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SYNTHESIS OF 2H-THIOPYRANS FROM 3-DIALKYLAMINODITHIOACRYLATES AND MALEIC ANHYDRIDE

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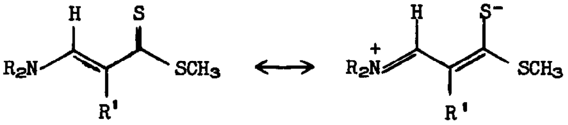
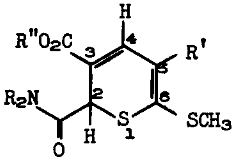
In the course of a study[1] of the chemistry of the 3-dialkylaminodithioacrylates, a reactive group of compounds readily derived[1a] from the trithiones, dithioacrylates 1a-c were observed to undergo rapid (ca. 1 hr) reaction with maleic anhydride in benzene at ambient temperature to afford in high yield (91, 69, and 73%, respectively) a series of isostructural 1:1 adducts[2] which have now been shown by single-crystal X-ray analysis to possess the 2H-thiopyran structure 2.





1 a: R'=H, R_2N=ON
b: R'=CH_3, R_2N=ON
c: R'=H, R_2N=$(CH_3)_2N$

2 a: R'=H, R_2N=ON, R"=H
b: R'=CH_3, R_2N=ON, R"=H
c: R'=H, R_2N=$(CH_3)_2N$, R"H
d: R'=CH_3, R_2N=ON, R"=Br-◯-CH_2

Although the infrared and nmr spectra[3] of these adducts clearly show them to be unsaturated carboxylic acids, neither the spectral parameters nor the results of chemical degradation allowed assignment of a unique structure. The adduct from dithioacrylate 1b and maleic anhydride was therefore converted to the corresponding p-bromobenzylester 4 in 66% yield by treatment with p-bromophenyldiazomethane (from nickel peroxide-oxidation of p-bromobenzaldehyde hydrazone).

Crystals of the ester, mp 140-141°, were grown by slow cooling of a saturated cyclohexane-benzene solution. The unit cell is monoclinic, space group $P2_1$-C_2^2, a = 11.36(1), b = 8.052(5), c = 11.77(1) A, β = 99.86(5)°. The measured density is 1.52 ± 0.02 g-cm^{-3} and the calculated density is 1.516 g-cm^{-3} for $C_{20}H_{22}O_4NS_2Br$ with Z = 2. The intensity data were collected by the Θ-2Θ scan technique on a Picker Automatic four-circle diffractometer using graphite monochromatized Mo Kα radiation. The structure was solved by interpretation of a series of three-dimensional Patterson functions, Fourier and difference Fourier syntheses, and least-square calculations, and was refined by full-matrix least squares to an R value of 0.057 for 1429 observed reflections. The molecular structure and principal bond distances are shown in Figure I; C(9)-C(10) and C(11)-C(12) and double bonds. All of the hydrogen atoms were located from a difference Fourier synthesis. Full structural details will be reported later.[5]

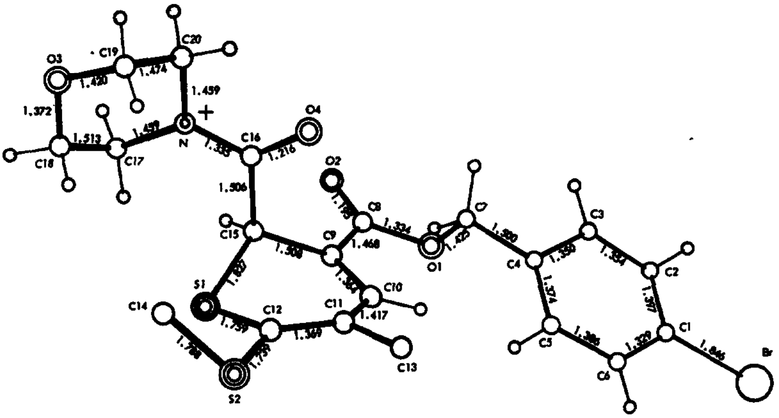
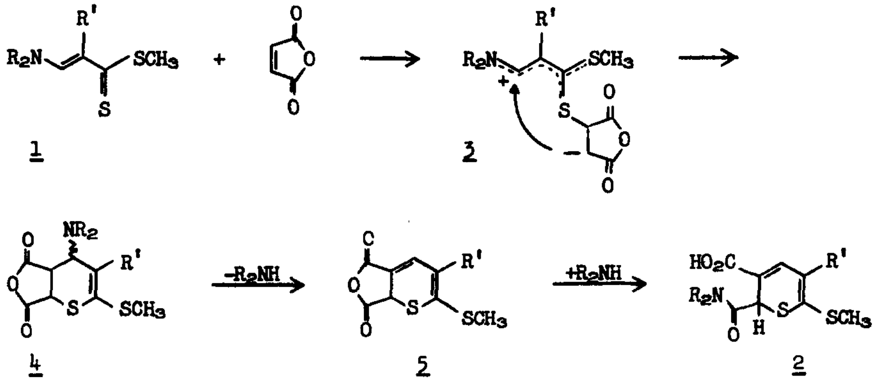


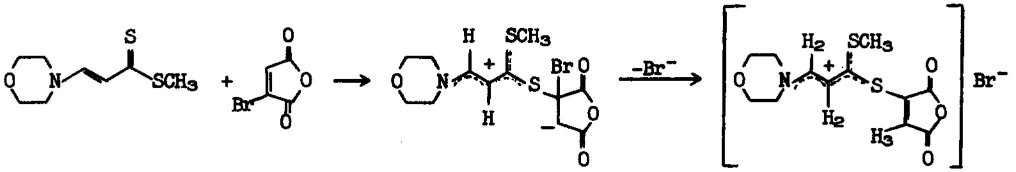
Figure I
The molecular structure of 2H-thiopyran 2d

A reasonable mechanism congruent with formation of 2H-thiopyrans 2a-c is presented in Scheme I. That the reaction is initiated by attack of the nucleophilic thiono sulfur atom of



Scheme I

the dithioacrylate at the electrophilic double bond of maleic anhydride to give the delocalized zwitterionic intermediate 3 follows from (a) the known chemistry of the dithioacrylates;[1b] (b) the observation that both succinic and phthalic anhydride, compounds in which the double bond is either absent or rendered unreactive, are inert towards the dithioacrylates, even under more vigorous conditions than required for reaction with maleic anhydride; and (c) the quantitive formation of salt 6[2,7,8], mp 143-144° dec, from the reaction of dithioacrylate 1b with bromomaleic anhydride (benzene, ambient temperature); loss of bromide ion from zwitterion 7 is apparently more rapid than cyclization.



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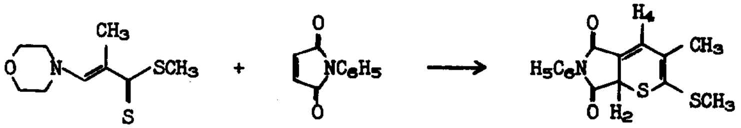
Elimination of dialkylamine from 4 (formally the Diels-Alder adduct of 1 and maleic anhydride) is presumably facilitated by the increased delocalization in adduct 5 which, in turn, apparently undergoes rapid ring-opening by the liberated amine specifically at the higher-energy unconjugated carbonyl group with concomitant relief of strain to afford the observed 2*H*-thiopyrans. Although attempts to isolate or detect (nmr) intermediate adducts 4 and 5 were uncucessful, adduct 8[2,10] was obtained in 62% yield from the reaction of dithioacrylate 1b with N-phenylmaleimide (benzene, ambient temperature); as expected, the imide ring in 8 apparently undergoes ring opening by the liberated amine less readily than does the anhydride function of 5.



1b

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Further discussion of the mechanism of this reaction as well as the reaction of the dithioacrylates with other unsaturated systems is reserved for the full paper.

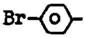
Acknowledgement

We wish to acknowledge the skillful technical assistance of Mr. Raymond T. Moy.

References

1. (a) E. J. Smutny, W. V. Turner, E. D. Morgan, and R. Robinson, *Tetrahedron*, **23**, 3785 (1967); (b) E. J. Smutny, *J. Amer. Chem. Soc.*, **91**, 208 (1967).
2. Satisfactory elemental analyses and/or high-resolution mass spectral molecular weights were obtained for all new compounds.

3. Nmr spectra: <u>2a</u> (DMSO-<u>d</u>$_6$): τ 2.74 (1 H, d, $|J| = 7.2$ Hz, H_4), 3.74 (1 H, d, $|J| = 7.2$ Hz, H_5), 4.90 (1 H, s, H_2), 6.47 (8 H, m, -), 7.55 (3 H, s, $-SCH_3$); <u>2b</u> ($CDCl_3$): τ -1.23 (1 H, s, exchangeable with D_2O, $-CO_2H$), 2.61 (1 H, s, H_4), 5.18 (1 H, s, H_2), 6.33 (8 H, m, -), 7.57 (3 H, s, $-SCH_3$), 7.89 (3 H, s, $CH_3-\overset{|}{C}=C\langle$); <u>2c</u> ($CDCl_3$): τ -0.48 (1 H, d, $|J| = 7.4$ Hz, H_4), 3.77 (1 H, d, $|J| = 7.4$ Hz, H_5), 5.10 (s, 1 H, H_2), 6.95 (6 H, broad d, $-N\langle^{CH_3}_{CH_3}$), 7.55 (3 H, s, SCH_3).

4. Nmr ($CDCl_3$): τ 2.62 (4 H, AA'BB' m, Br--), 2.65 (1 H, s, H_4), 4.88 (2 H, d, $|J| = 13.7$ Hz, Br--<u>CH$_2$</u>O_2C-), 5.20 (1 H, s, H_1), 6.40 (8 H, m, -), 7.62 (3 H, s, $-SCH_3$), 7.92 (3 H, s, $-CH_3$); ir (Nujol): 1690 (conjugated ester carbonyl), 1630 cm^{-1} (amide carbonyl).

5. The crystal structure of 2,6-diphenyl-3-benzyl-2<u>H</u>-thiopyran-5-carboxaldehyde has been determined previously.[6] Comparisons with the structure of 2<u>H</u>-thiopyran <u>2d</u> will be made in the full paper.

6. M.-U. Haque and C. N. Caughlan, <u>J</u>. <u>Org</u>. <u>Chem</u>., <u>32</u>, 3017 (1967).

7. Nmr (D_2O): τ 0.03 (1 H, d, $|J| = 7.2$ Hz, H_1), 3.52 (1 H, d, $|J| = 7.2$ Hz, H_2), 3.65 (1 H, s, H_3), 6.35 (8 H, m, -), 7.47 (3 H, s, $-SCH_3$); ir (KBr): 1830, 1760 cm^{-1} (anhydride carbonyl).

8. Examination of molecular models indicates that in all probability <u>6</u> possesses the <u>trans</u>-configuration at the (formal) carbon-carbon double bond. The observed 7.2 Hz coupling constant is in accordance with the known[9] decrease in $|J|_{trans}$ with increase in the electronegativity of substituents on the double bond.

9. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Oxford, 1966, Vol. 2, pp 714-716.

10. Nmr ($CDCl_3$): τ 2.57 (5 H, broad s, $>NC_6H_5$), 2.98 (1 H, broadened d, $|J| = 1.7$ Hz, H_4), 7.41 (3 H, s, $-SCH_3$), 7.80 (3 H, s, $CH_3-\overset{|}{C}=C\langle$); ir ($CHCl_3$): 1770, 1710, 1650 cm^{-1}.