Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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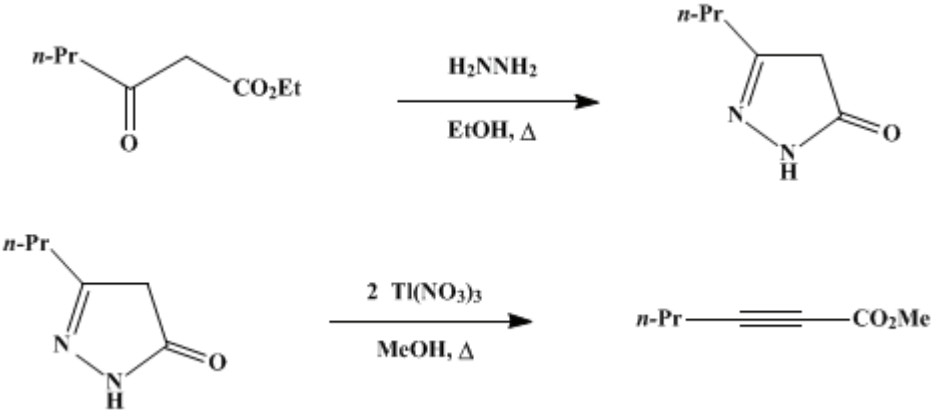
METHYL 2-ALKYNOATES FROM 3-ALKYL-2-PYRAZOLIN-5-ONES: METHYL 2-HEXYNOATE

[2-Hexynoic acid, methyl ester]



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1. Procedure

Caution! Thallium compounds are highly toxic.[3] However, they may be safely handled if prudent laboratory procedures are practiced. Rubber gloves and laboratory coats should be worn and reactions should be carried out in an efficient hood. In addition, thallium wastes should be collected and disposed of separately (Note 1).

A. *3-(1-Propyl)-2-pyrazolin-5-one*. A 500-ml., round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser is charged with 23.7 g. (0.150 mole) of ethyl 3-oxohexanoate (Note 2), 250 ml. of ethanol, and 9.8 g. (0.17 mole) of 85% aqueous hydrazine hydrate (Note 3). The mixture is stirred for 2 hours at 0° and 2 hours at reflux, then reduced in volume to 50–100 ml. on a rotary evaporator. The resulting suspension is cooled to 0–5° and suction filtered, giving 14–16 g. (77–83%) of 3-(1-propyl)-2-pyrazolin-5-one as colorless crystals, m.p. 204–206°, which are dried for 1–2 hours over anhydrous calcium chloride and used without further purification (Note 4).

B. *Methyl 2-hexynoate*. A 1-l., round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser is charged with 12.62 g. (0.1002 mole) of 3-(1-propyl)-2-pyrazolin-5-one and 500 ml. of methanol (Note 5). To this solution, 93.20 g. (0.2097 mole) of thallium(III) nitrate trihydrate (Note 6) is slowly added so as to avoid foaming. The reaction mixture is stirred for 20 minutes at room temperature and 20 minutes at reflux (Note 7) and (Note 8), then reduced to approximately half its volume by evaporation on a rotary evaporator. It is then cooled to 0–5° and filtered through fluted filter paper, removing precipitated thallium(I) nitrate. The filter cake is washed with 150 ml. of chloroform, and 250 ml. of water is added to the filtrate. The chloroform layer is separated, and two additional extractions with 100 ml. of chloroform are carried out. The combined chloroform layers are washed once with 100 ml. of 5% aqueous sodium hydrogen carbonate, twice with 100 ml. of water, and dried over anhydrous magnesium sulfate. The chloroform is removed on a rotary evaporator, and the residue is filtered through a 2 cm. by 12 cm. column of 100–200 mesh Florisil (Note 9) using approximately 250 ml. of chloroform as eluent. The chloroform is removed on a rotary evaporator, and the resulting pale yellow liquid is vacuum distilled through a 19-cm., unpacked column (Note 10), yielding 8.63–9.24 g. (68–73%) of methyl 2-hexynoate, b.p. 47–50° (5 mm.), as a colorless to slightly yellow liquid (Note 11).

2. Notes

1. The submitters recommend collection of solid wastes in an appropriate solid waste container, and liquid wastes (filtrates containing thallium residues, etc.) in suitably labeled bottles or cans. For the disposal of thallium wastes, a commercial organization specializing in the disposal of toxic materials was employed.
2. Ethyl 3-oxohexanoate is available under the name of ethyl butyrylacetate from Aldrich Chemical Company, Inc.
3. This product is available from Matheson, Coleman and Bell.
4. The pyrazolinone should be colorless. If it is not, it may be washed with a minimum of ice-cold ethanol. This procedure is convenient and yields material of adequate purity for the subsequent reaction. Additional pyrazolinone may be obtained by evaporating the filtrate and recrystallizing the residue from ethanol.
5. Commercially available anhydrous methanol was used without further treatment.
6. Thallium(III) nitrate trihydrate is best prepared fresh by dissolving, with stirring, 200 g. (0.439 mole) of thallium(III) oxide (available from American Smelting and Refining, Denver, Colorado) in 400 ml. of concentrated nitric acid. The submitters have found the proportion of 1 g. of thallium(III) oxide to 2 ml. of nitric acid to be best. Any suspended matter is removed by suction filtration through a medium fritted-glass funnel. The filtrate is cooled in an ice bath with mechanical stirring, yielding thallium(III) nitrate trihydrate as a fine white powder. The precipitate is separated by suction filtration through a medium fritted-glass funnel, pressed as dry as possible, and dried for approximately 6 hours in a vacuum desiccator over phosphorus pentoxide and potassium hydroxide. Longer drying times result in thallium(III) nitrate trihydrate of poorer quality. These crystals of thallium(III) nitrate trihydrate often occlude a considerable amount of nitric acid, with a consequent decrease in reactivity. To assure removal of occluded nitric acid, the submitters recommend grinding the initially dried material to a fine powder with a mortar and pestle and redrying in a vacuum desiccator, again over phosphorus pentoxide and potassium hydroxide, for an additional 6 hours. The resulting extremely reactive thallium(III) nitrate trihydrate should be stored in a desiccator, since it rapidly turns brown upon contact with moist air. Thallium residues may conveniently be removed with aqueous 1 *N* hydrochloric acid.
7. The reaction mixture first turns muddy brown, due to the hydrolysis of thallium(III) nitrate to thallium(III) hydroxide and thallium(III) oxide, and then yellow with the separation of colorless thallium(I) nitrate.
8. The reduction of thallium(III) to thallium(I) may be followed with potassium iodide–starch paper. A drop of solution is placed on the paper and allowed to dry. Thallium(III) gives a purple color when the paper is moistened with water, due to the oxidation of iodide to iodine by thallium(III). Thallium(I) gives a lemon-yellow color due to the formation of thallium(I) iodide.
9. This product is available from Floridin Company, Berkley Springs, West Virginia 25411. The checkers found that this filtration was not necessary.
10. Best results were obtained with an oil bath maintained at 80–85°. The bath temperature should never exceed 100°.
11. The spectral properties of the product are as follows; IR (film) $cm.^{-1}$: 2230 strong, 1718 strong, 1428 strong, 1261 strong, 1075 strong; ^1H NMR (neat), δ (multiplicity, coupling constant *J* in Hz., number of protons, assignment): 1.01 (t, $J = 7.2$, 3H, CH_3), 1.63 (m, 2H, CH_2), 2.34 (t, $J = 6.8$, 2H, $CH_2C{\equiv}C$), 3.68 (s, 3H, OCH_3). GC analysis may be conveniently carried out using 10% Carbowax 20M on 60/80 Diatoport S.

3. Discussion

Methyl 2-hexynoate has been prepared by the esterification of 2-hexynoic acid, which was prepared by the carboxylation of sodium hexynylide.[4] α,β-Alkynoic acids have generally been obtained by either carboxylation of metal alkynylides or by elimination reactions.[5] In particular, they have been prepared by the elimination of enol brosylates and tosylates,[6] an intramolecular Wittig reaction involving triphenylphosphinecarbomethoxymethylene and carboxylic acid chlorides,[7] and the base-promoted elimination reaction of 3-substituted-4,4-dichloro-2-pyrazolin-5-ones.[8]

The present method[9] affords the methyl ester directly in high yields from 2-pyrazolin-5-ones, which

are readily prepared in nearly quantitative yields from readily accessible β-keto-esters. In addition, the reaction is simple to carry out, conditions are mild, and the product is easily isolated in a high state of purity. A limitation of the reaction is that only the methyl ester can be made, as other alcohols have been found to give poor yields and undesirable mixtures of products. Table I illustrates other examples of the reaction.[10]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 348
- Org. Syn. Coll. Vol. 6, 488
- Org. Syn. Coll. Vol. 6, 709
- Org. Syn. Coll. Vol. 7, 81

TABLE I[a]
METHYL 2-ALKYNOATES FROM 2-PYRAZOLIN-5-ONES SUBSTITUTED AT POSITION 3

Substituent	Yield of Ester (%)
CH_3-	53
CH_3CH_2-	70
$(CH_3)_2CHCH_2$-	79
$CH_3(CH_2)_3CH_2$-	79
$CH_3(CH_2)_4CH_2$-	78
C_6H_5-	67
4–ClC_6H_4-	43

[a] Yields are for 0.01 mole reactions.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

triphenylphosphinecarbomethoxymethylene

ethanol (64-17-5)

calcium chloride (10043-52-4)

hydrochloric acid (7647-01-0)

methanol (67-56-1)

chloroform (67-66-3)

sodium hydrogen carbonate (144-55-8)

nitric acid (7697-37-2)

potassium iodide (7681-11-0)

iodine (7553-56-2)

potassium hydroxide (1310-58-3)

hydrazine hydrate (7803-57-8)

magnesium sulfate (7487-88-9)

Thallium (7440-28-0)

thallium(I) iodide

thallium(I)

thallium(III)

thallium(III) oxide (1314-32-5)

Methyl 2-hexynoate,
2-Hexynoic acid, methyl ester (18937-79-6)

ethyl 3-oxohexanoate,
ethyl butyrylacetate (3249-68-1)

3-(1-Propyl)-2-pyrazolin-5-one (29211-70-9)

thallium(III) nitrate trihydrate

thallium(I) nitrate (10102-45-1)

pyrazolinone

thallium(III) nitrate (13746-98-0)

thallium(III) hydroxide

2-hexynoic acid (764-33-0)

sodium hexynylide

phosphorus pentoxide (1314-56-3)