Kurzmitteilungen:

Electron-impact Induced and Thermal Decomposition of Dithranol Derivatives, I:

Thermolysis of 10-Phenylthio-dithranol in the Mass Spectrometer

Elektronenstoß-induzierter und thermischer Zerfall von Dithranol Derivaten, 1. Mitt.: Thermolyse von 10-Phenylthio-dithranol im Massenspektrometer

Hsu-Shan Huang[a)+)], Klaus K. Mayer[b)], and Wolfgang Wiegrebe[a)]

Institut für Pharmazie[a)] and Zentrale Analytik[b)], NWF IV, Universität Regensburg, Universitätsstr. 31, D-93040 Regensburg, Germany

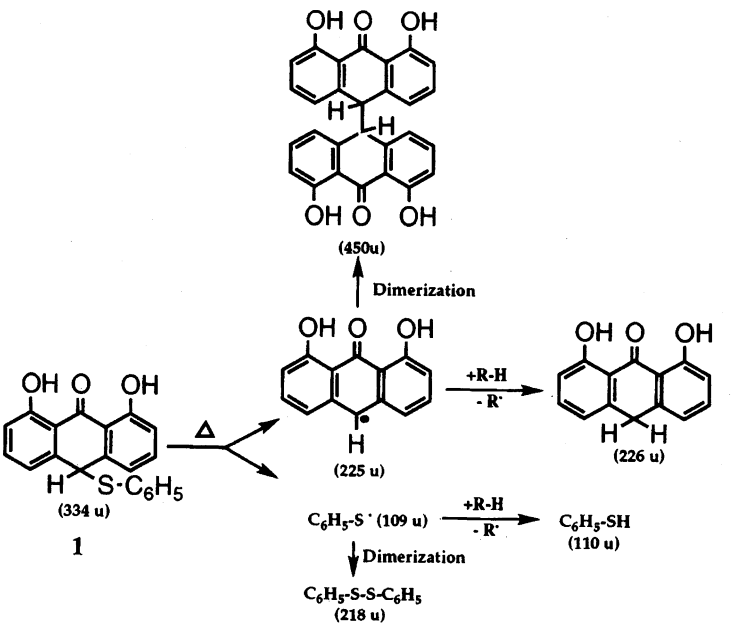
Received May 18, 1994

Dithranol (anthralin; 1,8-dihydroxy-9-anthrone) and its derivatives bearing a variety of substituents in the 10-position are of actual interest in research on psoriasis[1)]. In connection herewith 10-alkylthio- and 10-arylthio-1,8-dihydroxy-9(10*H*)-anthracenones were synthetized and used for anti-psoriatic activity[2,3)].

In the scope of our studies on dithranol[4)] we examined several 10-arylthio-derivatives[5)] and worked out ms procedures for their unequivocal identification and purity determination. As expected, the 70 eV and 12 eV EI-MS of 10-phenylthio-dithranol (**1**) are in accordance with those of simple benzylic sulphides displaying the base peak at m/z = 225 in the case of **1** as a result of benzylic cleavage. However, if a heated insertion probe is used, ions at m/z = 226 ($C_{14}H_{10}O_3$), m/z = 218 ($C_{12}H_{10}S_2$) and m/z = 110 (C_6H_6S) appear with varying intensity depending on inlet system and ion-source temp. and crucible materials (Al, Au, quartz). These ions are not found in FD mass spectra which show signals at m/z = 334 ($M^{+\cdot}$; 100%) and m/z = 225 (10%) only, even in case of high emitter currents. Furthermore, metastable molecular ions (B/Z = const., linked scan; 70 eV) are not fragmented to m/z 226; 218; and 110 ions (Exp. Part).

From these results it seems reasonable to infer thermal decomposition of **1** in the inlet-system (and the ion source) before ionization can take place, and homolytic fission[7,8)] of the C(10)-S bond followed by H·-abstraction by the resulting C- and S-radicals forming $C_{14}H_{10}O_3$ (dithranol) and C_6H_6S (thiophenol) neutrals, or their recombination to C-C or S-S dimers, *e.g.* diphenyldisulphide ($C_{12}H_{10}S_2$).

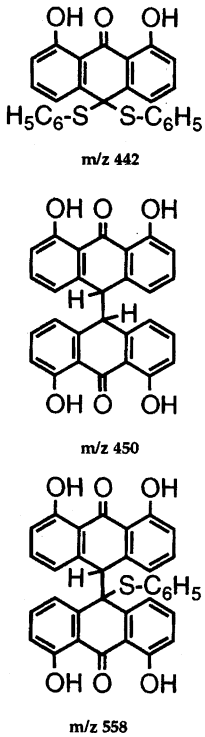
In order to prove this concept, thoroughly purified samples of **1** (Exp. Part) were heated (150°C) in quartz tubes for 1 to 30 min and the products identified by EI-MS and



Scheme 1

+) On leave from the Institute of Pharmacy, National Defense Medical Center, Taipei, Taiwan, Republic of China.

  0366-6233/94/1010-0669 $ 5.00 + .25/0



Scheme 2: Structures of thermolytic products

FD-MS. The data in Table 1 show a dramatic decrease of intensity of $M^{+\cdot}$ (m/z 334) and m/z 225 ions with extended heating periods, whereas the ions at m/z = 109, 218, and 226 give rise to stronger signals. Correspondingly, the FD-MS reveal an increase in radical recombination products of higher molecular mass at m/z = 442, 450, and 558.

The thermolytic products were identified by HR-MS, the structures derived thereby (Scheme 2) are in good accord with results of analogous decomposition studies on sulphides[8-11]. Therefore, we conclude that the unexpected compounds encountered in the EI-mass spectra of **1** are of thermal origin. The amount of these analytically unwelcome concomitants can be reduced by the use of quartz cru-

cibles, low inlet-system- and ion-source-temp. and short dwelling times (EI-MS) or by application of low-temp. ionization methods, *e.g.* FD-MS.

H.-S. Huang gratefully acknowledges financial support by National Defense Medical Center, Taipei, Taiwan, R.O.C. - This project was partially supported by Fonds der Chemischen Industrie, Germany.

Experimental Part

EI-MS (70/12 eV), FD-MS and MI-MS: MAT 95 double-focusing instrument. The samples were introduced *via* the direct insertion probe (quartz crucibles), at T = 100°C; ion source temp. 100-120°C. High resolution measurements with m/Δm = 15000.- Melting points: Büchi 510 melting point apparatus, uncorrected.- ^{1}H-NMR spectra: Varian EM 390 (90 MHz), TMS as an internal standard.- Fourier-transform IR spectra (KBr): Nicolet 510M FT-IR spectrometer.

10-Phenylthio-1,8-dihydroxy-9-anthrone (**1**)

To a solution of 10-bromo-1,8-dihydroxy-9-anthrone[12] (305 mg, 1.0 mmole) and 0.1 ml of trifluoroacetic acid in dry CH_2Cl_2 (20 ml), a solution of thiophenol (2.0 mmole) in dry CH_2Cl_2 (10 ml) was added dropwise. The reaction mixture was allowed to stir at room temp. for 6 h under N_2. The yellow solution was washed thoroughly with water and diluted with $CHCl_3$ (20 ml). The org. phase was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by three recrystallizations yielding yellow crystals of **1** (220 mg, 66%), mp. 149-150°C [lit. 145°C[2]].- FT-IR (KBr) 1629 (CO···HO) cm^{-1}.- ^{1}H-NMR (90 MHz, $CDCl_3$): δ (ppm) 5.40 (s; 1H, 10-H), 6.70 (d; J = 8 Hz, 2H, 2-H, 7-H), 6.90 (d; J = 8 Hz, 2H, H-4, H-5), 7.05 (d; J = 8 Hz, 2H, 2'-H, 6'-H), 7.15 (t; J = 8 Hz, 2H, 3'-H, 5'-H), 7.35 (t; J = 7.7 Hz, 1H, 4'-H), 7.49 (t; J = 7.7 Hz, 2H, 3-H, 6-H), 11.80 (s; 2H, 1-OH, 8-OH).- $C_{20}H_{14}O_3S$ (334.4) Calcd. C 71.8 H 4.22 Found C 71.3 H 4.19.

a) EI-MS: m/z (70/12 eV, % rel. int.) 334 (7/16), 226 (35/40), 225 (100/100), 197 (43/1), 151 (15/-), 110 (13/11), 109 (9/-).

b) FD-MS: m/z (% rel. int.) 334 (100), 225 (15).

c) MI-MS: $M^{+\cdot}$ (m/z 334; B/E): 333 (100), 302 (3), 301 (1), 256 (2), 225 (15) (quartz crucible).

d) EI-MS: m/z (70 eV; Al/Au crucibles; % rel. int.): 334 (2/3), 226 (95/80), 225 (100/100), 197 (55/50), 151 (25/25), 110 (40/35), 109 (25/20).

Table 1: Thermolysis (150°C) of **1** (EI-MS; 70 eV, % rel.int.)[a]

t(min)	m/z 334 $C_{20}H_{14}O_3S$	m/z 226 $C_{14}H_{10}O_3$	m/z 225 $C_{14}H_9O_3$	m/z 218 $C_{12}H_{10}S_2$	m/z 110 C_6H_6S	m/z 109 C_6H_5S
0	20	10	100	1	18	5
1	15	25	100	1	20	35
5	2	35	20	100	10	85
15	<0.5	40	1	100	5	70
30	<0.5	50	2	100	10	80

a) Data ^{13}C-corrected; ion-source temp. 100°C; average of 5 runs.

Table 2: Thermolysis (150°C) of **1** (FD-MS; % rel.int.)[a]

t(min)	m/z 558 $C_{34}H_{22}O_6S$	m/z 450 $C_{28}H_{18}O_6$	m/z 442 $C_{26}H_{18}O_3S_2$	m/z 334 $C_{20}H_{14}O_3S$	m/z 226 $C_{14}H_{10}O_3$	m/z 225 $C_{14}H_9O_3$	m/z 218 $C_{12}H_{10}S_2$
0	<0.5	<0.5	<0.5	100	-	10	-
1	1	1	2	100	12	15	2
5	15	20	10	100	15	40	2
10	20	55	15	100	35	75	15

a) Data ^{13}C-corrected; average of 5 runs.

Thermolysis of **1**

Pure **1** (1.0 mg) was placed in a silylated quartz tube (0.2 mm diameter) and kept for 1 to 30 min in a thermostated oil bath at 150°C. After cooling, the lower part of tube together with the dark solid was pulverized and the org. substance dissolved in absol. CH_2Cl_2 (1 ml). The homogenous solution was used immediately for FD-MS analysis.

References

1 K. Müller, D. Gürster, S. Piwek, W. Wiegrebe, *J. Med. Chem.* **1993**, *36*, 4099-4107, and lit. cited therein.
2 M. d'Ischia, G. Prota, *Synthesis* **1986**, 430-431.
3 J. Khalafy, J.M. Bruce, *Iran J. Chem., Chem. Eng.* **1990**, *13*, 35-42; *Chem. Abstr.* **1991**, *115*, 232150v.
4 W. Wiegrebe, K. Müller, *Skin Pharmacol.* **1994**, *7*, in press.
5 H.-S. Huang, forthcoming PhD Thesis, Universität Regensburg.
6 Y.M. Sheikh, A.M. Duffield, C. Djerassi, *Org. Mass Spectrom.* **1968**, *1*, 251-262; J.K. MacLeod, C. Djerassi, *J. Am. Chem. Soc.* **1967**, *89*, 5182-5190.
7 A.J. Colussi, S.W. Benson, *Int. J. Chem. Kinetics* **1977**, *9*, 295-306.
8 R.L. Failes, J.S. Shapiro, V.R. Stimson in "The Chemistry of Functional Groups", Suppl. S (Ed.: S. Patai, Z. Rappoport), Wiley, New York, **1993**, p. 466-468.
9 H. Butzert, H.D. Beckey, *Z. Phys. Chem.* **1968**, *NF 62*, 83-102.
10 Z. Dolejsek, J. Navakova, *Can. J. Chem.* **1981**, *59*, 1824-1828.
11 Ch.N. McEwen, *Mass Spectrom. Rev.* **1986**, *5*, 521-547.
12 O.-E. Schultz, H.H. Schultze-Mosgau, *Arch. Pharm. (Weinheim)* **1965**, *298*, 273-281.

[KPh624]