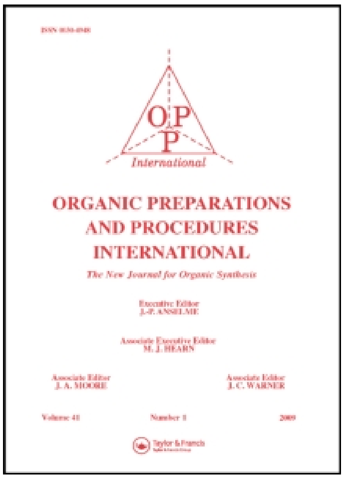


OP P International

ORGANIC PREPARATIONS AND PROCEDURES INTERNATIONAL

The New Journal for Organic Synthesis

Executive Editor
J.-P. ANSELME

Associate Executive Editor
M. J. HEARN

Associate Editor
J. A. MOORE

Associate Editor
J. C. WARNER

Volume 41 Number 1 2009

Taylor & Francis

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

SYNTHESIS OF 4-ARYL-5,6-BIS (CARBOMETHOXY)-2H-THIOPYRAN-2-THIONES. A NEW SERIES OF CYCLIC DITHIOESTERS OR α-DITHIOPYRONES

Jayalakshmi Ramachandran[a]; S. R. Ramadas[a]; C. N. Pillai[a]
[a] Department of Chemistry, Indian Institute of Technology, Madras, INDIA

To cite this Article Ramachandran, Jayalakshmi , Ramadas, S. R. and Pillai, C. N.(1981) 'SYNTHESIS OF 4-ARYL-5,6-BIS (CARBOMETHOXY)-2H-THIOPYRAN-2-THIONES. A NEW SERIES OF CYCLIC DITHIOESTERS OR α-DITHIOPYRONES', Organic Preparations and Procedures International, 13: 2, 81 — 86

To link to this Article: DOI: 10.1080/00304948109356099

URL: http://dx.doi.org/10.1080/00304948109356099

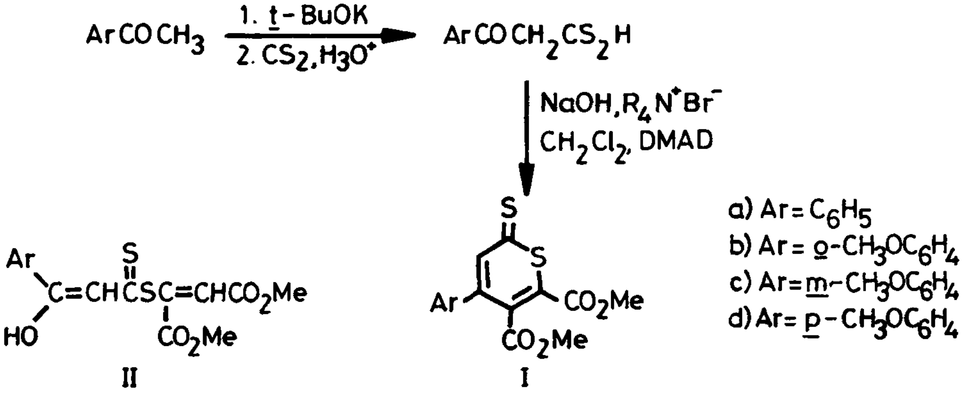
ORGANIC PREPARATIONS AND PROCEDURES INT. 13(2), 81-86 (1981)

SYNTHESIS OF 4-ARYL-5,6-BIS(CARBOMETHOXY)-2H-THIOPYRAN-2-THIONES. A NEW SERIES OF CYCLIC DITHIOESTERS OR α-DITHIOPYRONES

Jayalakshmi Ramachandran, S. R. Ramadas* and C. N. Pillai

Department of Chemistry, Indian Institute of Technology
Madras-600036, INDIA

Pradere and coworkers[1] have reported the preparation of aroyl-2-aryl-2H-thiopyran-2-thione derivatives utilizing the rather difficultly available 3-aryl-3-chloropropenals and aroyldithioacetic acid derivatives. The same year, Meyer and Scheithauer[2] also described the preparation of α-dithiopyrones employing β-halo-α,β-unsaturated ketones and suitable dithioacids. The present paper reports a very convenient procedure for the preparation of the hitherto unknown[3,4] α-dithio-



a) Ar = C_6H_5
b) Ar = o-$CH_3OC_6H_4$
c) Ar = m-$CH_3OC_6H_4$
d) Ar = p-$CH_3OC_6H_4$

pyrone system, specifically 4-aryl-5,6-bis(carbomethoxy)-2H-thiopyran-2-thione derivatives (Ia-d), employing readily available reagents under very mild conditions.

The aroyldithioacetic acid prepared by the reported procedure,[5] was neutralized with aqueous sodium hydroxide and the resulting solution was treated with dimethyl acetylenedicarboxylate (DMAD) in methylene chloride in the presence of cetyl trimethylammonium bromide (PTC catalyst). Compounds Ia-d were synthesize by this procedure. In the case where Ar = phenyl, the uncyclized product II could also be isolated. Attempts to conduct the reaction using the solution of the crude potassium salt (formed in the first stage) without isolation, gave an intractable mixture of products. This is presumably due to the fact that carbon disulfide itself reacts with dimethyl acetylenedicarboxylate to furnish a number of products.[6] Attempts to bring about the reaction using the isolated sodium salt (dry) in chloroform without the phase-transfer catalyst also proved unsuccessful.

All the dithioesters reported here were characterized by spectral and analytical data (vide Experimental). The PMR spectrum of II indicated features suggesting that it was a mixture of the _keto_ and _enol_ forms.

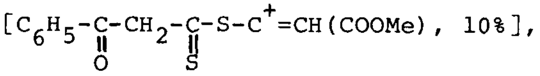
EXPERIMENTAL

Synthesis of 4-Phenyl-5,6-bis(carbomethoxy)-2H-thiopyran-2-thione (Ia) and (1,2-biscarbomethoxy)vinyl β-hydroxydithiocinnamate (II).- (a) An aqueous solution of the sodium salt of benzoyldithioacetic acid[5] (5.88 g, 0.03 mole), obtained by treating it with a calculated volume (34.6 ml) of a standard solution (1N) of sodium hydroxide was added to a stirred mixture of 75 ml of methylene chloride containing cetyl trimethylammonium bromide (1.086 g, 0.003 mole) with continuous stirring. After 10 minutes, a solution of DMAD (4.3 g, 0.03 mole) in methylene chloride (25 ml) was added dropwise over a period of 15 minutes with stirring. The reaction mixture was stirred at room temperature for 1 hr. and at 45° for 12 hrs.

After cooling, 50 ml of ice-cold water was added to the reaction mixture and the organic layer was separated. The aqueous layer was extracted with methylene chloride (2 x 30 ml). The combined organic extract was washed with ice-cold water, then with saturated sodium bicarbonate solution and finally with water. The organic extract was dried over anhydrous sodium sulphate and the solvent distilled. The crude product was obtained as a viscous red liquid.

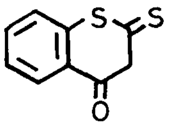
It was purified by repeated column chromatography (three times) over silica gel (120 g, 60-120 mesh, BDH, column dia. 11.5 cm, column height 80 cm). The eluate obtained with ethyl acetate-benzene (1:20) (500 ml) gave a gummy product. A few drops of carbon tetrachloride were added to this gum which was left aside at room temperature for a couple of days. A yellow solid separated. It was filtered and recrystallized from carbon tetrachloride. The pure sample of the initial Michael adduct (II) was obtained as a yellow solid, mp. 120-121°, in 21% yield.

IR (CCl_4): 1720 (ester carbonyl), 1610, 1575, 1560 (aromatic C=C) and 1200 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 3.45 [s, about 0.4 H, (-OH, enolic which disappears on exchange with D_2O)], 3.8 (s, 6H, $COOCH_3$), 4.9 (q, about 1.5 H, methylene protons of the <u>keto</u> form), 7.25 (d, about 1.4 H, due to the terminal vinylic H and the -H of the enolic double bond) and 7.45 and 7.95 (m, 5H, aromatic protons). MS: m/e 338 (M^+, 14%), 306 (M^+ - 32, -S, 3%) 279



$[C_6H_5\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_2\text{-}\underset{\underset{S}{\|}}{C}\text{-}S\text{-}C^+{=}CH(COOMe)$, 10%],

194 [



, 100%] and 105 (Ph-$\overset{+}{C}$=O, 71%)

<u>Anal</u>. Calcd. for $C_{15}H_{14}O_5S_2$: C, 53.26; H, 4.13.
Found: C, 53.69; H, 4.38.

(b) The filtrate from the isolation of compound II was evaporated under reduced pressure. The red viscous material obtained, was purified by repeated column chromatography (three times) over silica gel (120 g, BDH, 60-120 mesh, column dia. 11.5 cm, column height 80 cm). The eluate obtained with ethyl acetate-benzene (1:20) (500 ml) furnished the pure cyclic dithioester (Ia) as a thick red gum in 18% yield. The IR (CCl_4) of Ia: 1710 (conjugated ester carbonyl), 1660, 1600, 1570 (aromatic C=C) and 1160 cm^{-1} (C=S); ^1H NMR (CCl_4): δ 3.66 (s, 6H, $COOCH_3$), 3.78 (s, 3H, $-OCH_3$), 4.85 (s, 1H, olefinic proton) and 7.1-8.0 (m, 5H, aromatic protons).

<u>Anal</u>. Calcd. for $C_{15}H_{12}O_4S_2$: C, 56.26; H, 3.75.
Found: C, 55.79; H, 3.30.

<u>o</u>-Methoxyacetophenone, <u>m</u>-methoxyacetophenone and <u>p</u>-methoxyacetophenone led to the formation of Ib-d, respectively in 31%, 28% and 32% as described above.

Compounds (Ib-d) displayed the expected IR and NMR characteristics. The assigned structures for these compounds were further confirmed by ^{13}C NMR spectral data.

^{13}C NMR data ($CDCl_3$) δ values: Compound Ib: 52.5 (q, $-OCH_3$), 54.7 (q, $-CO_2CH_3$), 111.0, 112.4, 119.9, 130.1, 132.6 (d, due to one -CH- of the thiopyran ring and four =CH- of the phenyl ring), 126.8, 157.3, 159.7, 167.1, 167.7 and 168.2 (singlets, the last probably due to the ester carbonyls), and 185.5 (s, cyclic >C=S).

Anal. Calcd. for $C_{16}H_{15}O_5S_2$: C, 57.49; H, 4.19.
Found: C, 57.15; H, 3.96.

Compound Ic: 52.2 (q, $-OCH_3$), 54.1 (q, $-CO_2CH_3$), 107.8, 113.2, 129.5 (d, due to =CH- of the thiopyran and of the phenyl ring) 159.6, 161.0, 162.0, 162.8, 166.8, 167.8, and 168.5 (singlets, the last one probably due to the ester carbonyls) and 184.2 (s, cyclic >C=S).

Anal. Calcd. for $C_{16}H_{14}O_5S_2$: C, 57.49; H, 4.19.
Found: C, 56.95; H, 3.89.

Compound Id: 52.9 (q, $-OCH_3$), 53.2 (q, $-CO_2CH_3$), 107.9, 112.1, 118.7, 119.9, 129.1 (d, one=CH- of the thiopyran and the rest due to =CH- of the phenyl ring), 138.6, 159.5, 162.2, 167.8, 168.1 (singlets, the last one probably due to the ester carbonyls) and 185.5 (s, cyclic >C=S).

Anal. Calcd. for $C_{16}H_{14}O_5S_2$: C, 57.49; H, 4.19.
Found: C, 57.88; H, 4.58.

REFERENCES

1. J. P. Pradere, G. Alain, D. Guy, J. P. Guemas and H. Quiniou, C. R. Acad. Sci. [C], 269, 929 (1969).
2. R. Meyer and S. Scheithauer, Z. Chem., 9, 59 (1969).

3. E. Jansons, Usp. Khim., 45, 2020 (1976); Chem. Abstr., 86, 70959 (1977).

4. "Organic Chemistry of Sulfur", Ed. by S. Oae, Plenum Press, New York, 1977, p. 160.

5. F. C. V. Larsson and S. O. Lawesson, Tetrahedron, 28, 5341 (1972).

6. H. D. Hartzler, J. Am. Chem. Soc., 95, 4379 (1973).

(Received December 3, 1979; in revised form October 8, 1980)