation 6D)	
	7-(4-fluorobenzoyl)-5-chloroindolin-2-one, (see Preparation 6E)	
	7-(4-fluorobenzoyl)-6-chloroindolin-2-one, (see Preparation 6F)	
10	7-(4-fluorobenzoyl)-5-methoxyindolin-2-one, (see Preparation 6G)	10
	7-(2-fluorobenzoyl)indolin-2-one, (see Preparation 7)	
	7-(3-fluorobenzoyl)indolin-2-one, (see Preparation 8)	
	there are obtained:	
	7-(4-methylthiobenzoyl)-4-methylindolin-2-one, (Example 12A)	
15	7-(4-methylthiobenzoyl)-5-methylindolin-2-one, (Example 12B)	15
	7-(4-methylthiobenzoyl)-6-methylindolin-2-one, (Example 12C)	
	7-(4-methylthiobenzoyl)-4-chloroindolin-2-one, (Example 12D)	
	7-(4-methylthiobenzoyl)-5-chloroindolin-2-one, (Example 12E)	
	7-(4-methylthiobenzoyl)-6-chloroindolin-2-one, (Example 12F)	
20	7-(4-methylthiobenzoyl)-5-methoxyindolin-2-one, (Example 12G)	20
	7-(2-methylthiobenzoyl)indolin-2-one (Example 12H)	
	7-(3-methylthiobenzoyl)indolin-2-one (Example 12I).	

PREPARATION 13A TO 13C

25	Utilizing the procedure of Example 1 but substituting for sodium methyl mercaptide, equal molar amounts of the following:	25
	sodium ethylmercaptide,	
	sodium isopropylmercaptide,	
	sodium-n-butylmercaptide,	
30	there are obtained the following:	30
	7-(4-ethylthiobenzoyl)indolin-2-one, (Example 13A)	
	7-(4-isopropylthiobenzoyl)indolin-2-one, (Example 13B)	
	7-(4-n-butylthiobenzoyl)indolin-2-one (Example 13C).	

35	EXAMPLE 1	35
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Sodium 2-amino-3-(4-methylthiobenzoyl)phenylacetic acid monohydrate)

	A mixture of 5.2 g (0.018 mole) of 7-(4-methylthiobenzoyl)indolin-2-one (see Preparation 11) in 75 ml of 3N sodium hydroxide was heated at reflux for 20 hrs. The red solution was cooled and a yellow precipitate formed. The precipitate was collected by filtration and washed with a small amount of cold water and then	
40	trituted with tetrahydrofuran. The precipitate was again separated by filtration, dried, and recrystallized from 95% ethanol to give 4.9 g (83%) of bright yellow needles, m.p. 244-247°C.	40
	Analysis:	

	Calculated for $C_{16}H_{16}NO_4SNa$:	C, 56.30; H, 4.72; N, 4.10	
45	Found:	C, 56.38; H, 4.62; N, 4.17	45

EXAMPLES 2A to 2L

50	Utilizing the procedure of Example 1 but substituting for 7-(4-methylthiobenzoyl)indolin-2-one, equal molar amounts of the following:	50
	7-(4-methylthiobenzoyl)-4-methylindolin-2-one, (see Example 12A)	
	7-(4-methylthiobenzoyl)-5-methylindolin-2-one, (see Example 12B)	
	7-(4-methylthiobenzoyl)-6-methylindolin-2-one, (see Example 12C)	
	7-(4-methylthiobenzoyl)-4-chloroindolin-2-one, (see Example 12D)	
55	7-(4-methylthiobenzoyl)-5-chloroindolin-2-one, (see Example 12E)	55
	7-(4-methylthiobenzoyl)-6-chloroindolin-2-one, (see Example 12F)	
	7-(4-methylthiobenzoyl)-5-methoxyindolin-2-one, (see Example 12G)	
	7-(2-methylthiobenzoyl)indolin-2-one, (see Example 12H)	
	7-(3-methylthiobenzoyl)indolin-2-one, (see Example 12I)	
60	7-(4-ethylthiobenzoyl)indolin-2-one, (see Example 13A)	60
	7-(4-isopropylthiobenzoyl)indolin-2-one, (see Example 13B)	
	7-(4-n-butylthiobenzoyl)indolin-2-one, (see Example 13C)	
	there are obtained,	
	Sodium 2-amino-3-(4-methylthiobenzoyl)-6-methylphenylacetic acid, (Example 25A)	
65	Sodium 2-amino-3-(4-methylthiobenzoyl)-5-methylphenylacetic acid, (Example 25B)	65

- Sodium 2-amino-3-(4-methylthiobenzoyl)-4-methylphenylacetic acid, (Example 25C)
 Sodium 2-amino-3-(4-methylthiobenzoyl)-6-chlorophenylacetic acid, (Example 25D)
 Sodium 2-amino-3-(4-methylthiobenzoyl)-5-chlorophenylacetic acid, (Example 25E)
 Sodium 2-amino-3-(4-methylthiobenzoyl)-4-chlorophenylacetic acid, (Example 25F)
 5 Sodium 2-amino-3-(4-methylthiobenzoyl)-5-methoxyphenylacetic acid (Example 25G) 5
 Sodium 2-amino-3-(2-methylthiobenzoyl)-phenylacetic acid, (Example 25H)
 Sodium 2-amino-3-(3-methylthiobenzoyl)-phenylacetic acid, (Example 25I)
 Sodium 2-amino-3-(4-ethylthiobenzoyl)-phenylacetic acid, (Example 25J)
 Sodium 2-amino-3-(4-isopropylthiobenzoyl)-phenylacetic acid, (Example 25K)
 10 Sodium 2-amino-3-(4-n-butylthiobenzoyl)-phenylacetic acid, (Example 25L) 10

PREPARATION 14

7-(4-Methylthiobenzoyl)-3-methylindolin-2-one.

- Utilizing the procedure of Preparation 11 but substituting 7-(4-fluorobenzoyl)-3-methylindolin-2-one (see
 15 Preparation 10) for 7-(4-fluorobenzoyl)indolin-2-one, the titled compound is obtained. 15

EXAMPLE 3

Sodium 2-amino-3-(4-methylthiobenzoyl)- α -methylphenylacetic acid.

- A suspension of 7-(4-methylthiobenzoyl)-3-methylindolin-2-one (see Preparation 14) in 3N sodium
 20 hydroxide is refluxed under nitrogen, stripped of water under vacuum, and the product is isolated by
 trituration with organic solvent. 20

EXAMPLE 4

Ethyl 2-amino-3-(4-methylthiobenzoyl)phenylacetate.

- 25 Seventeen grams (0.05 mole) of sodium 2-amino-3-(4-methylthiobenzoyl)phenylacetic acid monohydrate 25
 (see Example 1) are dissolved in approximately 150 ml of dimethylformamide and the solution treated with
 33 g ethyl iodide. The solution is stirred at room temperature for 2.5 hrs and added to water and the mixture
 extracted several times with benzene. The combined benzene extracts are washed with dilute base and
 water, dried over sodium sulphate and concentrated to obtain the titled compound.

- 30 The present invention also contemplates novel compositions containing the compounds of the invention 30
 as active ingredients. Effective quantities of any of the foregoing pharmacologically active compounds may
 be administered to a living animal body in any one of various ways, for example, orally as in capsules or
 tablets, parenterally in the form of sterile solutions or suspensions, and in some cases intravenously in the
 form of sterile solutions. In forming the novel compositions of this invention, the active ingredient is
 35 incorporated in a suitable carrier, illustratively, a pharmaceutical carrier. Suitable pharmaceutical carriers 35
 which are useful in formulating the compositions of this invention include starch, gelatin, glucose,
 magnesium carbonate, lactose and malt. Liquid compositions are also within the purview of this invention
 and suitable liquid pharmaceutical carriers include ethyl alcohol, propylene glycol, glycerine and glucose
 syrup.

- 40 The pharmacologically active compounds may be advantageously employed in a unit dosage of from 0.1 40
 to 150 milligrams. The unit dosage may be administered once daily or in multiple or divided daily doses. The
 daily dosages may vary from 0.3 to 450 milligrams. Five to 25 milligrams appears optimum per unit dose.

- It is only necessary that the active ingredient constitute an effective amount, i.e. such that a suitable
 effective dosage will be obtained consistent with the dosage form employed. The exact individual dosages
 45 as well as daily dosages will, of course, be determined according to standard medical principles under the 45
 direction of a physician or veterinarian.

The active agents of the invention may be combined with other pharmacologically active agents, or with
 buffers, antacids or the like, for administration and the proportion of the active agent in the composition may
 be varied widely.

- 50 The following are examples of pharmaceutical compositions formed in accordance with this invention. 50

EXAMPLES 5A to 5D

Capsules

Capsules of 5 mg. (Example 5A), 25 mg. (Example 5B), and 50 mg. (Example 5C) of active ingredient per capsule are prepared. With the higher amounts of active ingredient, adjustment may be made in the amount of lactose.

	Typical blend for encapsulation	Per capsule, mg.	
10	Active ingredient	5.0	10
	Lactose	296.7	
	Starch	129.0	
	Magnesium stearate	4.3	
15	Total	435.0 mg.	15

Additional capsule formulations preferably contain a higher dosage of active ingredient and are as follows:

20 EXAMPLE 5D

	Ingredients	Per capsule, mg.	
25	Active ingredient	25.0	25
	Lactose	306.5	
	Starch	99.2	
	Magnesium stearate	4.3	
30	Total	435.0 mg.	30

In Each of Examples 5A to 5D the selected active ingredients are uniformly blended with lactose, starch, and magnesium stearate and the blend is encapsulated.

35 EXAMPLE 6

Tablets

A typical formulation for a tablet containing 5.0 mg. of active ingredient per tablet follows. The formulation may be used for other strengths of active ingredient by adjustment of weight of dicalcium phosphate.

		Per tablet, mg.	
40	(1) Active ingredient	5.0	40
	(2) Corn starch	13.6	
	(3) Corn starch (paste)	3.4	
45	(4) Lactose	79.2	45
	(5) Dicalcium phosphate	68.0	
	(6) Calcium stearate	0.9	
		170.1 mg	

The procedure for making the tablets is to uniformly blend ingredients 1, 2, 4 and 5. Ingredient 3 is formed into a 10 per cent paste in water. The blend is granulated with the starch paste and the wet mass is passed through an eight mesh screen. The wet granulation is dried and sized through a twelve mesh screen. The dried granules are blended with the calcium stearate and pressed.

EXAMPLE 7

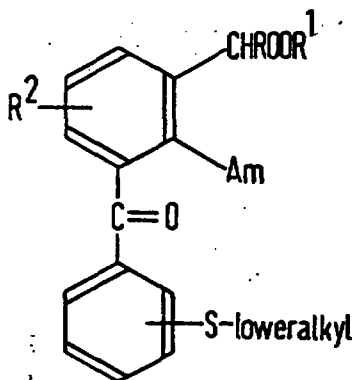
Injectable - 2% sterile solutions

		Per cc	
60	Active ingredient	20 mg.	60
	Preservative, e.g., chlorobutanol	0.5% weight/volume	
	Water for injection	q.s.	

The procedure is to prepare the solution, clarify it by filtration, and fill it into vials, which are then sealed and autoclaved.

CLAIMS

1. A compound having the formula:



wherein;

R represents a hydrogen atom or a lower alkyl group,

R^1 represents a hydrogen atom or a lower alkyl group or a pharmaceutically acceptable metal cation,

R^2 represents a hydrogen or halogen atom or a lower alkyl or lower alkoxy group and

Am represents a primary amino ($-NH_2$), methylamino or dimethylamino group.

2. 2-Amino-3-(3-methylthiobenzoyl)-phenylacetic acid.

3. Sodium 2-amino-3-(4-methylthiobenzoyl)-phenylacetate monohydrate.

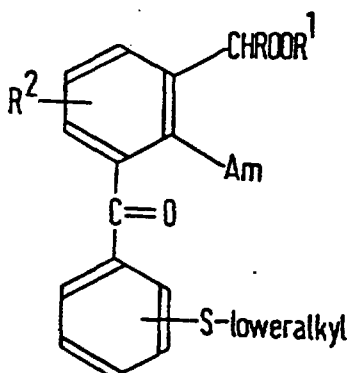
4. A compound as claimed in claim 1 and as specifically described with reference to Example 1, 2A to 2L, 3 or 4.

5. A compound as claimed in claim 1, 2, 3 or 4 for use in alleviating inflammation in a living animal body.

6. A compound as claimed in claim 1, 2, 3 or 4 for use in alleviating pain in a living animal body.

7. A compound as claimed in Claim 1, 2, 3 or 4 for use in inhibiting blood platelet aggregation in a warm-blooded animal.

8. A therapeutic pharmaceutical composition suitable for alleviating inflammation and pain and inhibiting blood platelet aggregation in a living animal body comprising an effective amount of a compound having the formula:



wherein,

R represents a hydrogen atom or a loweralkyl group,

R^1 represents a hydrogen atom or a loweralkyl group or a pharmaceutically acceptable metal cation,

R^2 represents a hydrogen or a halogen atom or a loweralkyl or lower alkoxy group and

Am represents a primary amino ($-NH_2$), methylamino or dimethylamino group and a pharmaceutically acceptable carrier or diluent.

9. A composition as claimed in Claim 8 in which the compound is present in a unit dosage form in an amount in the range 0.1 to 150 milligrams.

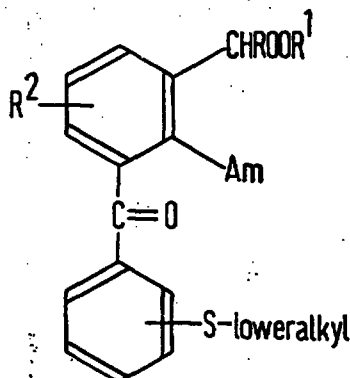
10. A composition as claimed in Claim 8 or Claim 9 in which compound is 2-amino-3-(4-methylthiobenzoyl)phenylacetic acid.



The procedure is to prepare the solution, clarify it by filtration, and fill it into vials, which are then sealed and autoclaved.

CLAIMS

1. A compound having the formula:



wherein;

R represents a hydrogen atom or a lower alkyl group,

R¹ represents a hydrogen atom or a lower alkyl group or a pharmaceutically acceptable metal cation,

R² represents a hydrogen or halogen atom or a lower alkyl or lower alkoxy group and

Am represents a primary amino (-NH₂), methylamino or dimethylamino group.

2. 2-Amino-3-(3-methylthiobenzoyl)-phenylacetic acid.

3. Sodium 2-amino-3-(4-methylthiobenzoyl)-phenylacetate monohydrate.

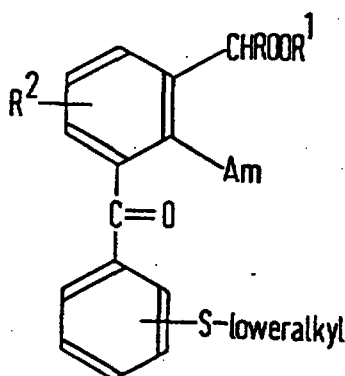
4. A compound as claimed in claim 1 and as specifically described with reference to Example 1, 2A to 2L, 3 or 4.

5. A compound as claimed in claim 1, 2, 3 or 4 for use in alleviating inflammation in a living animal body.

6. A compound as claimed in claim 1, 2, 3 or 4 for use in alleviating pain in a living animal body.

7. A compound as claimed in Claim 1, 2, 3 or 4 for use in inhibiting blood platelet aggregation in a warm-blooded animal.

8. A therapeutic pharmaceutical composition suitable for alleviating inflammation and pain and inhibiting blood platelet aggregation in a living animal body comprising an effective amount of a compound having the formula:



wherein,

R represents a hydrogen atom or a loweralkyl group,

R¹ represents a hydrogen atom or a loweralkyl group or a pharmaceutically acceptable metal cation,

R² represents a hydrogen or a halogen atom or a loweralkyl or lower alkoxy group and

Am represents a primary amino (-NH₂), methylamino or dimethylamino group and a pharmaceutically acceptable carrier or diluent.

9. A composition as claimed in Claim 8 in which the compound is present in a unit dosage form in an amount in the range 0.1 to 150 milligrams.

10. A composition as claimed in Claim 8 or Claim 9 in which compound is 2-amino-3-(4-methylthiobenzoyl)phenylacetic acid.

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11. A composition as claimed in Claim 8 or Claim 9 in which compound is sodium 2-amino-3-(4-methylthiobenzoyl)-phenyl-acetate monohydrate.
12. A pharmaceutically composition as claimed in Claim 8 substantially as specifically described herein with reference to Example 5, 6 or 7.

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