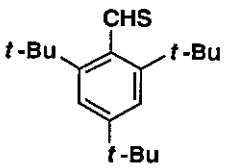
A NOVEL DITHIOPHTHALIDE SYNTHESIS

Peter N. Nugara, Nai-Zhong Huang, M. V. Lakshmikantham, and Michael P. Cava*

Department of Chemistry, The University of Alabama, Box 870336, Tuscaloosa, Alabama 35487-0336, U.S.A.

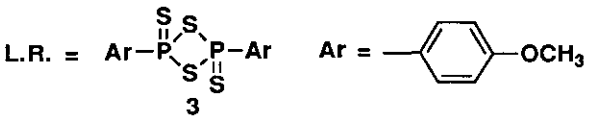
Abstract - Thionation of *o*-phthalaldehyde and naphthalene-2,3-dicarboxaldehyde with Lawesson's reagent led to the efficient formation of dithiophthalide and 2,3-dithionaphthalide respectively. Dithioaldehydes are presumed intermediates in these conversions.

In contrast to aromatic thioketones, aromatic thioaldehydes represent a highly reactive and little known class of compounds. The only stable monomeric examples are certain heterocyclic push-pull stabilized thioaldehydes, and the highly sterically stabilized 2,4,6-tri-*tert*-butylthiobenzaldehyde.[1,2]



1

Nothing appears to be known regarding the generation and subsequent fate of an aromatic *o*-dithioaldehyde. For this reason, we now record our observations concerning the reaction of *o*-phthalaldehyde (2) with Lawesson's Reagent (LR, 3), a useful thionating agent for a variety of carbonyl functions.[3]

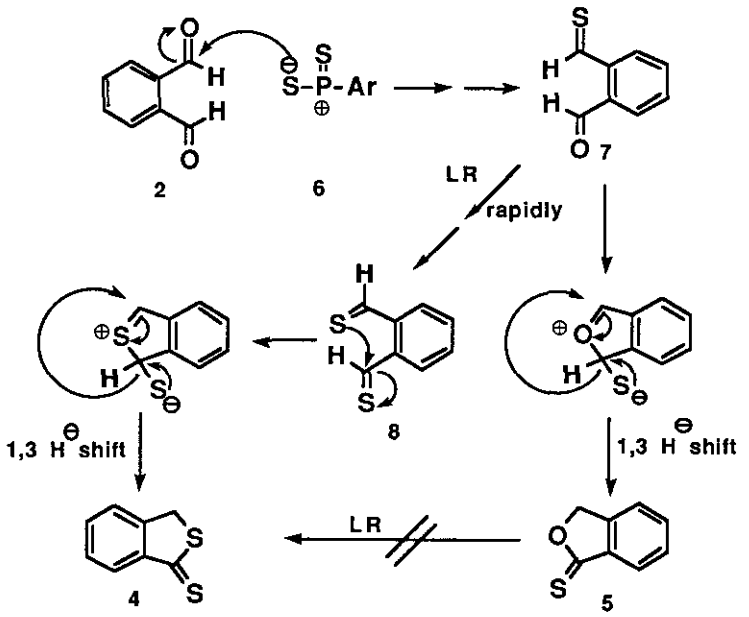


3

1

o-Phthalaldehyde reacted with LR in refluxing chlorobenzene to give dithiophthalide (4, 51%) in addition to 1 or 2% of thionophthalide (5). A similar reaction in chloroform at room temperature was complete in thirty minutes, and afforded 4 in 78% yield, making this the most convenient synthesis of dithiophthalide.[4]

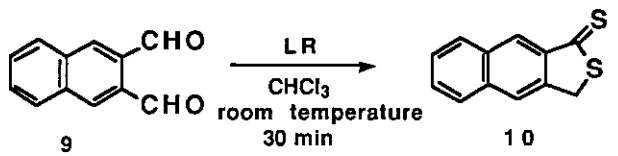
The suggested mechanism of this transformation is shown in Scheme 1. Thionation of *o*-phthalaldehyde by the reactive monomeric form (6) of LR first produces the monothioaldehyde (7), which is then rapidly thionated to *o*-dithiophthalaldehyde (8). Intramolecular cyclization of the two thione functions, followed by a 1,3-hydride shift, leads to the dithiolactone (4). If a small amount of monothioaldehyde (7) cyclizes in a similar manner prior to further thionation, the thionophthalide (5) is produced. The thionolactone (5) does not react with LR under the thionation conditions employed, showing it is not an intermediate in the synthesis of dithiophthalide.



Scheme 1

The visible spectrum of a thionation reaction run in dichloromethane showed, in addition to the strong maximum of dithiophthalide at 493 nm, transient peaks at 545, 606 and 706 nm. Since 2,4,6-tri-*tert*-butylthiobenzaldehyde (**1**) and thiobenzaldehyde are reported to exhibit maxima at 552 and 590 nm,[1,2] we suggest that the 545 and 606 nm bands may be attributed to the monothioaldehyde (**7**) while that at 706 nm may be attributed to the dithioaldehyde (**8**).

The thionation of 2,3-naphthalenedicarboxaldehyde[5] (**9**) was also examined. The reaction in chloroform was rapid and very clean, and afforded the previously unreported dithio-2,3-naphthalide (**10**) in 96% yield.



EXPERIMENTAL SECTION

Dithiophthalide **4**

To a solution of *o*-phthalaldehyde (0.54 g, 4.0 mmol) in chloroform (30 ml) was added LR (2.0 g, 5 mmol).The reaction mixture was stirred at room temperature for 30 min and the chloroform was then removed under reduced pressure. The residue was heated with ethanol until the evolution of hydrogen sulfide ceased. Evaporation of the ethanol, followed by extraction of the residue with eight 10 ml-portions of hexane and filtration through a short pad of silica gave a dark solution which was concentrated to approximately 6 ml and cooled in an ice bath to give **4**, 0.52 g (77.7%) as orange needles, mp 63-64 °C, (lit.[4] mp 67 °C). ^{1}H Nmr (360 MHz, $CHCl_3$) δ 8.08 (d, J = 7 Hz, 1H), 7.64 (t, J = 7 Hz, 1H), 7.56 (d, J = 8 Hz, 1H), 7.48 (t, J = 8 Hz, 1H), 4.54 (s, 2H). ^{13}C Nmr(90 MHz, $CDCl_3$) δ 228.5, 147.3, 144.3, 132.6, 128.1, 125.5, 124.7, 40.8.

When the thionation of *o*-phthalaldehyde was done in refluxing chlorobenzene the major product (**4**) and the minor product (**5**), mp 106-108 °C, (lit.[4] mp 109-110 °C) were isolated by radial chromatography. ^{1}H Nmr for **5** (200 MHz, $CDCl_3$) δ 8.09-7.49 (m, 4H), 5.59 (s, 2H).

Dithio-2,3-naphthalide **10**

To a solution of 2,3-naphthalaldehyde[5] (0.32 g, 1.8 mmol) in 20 ml of chloroform was added LR (1.5 g, 3.7 mmol). The reaction mixture was stirred at room temperature for 30 min and the chloroform was then removed under reduced pressure. The residue was heated with ethanol until the evolution of hydrogen sulfide ceased. Filtration of the ethanolic solution gave a red flaky solid, which was recrystallized from methanol/water to give **10**, 0.36 g, (96 %) mp 153-154 °C. ^{1}H Nmr(360 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.08 (d, J = 11 Hz, 1H), 7.97 (s, 1H), 7.90 (d, J =11 Hz, 1H), 7.65 (t, J =7 Hz, 1H), 7.56 (t, J = 7 Hz, 1H), 4.71 (s, 2H). ^{13}C Nmr(90 MHz, $CDCl_3$) 228.5, 147.3, 144.0, 132.6, 128.1, 125.5, 124.6, 40.8. Ir(KBr) 1280, 1175, 1120, 1070, 750 cm^{-1}. Ms m/z 216. Anal. Calcd for $C_{12}H_8S_2$: C, 66.66; H, 3.70; S, 29.63. Found: C, 66.47; H, 3.79; S. 29.57.

ACKNOWLEDGMENT

We thank the National Science Foundation for a grant (CHE 9001714) in support of this work.

REFERENCES

1. J. E. Baldwin and R. C. G. Lopez, Tetrahedron, 1983, 39, 1487 and references cited therein.
2. R. Okazaki, A. Ishii, N. Fukuda, H. Oyama, and N. Inamoto, J. Chem. Soc., Chem. Commun., 1982, 1187.
3. M. P. Cava and M. I. Levinson, Tetrahedron , 1985, 41, 5061.
4. M. Renson and R. Collienne, Bull. Soc. Chim. Belg., 1964, 73, 491.
5. W. Ried and H. Bodem, Chem. Ber., 1956, 89, 708.

Received, 17th May, 1991