(12) J. L. Cotter and A. G. Evans, *J. Chem. Soc.*, 2988 (1959).
(13) See, for example, M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1435 (1957).
(14) S. Sugasawa and K. Fujiwara, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 72.
(15) M. Schlosser, *Newer Methods Prep. Org. Chem.*, **5**, 301 (1968).
(16) H. Wolff, *Org. React.*, **3**, 327 (1946).
(17) Yu. A. Bruk and F. Yu. Rachinskii, *Zh. Org. Khim.*, **3**, 2174 (1967).
(18) L. Horner and H. Fernekess, *Chem. Ber.*, **94**, 712 (1961).

Salicylidene–Thiolactone Rearrangement. A Direct Synthesis of 4*H*-2-Arylthieno[3,2-*c*][1]benzopyran-4-ones

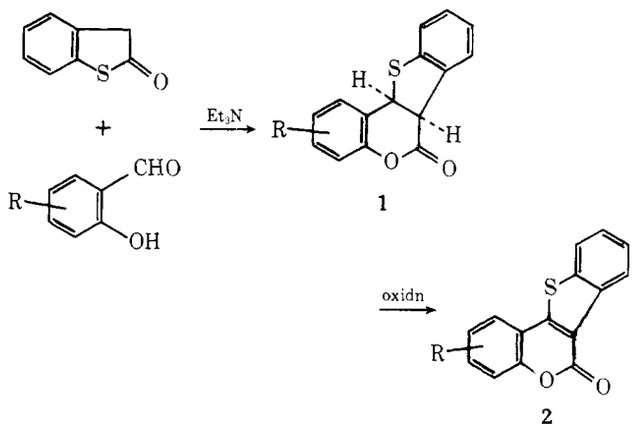
Ned D. Heindel,* John A. Minatelli, and Diane Harris

Department of Chemistry, Lehigh University, Bethiehem, Pennsylvania 18015

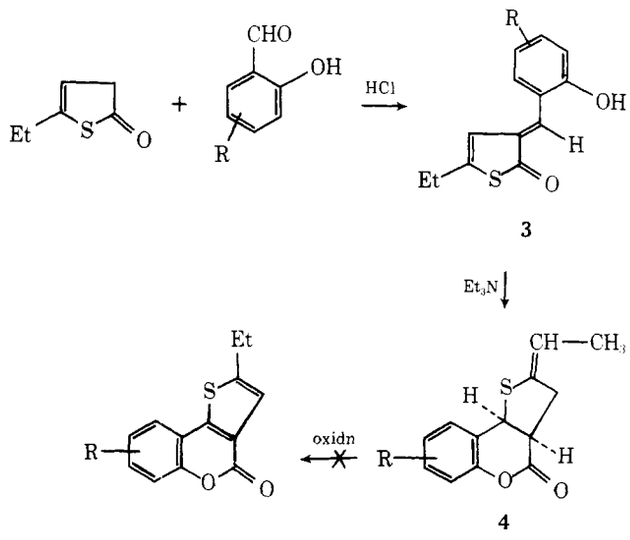
Received November 2, 1976

Previous publications from these laboratories have reported two related molecular transformations: the benzylidene–thiolactone rearrangement[1] and the salicylidene–thiolactone rearrangement.[2,3] In one of these, condensation of salicylaldehydes with thianaphthen-2-ones led to dihydrothienobenzopyranones (1) which upon oxidation gave the fully aromatized forms (**2**)[2] (see Scheme I). The salicylidene intermediates (**3**) were actually isolated in the condensation of 5-ethyl-4-thiolen-2-one and were rearranged to dihydrothienobenzopyranones (**4**).[3] Oxidations of the latter were unsuccessful and this resistance has been attributed to the exocyclic unsaturation in **4** (see Scheme II).

Scheme I



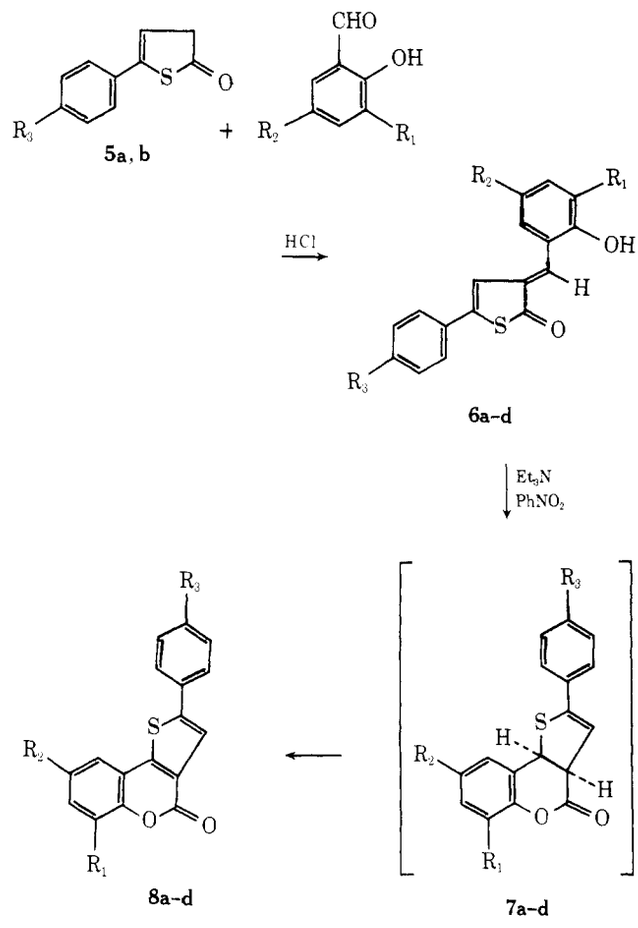
Scheme II



Several new thienobenzopyrans which bear unsaturation at the ring fusion locus have demonstrated potency as tranquilizers, analgesics, and antipyretics.[4-6] Although our earlier studies with 5-ethyl-4-thiolen-2-one did not lead to such oxidized products, we wish to report a new method which applies the salicylidene–thiolactone rearrangement to the direct preparation of such fully aromatized thienobenzopyranones. In this procedure, attachment of an aryl moiety at C-5 of the thiolenone prevents exocyclic unsaturation in the rearranged intermediate and greatly facilitates dehydrogenative oxidation.

These 5-aryl-4-thiolen-2-ones (**5a, 5b**) were prepared by sulfuration and cyclization of β-aroylpropionic acid according to a method developed by Kosak.[7] Although highly labile to oxidative formation, especially in basic media, of indigoid dimers,[7] these thiolactones could be condensed with salicylaldehydes under acidic conditions to yield stable, crystalline salicylidene derivatives (see Scheme III). These compounds (**6a–d**) were orange to red solids which gave positive $FeCl_3$ tests and which displayed carbonyl absorptions at 1653 ± 10 cm^{-1}. Only one vinylic hydrogen could be detected in the ^1H NMR spectrum and that resonance invariably fell within the aromatic complex. It thus appears that these salicylidenes possess the more sterically favored trans configuration (vinyl proton cis to carbonyl). Earlier reports have indicated a greater anisotropic deshielding for trans vinyls in closely related systems.[8-10]

Scheme III



While stable to nonbasic refluxing solvents at temperatures up to 80 °C, these salicylidenes underwent facile rearrangement—apparently after initial isomerization to a cis configuration—with amine bases at temperatures as low as 5–10 °C. Rearrangements carried out with triethylamine in chloroform, even under nitrogen atmosphere, invariably gave difficultly

Table I. Thiolenone–Salicylidenes and the Thieno[3,2-*c*][1]benzopyran-4-ones Produced by Their Rearrangement

				6			8		
Compd	R_1	R_2	R_3	% yield	Mp, °C	Mol formula[a]	% yield	Mp, °C	Mol formula[b]
a	H	H	H	89	172–173	$C_{17}H_{12}O_2S$	60	155–157	$C_{17}H_{10}O_2S$
b	H	Cl	H	53	204–206	$C_{17}H_{11}ClO_2S$	74	215–217	$C_{17}H_9ClO_2S$
c	OCH_3	H	H	83	160–162	$C_{18}H_{14}O_3S$	44	204–206	$C_{18}H_{12}O_3S$
d	H	H	CH_3	28	184–186	$C_{18}H_{14}O_2S$	43	202–204	$C_{18}H_{12}O_2S$

[a] All compounds were analyzed for C and H and had values within ±0.4% of theoretical for these elements. [b] All compounds were analyzed for C, H, and S and had values within ±0.4% of theoretical for these elements.

separable mixtures whose infrared spectra implicated the presence of a nonconjugated lactone, presumably **7a–d** (C=O approximately 1745 cm^{-1}) and a conjugated one, **8a–d** (C=O approximately 1725 cm^{-1}). Low yields of the dehydrogenated compounds could, in fact, be isolated but **7a–d** could not be obtained in pure form.

If conditions were altered to provide a mildly oxidizing solvent (nitrobenzene) excellent yields of the rearranged and dehydrogenated products could be directly obtained (see Table I). These products were characterized as the 4*H*-2-arylthieno[3,2-*c*][1]benzopyran-4-ones (**8a–d**) by the absence of the usual ring-fusion methinyl doublets in the ^1H NMR, by the conjugated lactone carbonyls at 1727 ± 3 cm^{-1}, by suitable elemental analyses, and by unique mass spectral fragmentation patterns.

The electron impact scission pathways established for 2-arylthiophenes[11] and for coumarins[12] were evident in the spectra of these 2-arylthienobenzopyranones. The molecular ion constituted the base peak in each case with weak (approximately 10% relative intensity) peaks appearing at half mass ($M^+/2e$). The $ArC{\equiv}S^+$ peak reported for thiophene models was one of the few strong fragment ions (*m/e* 121 in **8a–c** and *m/e* 135 in **8d**). The typical coumarin-like successive scission from the parent ion of CO and CHO was found in **8a** and **8d.**[12] In the methoxy analogue (**8c**), these two carbon monoxide cleavages followed an initial demethylation ($M^+ - CH_3$ or *m/e* 293, then *m/e* 265 and 237). However, this pattern, too, is in exact accord with that reported by Barnes and Occolowitz for 7-methoxycoumarin in which a demethylation precedes two CO losses.[13] In the chlorinated thienobenzopyranone (**8b**) the dual CO fragmentations compete with the halogen scission. Thus the molecular ion decomposes ($M^+ \rightarrow 284 \rightarrow 249 \rightarrow 221$ amu) for loss of CO, Cl, and CO and decomposes ($M^+ \rightarrow 277 \rightarrow 249 \rightarrow 221$ amu) for loss of Cl, CO, and CO.

Experimental Section

All of the melting points are uncorrected. ^1H NMR spectra were recorded on a Hitachi R20A spectrometer. IR spectra were obtained on a Perkin-Elmer Model 257. Mass spectra were provided, in part, by Dr. James Sturm of the Lehigh University Mass Spectrometry Laboratory on a Hitachi RMU-6E double focusing mass spectrometer and, in part, by Dr. Barbara L. Jelus of the University of Delaware Mass Spectrometry Laboratory on a CEC 21-110B. In both facilities the ionizing voltage was 70 eV and the temperature of the direct solids inlet was 60–80 °C. Microanalyses were provided by Robertson Microanalytical Laboratory, Florham Park, N.J.

Preparation of 5-Aryl-4-thiolen-2-ones (5a,b). 5-Phenyl-4-thiolen-2-one (**5a**) was prepared from β-benzoylpropionic acid and P_2S_5 in anhydrous pyridine–chloroform according to Kosak's method.[7] A yield of 12% of light green crystals was isolated (from 1:1 ethyl ether–hexane) and these darkened rapidly in air as noted. A melting point of 85–86 °C (lit. mp 81–82 °C)[7] could be obtained by sublimation, leaving a purple residue behind. Elemental analyses were not in accepted accord with the theoretical values but spectral data supported the structure: IR (KBr) 1725 cm^{-1}; NMR ($CDCl_3$) δ 3.39 (d, J = 3 Hz, C_3H_2), 5.75 (t, J = 3 Hz, C_4H), and 7.30–7.90 (m, 5 H, ArH); mass spectrum *m/e* 176 (M^+), 148 ($M^+ - CO$), and 115 ($M^+ - HCSO$). Anal. Calcd for $C_{10}H_8OS$: S, 18.18. Found: 19.08.

5-*p*-Tolyl-4-thiolen-2-one (**5b**) was synthesized in 23% yield from β-toloylpropionic acid and P_2S_5 exactly as described for the phenyl analogue. This compound too was oxidatively labile and the initially obtained pale green solid (from 1:1 ether–hexane) became deep purple on exposure to air. Sublimation in vacuo gave white crystals, mp 95–97 °C: IR (KBr) 1730 cm^{-1} (CO); NMR ($CDCl_3$) δ 2.35 (s, 3 H, $ArCH_3$), 3.65 (d, J = 3 Hz, C_3H_2), 6.06 (t, J = 3 Hz, C_4H), and 7.07–7.50 (m, 4 H, ArH); mass spectrum *m/e* 190 (M^+), 162 ($M^+ - CO$), and 129 ($M^+ - HCSO$). Anal. Calcd for $C_{11}H_{10}OS$: C, 69.44; H, 5.30; S, 16.85. Found: C, 67.60; H, 5.45; S, 17.80.

Both compounds were employed immediately after synthesis in the preparation of the salicylidene derivatives, which were stable, isolable compounds.

Preparation of 3-(2′-Hydroxyarylidene)-5-aryl-4-thiolen-2-ones (6a–d). A well-stirred solution of equimolar amounts (5.75 mmol) of **5a** or **5b** and the appropriate salicylaldehyde in 35 mL of absolute ethanol was chilled in an ice–water bath. Anhydrous hydrogen chloride gas was introduced at a rapid rate through a bubbler and precipitation of a solid product commenced almost immediately. After 4 min the gas flow was terminated and the suspension stirred and chilled for an additional 3 h. It was then filtered, and the solid washed with 2 mL of cold ethanol and recrystallized from 1:1 ethanol–benzene. Yields and physical properties of the products, which were orange to red solids, are reported in Table I.

Preparation of 4*H*-2-Arylthieno[3,2-*c*][1]benzopyran-4-ones (8a–d). A suspension of 1.75 mmol of the appropriate salicylidene derivative **6a–d** in 20 mL of nitrobenzene was heated with stirring to 85 °C and treated to the dropwise addition of 10 drops of triethylamine. The temperature of the mixture was then raised to 125 °C, maintained there for 0.5 h, and cooled slowly to ambient temperatures. The nitrobenzene was removed in vacuo and the resulting crude crystals recrystallized twice from 1:1 benzene–cyclohexane. Yields and physical properties are given in Table I.

Registry No.—**5a,** 939-09-3; **5b,** 61477-86-9; **6a,** 61477-87-0; **6b,** 61477-88-1; **6c,** 61477-89-2; **6d,** 61477-90-5; **8a,** 61491-10-9; **8b,** 61477-91-6; **8c,** 61477-92-7; **8d,** 61477-93-8; β-benzoylpropionic acid, 2051-95-8; β-toloylpropionic acid, 4619-20-9; salicylaldehyde, 90-02-8; 5-chlorosalicylaldehyde, 635-93-8; 5-methoxysalicylaldehyde, 148-53-8.

References and Notes

(1) R. A. Conley and N. D. Heindel, *J. Org. Chem.*, **41,** 3743 (1976).
(2) R. A. Conley and N. D. Heindel, *J. Org. Chem.*, **40,** 3169 (1975).
(3) N. D. Heindel and J. A. Minatelli, *J. Heterocycl. Chem.*, **13,** 669 (1976).
(4) Y. Makisumi, Japanese Kokai 73 00 596; *Chem. Abstr.*, **78,** 72096u (1973).
(5) L. S. Harris, H. G. Pars, J. C. Sheehan, and R. K. Razdan, German Offen. 2 263 129; *Chem. Abstr.*, **79,** 78768g (1973).
(6) Y. Makisumi, Japanese Kokai 74 75 599; *Chem. Abstr.*, **83,** 164152r (1975).
(7) A. I. Kosak, R. J. F. Palchak, W. A. Steele, and C. M. Selwitz, *J. Am. Chem. Soc.*, **76,** 4450 (1954).
(8) D. C. Lankin, M. R. Scalise, J. C. Schmidt, and H. Zimmer, *J. Heterocycl. Chem.*, **11,** 631 (1974).
(9) N. D. Heindel and L. A. Schaeffer, *J. Org. Chem.*, **35,** 2446 (1970).
(10) D. N. Kevill, E. D. Weiler, and N. H. Cromwell, *J. Org. Chem.*, **29,** 1276 (1964).
(11) J. H. Bowie, R. G. Cooks, S. O. Lawesson, and C. Nolde, *J. Chem. Soc. B*, 616 (1967).
(12) Q. N. Porter and J. Baldas, "Mass Spectrometry of Heterocyclic Compounds", Wiley-Interscience, New York, N.Y., 1971, pp 148–149.
(13) C. S. Barnes and J. L. Occolowitz, *Aust. J. Chem.*, **17,** 975 (1964).