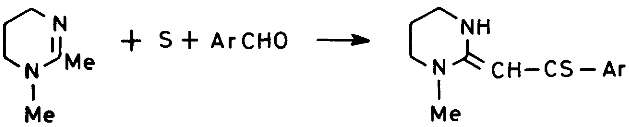
C-Thioacylation by the Willgerodt–Kindler Reaction. Structure of the Anomalous Products from Salicylaldehydes. *X*-Ray Crystal Structure of the Betaine from 1,2-Dimethyl-1,4,5,6-tetrahydropyrimidine, Sulphur, and 3,5-Dichlorosalicylaldehyde

Srinivasachari Rajappa * and Bhagwan G. Advani
CIBA-GEIGY Research Centre, Goregaon, Bombay 400063, India
Gopinath Kartha †
Roswell Park Memorial Institute, Buffalo, N.Y. 14263, U.S.A.

1,2-Dimethyl-1,4,5,6-tetrahydropyrimidine (**1**), on reaction with salicylaldehydes (**3**) in the presence of sulphur, does not lead to the expected *C*-thioacylated products (**4**); instead, the products obtained are the betaines (**5**). The structure of (**5b**) from 3,5-dichlorosalicylaldehyde has been established by *X*-ray diffraction analysis.

We have described[1] a novel *C*-thioacylation of 1,2-dimethyl-1,4,5,6-tetrahydropyrimidine (**1**) by reaction with aromatic aldehydes in the presence of sulphur to give the thioacylketene aminals (**2**). When salicylaldehydes were the substrates in this reaction anomalous products were obtained in low yields. This communication reports the structures of these products.



(**1**) (**2**)

Reaction of salicylaldehyde (**3a**) with the amidine (**1**) in the presence of sulphur under the usual conditions gave a single crystalline product (**5a**) in 20% yield. This was not the expected thioacylketene aminal (**4a**), but a compound with two hydrogen atoms less (molecular formula $C_{13}H_{14}N_2OS$; mass spectrum: M^+, 246). There was no spectroscopic evidence for the presence of NH or OH groups in the molecule (i.r., ^1H n.m.r.). Surprisingly, the same product was also formed, albeit in lower yield (8%), from 2-methoxybenzaldehyde; demethylation has thus been part of the sequence leading to the final product in this case. Neither 3-hydroxy- nor 4-hydroxy-benzaldehyde gave a crystalline product in this reaction.

Two substituted salicylaldehydes, (**3b**) and (**3c**), were subjected to this reaction; the products, (**5b**) and (**5c**), had molecular weights two units less than the values calculated for the respective thioacylketene aminals (**4b**) and (**4c**). All three products (**5**) exhibited long-wavelength absorption maxima around 390—400 nm. The similarity of the u.v., ^1H n.m.r., and mass spectra of these three compounds leaves no doubt that they have similar structures.

It is obvious that these anomalous products have arisen by an oxidative cyclization from (**4**), involving loss of the two hydrogen atoms attached to the nitrogen and oxygen. That these products had the betaine structure (**5**) was proved unambiguously by the *X*-ray crystallographic analysis of the product (**5b**) from 3,5-dichlorosalicylaldehyde (**3b**) (Figure).

The length of the bond joining the isothiazole and the phenyl rings in (**5b**) is 1.44 Å; this, together with the overall planarity of the molecule, suggests that there is considerable double-bond character for this bond as shown in (**6**). This *o*-quinonoid form

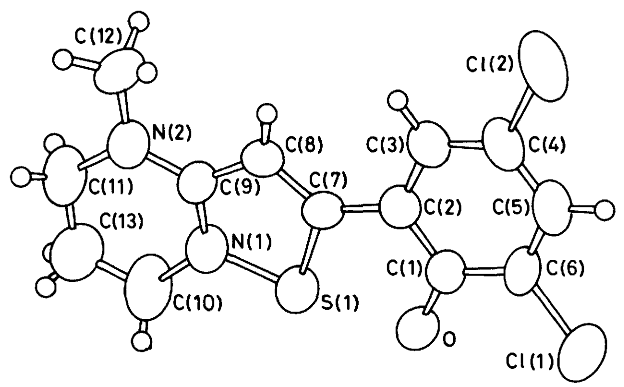
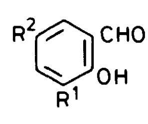
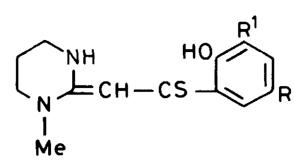
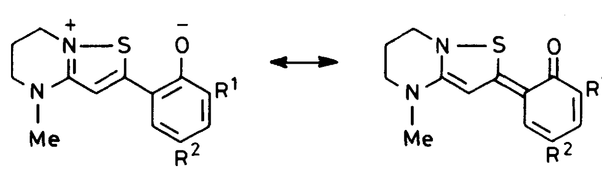


Figure. *X*-Ray crystal structure of (**5b**)



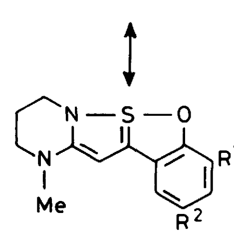


(**3**) (**4**)



(**5**) (**6**)

a; $R^1 = R^2 = H$
b; $R^1 = R^2 = Cl$
c; $R^1 = OMe, R^2 = H$

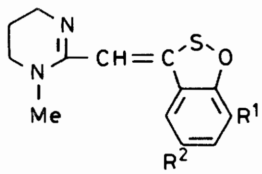


(**7**)

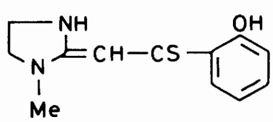
---

† To whom queries on the *X*-ray crystallography should be sent.

(**6**) may contribute to the long-wavelength absorption in ethanol solution; addition of acid causes a hypsochromic shift due to curtailment of conjugation consequent on *O*-protonation. The S–N(1)* bond length is 1.73 Å; hence there is no doubt that a covalent bond exists between these two atoms. It is interesting to note, however, that the S–O distance in (**5b**) is 2.26 Å; this is appreciably smaller than the usual van der Waals distance between S and O atoms, but not short enough to warrant postulation of a formal covalent bond between the two atoms as in structure (**7**). However, such a structure might be one of the contributors to the molecule. This would explain why an oxygen substituent adjacent to the thiocarbonyl group on the phenyl ring in (**4**) is necessary for the formation of such oxidatively cyclized products. It was tempting to speculate that these arise through the intermediacy of the benzoxathiole derivatives (**8**). However, 1,2-dimethylimidazolidine gave the normal product (**9**) when treated under the same conditions with salicylaldehyde and sulphur. It can be concluded that the spatial proximity of the three heteroatoms N, S, and O in compounds (**4**) is responsible for the unexpected oxidative cyclization to (**5**).



(**8**)



(**9**)

Experimental

U.v. spectra were measured for solutions in ethanol using a Beckman M 35 machine. ^{1}H N.m.r. spectra were recorded on a Varian A 60 instrument; chemical shifts are expressed in δ values (p.p.m.) downfield from Me_4Si. Mass spectra were determined on a Varian Mat CH 7 instrument at 70 eV utilizing direct insertion. Ether refers to diethyl ether.

General Procedure for the Willgerodt–Kindler Reaction.—A mixture of the amidine (0.02 mol), aldehyde (0.02 mol), and sulphur (0.025—0.03 mol) was stirred and refluxed in xylene (100 ml) under nitrogen for 5 h. After the solution had cooled, the xylene was decanted off. The decantate in some experiments deposited the product on either being kept or on treatment with a little hexane. The xylene-insoluble residue from the reaction was separately extracted with dichloromethane, the extract was evaporated, and the residue chromatographed over alumina (chloroform eluant). The product was sometimes obtained in this eluate.

The Betaine (**5a**).—M.p. 234—237 °C (from acetonitrile), yield from salicylaldehyde 20.7%; yield from 2-methoxybenzaldehyde 8.3% (Found: C, 63.7; H, 6.0; N, 11.7; S, 13.5. $C_{13}H_{14}N_2OS$ requires C, 63.4; H, 5.7; N, 11.4; S, 13.0%); *m/z* 246 (M^+); δ($CDCl_3$) 2.0 (m, CH_2), 2.87 (s, NMe), 3.12 (t, CH_2), 3.67 (t, CH_2), 6.35 (s, CH), and 6.5—7.7 (m, 4 ArH); δCD_3SOCD_3) 2.0 (m, CH_2), 3.05 (s, NMe), 3.27 (t, CH_2), 3.70 (t, CH_2), 6.97 (s, CH), and 6.3—8.0 (m, 4 ArH); λ_{max} 230 (ε 22 400), 281sh (9 700), 288 (10 500) and 387 nm (15 000); $\lambda_{max.}$(EtOH + HCl) 277 (ε 15 600), 286 (15 600) and 337 nm (17 600).

The Betaine (**5b**).—M.p. 278—280 °C (from acetonitrile), yield 6.5% (Found: C, 49.3; H, 4.1; N, 9.2. $C_{13}H_{12}Cl_2N_2OS$ requires C, 49.5; H, 3.8; N, 8.9%); *m/z* 314, 316, and 318 (M^+, isotope cluster); δ(CD_3SOCD_3) 2.1 (m, CH_2), 3.13 (s, NMe), 3.33 (t, CH_2), 3.83 (t, CH_2), 7.25 (s, CH), 7.37 (d, *J* 2.5 Hz, ArH), and 7.93 (d, *J* 2.5 Hz, ArH); $\lambda_{max.}$ 237 (ε 22 600), 284 (9 000), 295 (9 500), and 402 nm (15 200).

The Betaine (**5c**).—M.p. 228—231 °C (propan-2-ol-ether), yield 9% (Found: C, 60.6; H, 5.9; N, 9.9. $C_{14}H_{16}N_2O_2S$ requires C, 60.9; H, 5.8; N, 10.1%); *m/z* 276 (M^+); δ($CDCl_3$) 2.0 (m, CH_2), 2.77 (s, NMe), 3.04 (t, CH_2), 3.63 (t, CH_2), 3.90 (s, OMe), 6.25 (s, CH), and 6.4—7.4 (m, 3 ArH); $\lambda_{max.}$ 243 (ε 16 800), 300 (13 100), and 390 nm (13 050).

1-*Methyl*-2-[(2-*hydroxythiobenzoyl*)*methylene*]*imidazolidine* (**9**).—M.p. 156—159 °C (from propan-2-ol), yield 12.6% (Found: C, 61.8; H, 6.35; N, 12.0. $C_{12}H_{14}N_2OS$ requires C, 61.5; H, 6.0; N, 12.0%); *m/z* 234 (M^+); δ($CDCl_3$) 2.90 (s, NMe), 3.75 (m, 2 CH_2), 6.20 (s, CH), and 6.7—7.5 (m, 4 ArH); $\lambda_{max.}$ 240sh (ε 9 700), 279 (7 900), and 362 nm (13 900).

Crystal Data for (**5b**).—$C_{13}H_{12}Cl_2N_2OS$, M = 315.2, Triclinic, space group $P1$, a = 7.608(4), b = 12.990(3), c = 15.917(4) Å, α = 67.02(1), β = 85.66(3), γ = 73.41(3)°, U = 1 386.8(1), D_c = 1.51 g cm^{-3}, μ(Cu-K_α) = 56.3 cm^{-1}.

Table 1. Table of atomic co-ordinates and estimated standard deviations for non-hydrogen atoms

Atom	*x*	*y*	*z*
Cl(1A)	0.674 6(2)	0.193 0(1)	0.257 45(11)
Cl(2A)	0.683 0(2)	−0.209 2(1)	0.538 14(9)
Cl(1B)	0.892 7(2)	0.483 2(1)	0.116 07(9)
Cl(2B)	0.748 5(3)	0.353 2(1)	0.472 49(12)
S(1A)	1.040 5(2)	−0.115 2(1)	0.125 72(8)
S(1B)	0.532 1(2)	0.882 1(1)	0.134 09(8)
O(A)	0.880 1(4)	0.033 2(3)	0.166 5(2)
O(B)	0.693 0(5)	0.721 2(3)	0.110 0(2)
N(2A)	1.263 0(5)	−0.444 1(3)	0.183 5(2)
N(1A)	1.161 9(5)	−0.241 8(3)	0.111 8(2)
N(1B)	0.402 2(5)	0.990 9(3)	0.167 8(2)
N(2B)	0.250 4(5)	1.030 1(3)	0.289 3(3)
C(1A)	0.838 2(6)	−0.017 9(4)	0.249 5(3)
C(7A)	1.001 9(6)	−0.199 6(3)	0.236 7(3)
C(2A)	0.896 0(6)	−0.140 7(3)	0.291 6(3)
C(8A)	1.081 8(6)	−0.315 1(3)	0.258 4(3)
C(3A)	0.849 3(6)	−0.199 4(4)	0.380 6(3)
C(9A)	1.174 3(6)	−0.339 6(3)	0.184 9(3)
C(11A)	1.345 9(7)	−0.455 0(4)	0.099 8(3)
C(5A)	0.691 4(7)	−0.016 3(4)	0.391 0(3)
C(12A)	1.294 5(7)	−0.549 9(4)	0.265 8(4)
C(10A)	1.252 3(8)	−0.241 0(5)	0.027 0(3)
C(4A)	0.748 4(7)	−0.136 0(4)	0.427 8(3)
C(6A)	0.737 3(6)	−0.041 6(4)	0.304 0(3)
C(8B)	0.421 6(6)	0.834 0(4)	0.298 2(3)
C(7B)	0.522 1(6)	0.782 3(4)	0.243 1(3)
C(1B)	0.703 9(6)	0.638 3(4)	0.188 3(3)
C(11B)	0.187 9(8)	1.154 1(4)	0.234 2(4)
C(3B)	0.630 1(7)	0.575 2(4)	0.350 5(3)
C(5B)	0.807 5(7)	0.434 3(4)	0.292 5(4)
C(2B)	0.617 0(6)	0.662 9(4)	0.263 0(3)
C(6B)	0.794 7(6)	0.520 3(4)	0.206 2(3)
C(4B)	0.725 2(7)	0.464 1(4)	0.363 8(4)
C(12B)	0.197 2(7)	0.987 3(4)	0.384 7(3)
C(10B)	0.351 9(9)	1.112 2(5)	0.104 5(4)
C(9B)	0.351 3(6)	0.954 6(4)	0.254 1(3)
C(13B)	0.227 0(13)	1.184 4(5)	0.140 1(4)
C(13A)	1.259 1(11)	−0.346 6(5)	0.016 6(4)

* Crystallographic numbering.

Table 2. Table of atomic co-ordinates for hydrogen atoms

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
H(81A)	1.0764	−0.3736	0.3170	H(103)	0.2870	1.1151	0.0516
H(31A)	0.8868	−0.2820	0.4076	H(104)	0.4488	1.1399	0.0869
H(51A)	0.6212	0.0257	0.4256	H(133)	0.1062	1.2006	0.1107
H(81B)	0.4025	0.7925	0.3601	H(134)	0.2602	1.2520	0.1209
H(31B)	0.5742	0.5933	0.4002	H(113)	0.0592	1.1789	0.2396
H(51B)	0.8710	0.3557	0.3028	H(114)	0.2480	1.1931	0.2558
H(101)	1.3808	−0.2402	0.0332	H(121)	1.3594	−0.5430	0.3164
H(102)	1.1964	−0.1752	−0.0230	H(122)	1.1934	−0.5625	0.2988
H(131)	1.3238	−0.3488	−0.0360	H(123)	1.4160	−0.6055	0.2656
H(132)	1.1344	−0.3445	0.0082	H(124)	0.3047	0.9785	0.4316
H(111)	1.4751	−0.4633	0.1035	H(125)	0.1750	0.9130	0.4010
H(112)	1.3298	−0.5219	0.0947	H(126)	0.0820	1.0410	0.3984

Table 3. Bond Lengths (standard deviations in parentheses)

Bond	Molecule A	Molecule B
C(1)–C(2)	1.412(3)	1.417(3)
C(2)–C(3)	1.397(3)	1.402(3)
C(3)–C(4)	1.336(3)	1.356(3)
C(4)–C(5)	1.376(3)	1.388(4)
C(5)–C(6)	1.368(3)	1.380(3)
C(6)–C(1)	1.423(3)	1.411(3)
C(4)–Cl(2)	1.752(2)	1.747(3)
C(6)–Cl(1)	1.739(2)	1.738(3)
C(1)–O	1.289(3)	1.279(3)
C(2)–C(7)	1.435(3)	1.428(3)
C(7)–S(1)	1.733(2)	1.725(3)
S(1)–N(1)	1.730(2)	1.725(2)
N(1)–C(9)	1.331(3)	1.332(3)
C(9)–C(8)	1.417(3)	1.398(3)
C(8)–C(7)	1.359(3)	1.367(3)
N(1)–C(10)	1.465(3)	1.456(3)
C(10)–C(13)	1.430(4)	1.388(4)*
C(13)–C(11)	1.523(4)	1.424(4)*
C(11)–N(2)	1.470(3)	1.453(3)*
N(2)–C(9)	1.340(3)	1.341(3)
N(2)–C(12)	1.455(3)	1.468(3)

* Deviations considered significant.

Table 4. Bond angles (estimated standard deviation is 0.3°)

Bond angle	Molecule A	Molecule B
C(2)–C(1)–C(6)	116.3	116.2
C(1)–C(6)–C(5)	112.1	122.1
C(6)–C(5)–C(4)	118.9	119.1
C(5)–C(4)–C(3)	122.4	121.7
C(4)–C(3)–C(2)	118.9	119.4
C(3)–C(2)–C(1)	121.2	121.4
C(2)–C(1)–O	119.5	119.5
O–C(1)–C(6)	124.1	124.2
C(1)–C(6)–C(4)	118.0	118.5
Cl(1)–C(6)–C(5)	119.8	119.4
C(5)–C(4)–Cl(2)	118.4	117.7
Cl(2)–C(4)–C(3)	119.1	120.6
C(3)–C(2)–C(7)	123.0	123.2
C(1)–C(2)–C(7)	115.8	115.5
C(2)–C(7)–S(1)	117.7	117.9
C(2)–C(7)–C(8)	129.7	130.1
C(7)–S(1)–N(1)	88.5	88.8
S(1)–N(1)–C(9)	115.2	115.0
S(1)–N(1)–C(10)	122.4	121.1*
N(1)–C(9)–C(8)	110.6	110.8
C(9)–C(8)–C(7)	113.0	113.4
C(8)–C(7)–S(1)	112.6	112.0
N(2)–C(9)–C(8)	127.7	127.7
C(10)–N(1)–C(9)	122.3	123.8*
N(1)–C(9)–N(2)	121.6	121.2
C(9)–N(2)–C(11)	120.9	121.4
C(11)–C(13)–C(10)	112.9	124.9
N(2)–C(11)–C(13)	110.2	114.1*
C(9)–N(2)–C(12)	121.7	119.8
C(12)–N(2)–C(11)	117.1	118.8
N(1)–C(10)–C(13)	109.0	112.6*

* Deviations considered significant.

Crystallographic Measurements.—Compound (**5b**) crystallized as long lath-shaped yellow crystals from acetonitrile at room temperature. Cell parameters were obtained from least squares analysis of 25 reflections measured on an Enraf-Nonius CAD4 automatic diffractometer and diffraction data were collected to a Bragg angle of 77°. Out of 5 864 unique reflections collected, 3 783 having $I > 3\sigma(I)$ were considered observed. Intensities of three standard reflections were monitored every 200 reflections and empirical absorption corrections were applied.

Structure Determination and Refinement.—The structure was solved by the multi-solution tangent refinement program MULTAN.[2] An *E*-map with the set with highest combined figure of merit indicated locations for 36 out of 38 non-hydrogen atoms in the asymmetric unit. The remaining two atoms were obtained from a weighted Fourier map and all the co-ordinates were refined by the full matrix least-squares method, first with isotropic and then with anisotropic thermal parameters. The positional parameters of all hydrogen atoms found from a difference Fourier synthesis were also included in the refinement. The final *R* index $[(\Sigma||F_o| - |F_c||)/(\Sigma|F_o|)$ was 0.058 and the quantity minimized was $\Sigma w(||F_o - |F_c|)^2$, where the weight *w* was $1/\sigma^2(F)$. The refined atomic co-ordinates for the non-hydrogen atoms are listed in Table 1 and those for the hydrogen atoms in Table 2. Tables of observed and calculated structure factors and thermal paramaters for non-hydrogen atoms are listed in Supplementary Publication No. SUP 23964 (20 pp.).

Discussion

The structure of the molecule and the atom numbering scheme used are shown in the Figure. There are two molecules (A and B) in the asymmetric unit cell and both have very similar structure and conformation. However, the bond lengths and angles in the two molecules (Tables 3 and 4) indicate small but significant differences making the six-membered saturated ring in molecule B much flatter than in molecule A.

The distance O–S (2.26 Å) though much larger than the N(1)–S distance (1.73 Å) is still appreciably smaller than the usual van der Waals distance between S and O atoms (3.3 Å).

Acknowledgements

We thank Dr. S. Selvavinayakam and his associates for the analytical and spectral data. The possible contribution of structure (**7**) was first suggested by a referee.

References

1 S. Rajappa, M. D. Nair, R. Sreenivasan, and B. G. Advani, *Tetrahedron*, 1982, **38**, 1673.
2 G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect A*, 1971, **27**, 368.

Received 18*th April* 1983; *Paper* 3/610