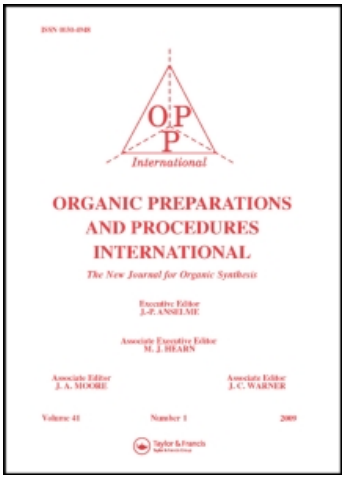

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Ramachandran, Jayalakshmi , Ramadas, S. R. and Pillai, C. N.(1981) 'MICHAEL ADDITION OF DITHIOBENZOIC ACID TO α,β-UNSATURATED KETONES. A NEW SERIES OF DITHIOESTERS', Organic Preparations and Procedures International, 13: 2, 71 — 79
To link to this Article: DOI: 10.1080/00304948109356098
URL: http://dx.doi.org/10.1080/00304948109356098

ORGANIC PREPARATIONS AND PROCEDURES INT. 13(2), 71-79 (1981)

MICHAEL ADDITION OF DITHIOBENZOIC ACID TO α,β-UNSATURATED KETONES. A NEW SERIES OF DITHIOESTERS

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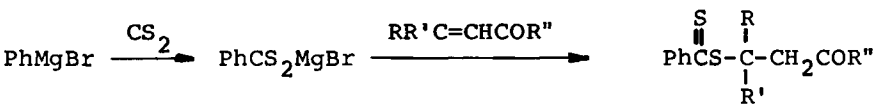
The chemistry of dithioacids and dithioesters has been extensively reviewed recently by Jansons.[1] A convenient method for the preparation of dithioacids is the reaction of Grignard reagents with carbon disulfide.[2] These dithioacids can be esterified by the use of alkylating agents such as alkyl halides, diazomethane, dimethyl sulfate to give the corresponding dithioesters.[3] Oae and coworkers[4] have reported that the Michael addition of dithioacetic acid to electrophilic olefins such as α,β-unsaturated acids, nitriles, ketones and esters under thermal conditions afforded the corresponding Michael adducts in unspecified yields.

The present study deals with the addition of the dithiocarboxylate anion (as the Grignard complex) to α,β-unsaturated



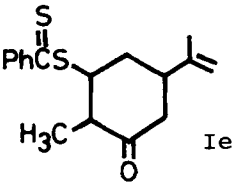
I

a) R = R" = Ph, R' = H

b) R = Ph, R' = H, R" = CH_3

c) R = R' = R" = CH_3

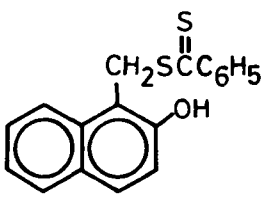
d) R = 2-furyl, R' = H, R" = CH_3



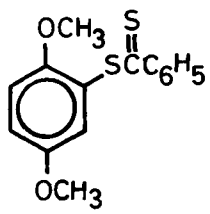
Ie

ketones as an alternate route for the preparation of a new series of dithioesters.

The halomagnesium salt $RCSS^- MgBr^+$ - obtained by the treatment of the Grignard reagent (C_6H_5MgBr) with carbon disulfide in ether-tetrahydrofuran - was treated, without isolation, with α,β-unsaturated ketones. This general procedure was adopted for the preparation of compounds Ia-e. Compound If was obtained by the addition of sodium dithiobenzoate to 1,2-dihydro-1-methylenenaphthalene-2-one formed in situ from 1-dimethylaminomethyl-2-naphthol in refluxing dioxane. The direct reaction with the halomagnesium salt in ether/THF was not successful in this case. The halomagnesium salt was also



If



Ig

unsuitable for the preparation of Ig where p-benzoquinone was the Michael acceptor. It appeared that benzoquinone was reduced to hydroquinone, probably by the excess of Grignard reagent. In this case too, the dithiobenzoic acid was isolated, converted to the sodium salt and then treated with benzoquinone in tetrahydrofuran and the product, without isolation, was methylated with dimethyl sulfate. Ester Ig is one of the few known aryl dithiobenzoates.

The products were characterized by their ir, nmr and mass spectra and gave satisfactory elemental analyses.

EXPERIMENTAL

ω-Phenyl-ω-benzenedithiocarboxypropiophenone (Ia).- Phenylmagnesium bromide, obtained from magnesium turnings (1.06 g, 0.04 mole) and bromobenzene (4 ml) in dry ether (100 ml), was cooled to -5°. A solution of carbon disulfide (4.8 ml) in dry tetrahydrofuran (30 ml) was added dropwise over a period of 15 min., with stirring under nitrogen atmosphere. The colourless Grignard complex immediately turned yellowish red. After stirring at room temperature for 0.5 hr., it was refluxed for 0.5 hr. The deep red reaction mixture was cooled to 10° and a solution of benzalacetophenone (8.32 g, 0.04 mole) in dry tetrahydrofuran (30 ml) was added dropwise over a period of 20 minutes. After stirring at room temperature for 0.5 hr., the reaction mixture was stirred at reflux temperature for 4 hrs. The reaction mixture was decomposed with ice-cold dilute hydrochloric acid (2:1) (100 ml) and the organic layer separated. The aqueous layer was extracted with ether (3 x 30 ml). The combined organic layers were washed with ice-cold water (3 x 30 ml), then with ice-cold 10% sodium hydroxide solution (3 x 50 ml) and finally with ice-cold water (3 x 30 ml). The ethereal layer was dried over anhydrous sodium sulfate and the solvent was distilled. An orange red solid was left as a residue in the flask.

The crude product was chromatographed over silica gel (120 g; 60-120 mesh, BDH; column dia. 11.5 cm; column height 80 cm) in 2 g portions. The initial fractions of the eluate with benzene-petroleum ether (2:1) (1500 ml) furnished a reasonably pure product, while the latter fractions of the eluate (200 ml) with the same solvent gave benzalacetophenone in ∿ 11% yield.

The chromatographed product (from initial fractions) was crystallized from carbon tetrachloride to give an analytically pure sample of the dithioester la in ∿ 69% yield, mp. 90-91° as orange red crystals.

IR (CCl_4): 1690 (conjugated carbonyl) 1600, 1590 and 1215 cm^{-1} (C=S). ^{1}H-NMR (CCl_4): δ3.4-4.2 (m, ABX pattern, 2H, $-CH_2-$), 5.6-5.9 (q, 1H, methine), 7.0-8.1 (m, 15H, aromatic).

Mass spectrum: m/e 209 (40%) ($M-C_6H_5CS_2$), 154 (26%) ($C_6H_5CS_2H$ McLafferty) and 105 (100%) ($C_6H_5CO^+$).

^{13}C-NMR ($CDCl_3$): δ 43.3 (t, $-CH_2-$), 40.4 (d, -CH-), 133.0, 132.3, 132.1, 128.4, 128.2, 128.1, 127.8, 127.6, 126.7, (doublets, aromatic =C-H), 144.2, 138.9, 136.1, (singlets, aromatic =C-), 195.8 (s, C=O) and 225.5 (s, C=S).

Anal. Calcd for $C_{22}H_{18}OS_2$: C, 72.93; H, 4.97.
Found: C, 72.46; H, 4.49.

The Michael addition of dithiobenzoate anion to other α,β-unsaturated ketones, viz., benzalacetone, mesityl oxide, carvone and furfural acetone were carried out in a similar fashion to afford Ib-Ie.

4-Phenyl-4-benzenedithiocarboxybutanone-2 (Ib).- Red liquid by chromatography over silica gel, 1:1 benzene-petroleum ether eluate, ∿ 59% yield.

IR (CCl_4): 1705 (saturated carbonyl) 1590, 1580, and 1215 cm^{-1} (C=S); ^{1}H-NMR: δ 1.92 (s, 3H, CH_3), 2.8-3.38 (m, ABX pattern, 2H, $-CH_2-$), 5.36-5.56 (m, 1H, methine) and 7.1-8.02 (m, 10H, aromatic).

Mass spectrum: m/e 285 (73%) ($M-CH_3$), 154 (27%) ($C_6H_5CS_2H$, McLafferty), 147 (39%) ($M-C_6H_5CS_2$), 121 (39%) (C_6H_5CS) and 43

(100%) (CH_3CO^+).

^{13}C-NMR: δ 32.9 (q, $-CH_3$), 51.0 (t, $-CH_2-$), 53.2 (d, -CH-), 129.7, 130.1, 130.8, 131.2, 131.7, 135.7 (doublets, aromatic =CH), 141.2, 147.2 (singlets, aromatic =C-), 207.0 (s, C=O) and 228.4 (s, C=S).

Anal. Calcd for $C_{17}H_{16}S_2O$: C, 68.00; H, 5.33.
Found: C, 67.72; H, 4.97.

4-Methyl-4-benzenedithiocarboxypentanone-2 (Ic).- Obtained as a violet liquid, by chromatography over silica gel, 2:2 benzene-petroleum ether eluate, followed by short path distillation, 130-135°/7 mm Hg, ∿ 58% yield.

IR (smear): 1705 (saturated carbonyl), 1595, 1580 and 1180 cm^{-1} (C=S). ^{1}H-NMR (CCl_4): δ 1.6 (s, 6H, gem-dimethyl), 1.9 (s, 3H, $-CO-CH_3$), 3.3 (s, 2H, $-CH_2-$) and 7.0-7.9 (m, 5H, aromatic).

Mass spectrum: m/e, 154 (85%) ($C_6H_5CS_2$), 98 (26%) ($M-C_6H_5CS_2H$, McLafferty), 83 (44%) [$(CH_3)_2C=C=CO$], 58 (40%) ($CH_3-C(OH)=CH_2$, McLafferty involving carbonyl) and 43 (100%) (CH_3CO^+).

Anal. Calcd for $C_{13}H_{16}S_2O$: C, 61.38; H, 6.30.
Found: C, 61.00; H, 6.55.

2-Methyl-3-benzenedithiocarboxy-5-isopropenylcyclohexanone (Id).- Obtained as orange-red needles, mp. 92°, 47% yield.

IR(CCl_4): 1705 (saturated carbonyl), 1630, 1580 and 1210 cm^{-1} (C=S); ^{1}H-NMR (CCl_4): δ 1.1-1.2 (d, 3H, $-CH_3$), 1.8 (s, 3H, vinylic CH_3), 2.06-3.18 (broad m, 7H, cyclohexyl protons), 4.83 (s, 2H, $=CH_2$) and 7.35-8.15 (m, 5H, aromatic).

Mass spectrum: m/e 154 (90%), ($C_6H_5CS_2H$, McLafferty), 151 (36%) ($M-C_6H_5CS_2$), 150 (12%) ($M-C_6H_5CS_2H$, McLafferty) and 121 (100%)

($C_6H_5CS^+$).

^{13}C-NMR($CDCl_3$): δ 11.9 (q, CH_3 on saturated carbon), 20.5 (q, CH_3 on vinylic carbon), 35.1, 46.0, 55.3 (triplets, $-CH_2-$ of cyclohexane ring), 43.1, 47.4 (doublets, -CH- of cyclohexane ring) 110.3 (t, $=CH_2$), 126.8, 128.0, 132.3 (doublets, aromatic = CH-) 144.6, 146.0 (singlets, quaternary carbons of the phenyl ring and of the unsaturated side chain), 208.3 (s, C=O) and 225.7 (s, C=S).

Anal. Calcd for $C_{17}H_{20}S_2O$: C, 64.76; H, 6.35.
Found: C, 65.12; H, 6.81.

4(2'-Furfuryl)-4-benzenedithiocarboxybutanone-2 (Ie).- Red liquid, by chromatography over silica gel, 2:1 benzene-petroleum ether eluate, ∿ 56% yield.

IR (CCl_4): 1705 (saturated carbonyl), 1625, 1590, and 1150 cm^{-1} (C=S). ^{1}H-NMR, δ 2.0 (s, 3H, $CO-CH_3$), 3.7-3.4 (d, 2H, $-CH_2-$), 5.6-5.9 (t, 1H, methine), 6.25 (broad, 3H, furan ring protons) and 7.2-8.15 (m, 5H, phenyl ring protons).

Anal. Calcd for $C_{15}H_{14}O_2S_2$: C, 62.06; H, 4.87.
Found: C, 62.12; H, 4.75.

Preparation of Sodium Dithiobenzoate.- The Grignard reagent obtained from bromobenzene (3 ml) and magnesium (0.82 g) in absolute ether (100 ml) was treated with carbon disulfide (4.5 ml) in dry tetrahydrofuran (30 ml) at -5°, following the procedure for the preparation of Ia. At the end of the reaction, the mixture was diluted with 50 ml of ether and was decomposed with ice-cold dilute hydrochloric acid (50 ml). The organic layer was separated and was extracted with ice-cold 10% sodium hydroxide solution (3 x 30 ml). The alkaline layer was acidi-

fied with ice-cold 10% hydrochloric acid. Dithiobenzoic acid separated as a red solid. It was filtered and dried. This free acid was treated with a calculated volume of 2N sodium hydroxide solution (70 ml). The red solid went into solution as sodium salt. The water was removed by azeotropic distillation with benzene and finally dried under vacuum.

1-Benzenedithiocarboxymethyl-2-hydroxynaphthalene (If).- A solution of α-dimethylaminomethyl-β-naphthol[5] (6.0 g, 0.025 mole) and sodium dithiobenzoate (4.4 g, 0.025 mole) in dioxane (75 ml), was stirred under reflux under nitrogen atmosphere for 8 hrs. At the end of the reaction, the solvent was distilled under reduced pressure. A viscous brown liquid was left. This was treated with 50 ml of ice-cold water. The resulting mixture was decomposed with ice-cold dilute hydrochloric acid and was worked out as in the preparation of Ia. The brown gum obtained was chromotographed over silica gel (120 g; 60-120 mesh; BHD; column dia 11.5 cm; column height 80 cm) in 2 g portions. The eluate with benzene-petroleum ether (2:1) (1500 ml) gave a dark red solid, which on repeated crystallization from carbon tetrachloride, gave the analytically pure sample of the dithioester, (1f), as orange red flakes in 52% yield, mp. 105-110°. IR (CCl_4): 3450-2950 (broad, OH), 1600-1560, and 1210 cm^{-1} (>C=S). ^{1}H-NMR (CCl_4): δ 5.0 (s, 2H, $-CH_2-$ and 6.7-8.0 (m, 12H, aromatic and OH protons).

Mass spectrum: m/e, 310 (27%) (M^+), 157 (25%) ($M-C_6H_5CS_2$), 156 (20%), ($M-C_6H_5CS_2H$, ortho-effect hydrogen migration), 154 (16%), ($C_6H_5CS_2H$), ortho-effect hydrogen migration) and 121 (100%) ($C_6H_5CS^+$).

Anal. Calcd for $C_{18}H_{14}S_2O$: C, 69.78; H, 4.61.
Found: C, 70.23; H, 5.11.

2-Benzenedithiocarboxy-1,4-dimethoxybenzene (Ig).- Sodium dithiobenzoate (5.28 g, 0.03 mole) and p-benzoquinone (3.24 g), 0.03 mole) in dry tetrahydrofuran were stirred at room temperature under nitrogen atmosphere for 1 hr. Stirring was continued at the reflux temperature of the solvent for 4 hrs., and the reaction mixture was cooled. Anhydrous potassium carbonate (10 g) and dimethyl sulfate (5 ml) were added and the reaction mixture was refluxed with stirring under nitrogen atmosphere for 8 hrs.

At the end, potassium carbonate was filtered and the filtrate was then diluted with 100 ml of ether. This organic layer was washed with ice-cold water (2 x 50 ml), then with ice-cold 10% sodium hydroxide and finally with ice-cold water. The organic layer was dried over anhydrous sodium sulfate and then the solvent distilled.

The crude product was obtained as a red liquid. Repeated chromatographic purification of this red liquid over silica gel (160 g, 60-120 mesh; BDH) furnished the analytically pure sample of the dithioester (1 g), with benzene-petroleum ether (1:4) eluate (1500 ml), as a red liquid in ∿ 38% yield.
IR (CCl_4): 1590, 1570, and 1215 cm^{-1} (>C=S); ^{1}H-NMR: δ 3.58 (s, 6H, $-OCH_3$), 7.5-8.4 (8H, aromatic).
Mass spectrum: m/e 168 (16%), 154 (100%) ($C_6H_5CS_2H$, hydrogen migration due to ortho-effect), 138 (69%), 136 (19%), 123 (89%), 121 (81%) and 105 (50%).
Anal. Calcd for $C_{15}H_{14}S_2O_2$: C, 57.93; H, 4.51

Found: C, 58.2; H, 4.64.

In addition methyl dithiobenzoate was also isolated in ∿ 18% yield from the petroleum ether eluate (500 ml).

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(Received December 3, 1979; in revised form August 11, 1980)