The Pummerer Rearrangement with 7-(Trifluoromethyl)dibenzo[*b*,*e*][1,4]-thiazepine-5(11*H*)-carboxaldehyde 10-Oxide. Formation of a Novel 5,11-Bridged Tetracycle

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13-Ethoxy-7-(trifluoromethyl)-11*H*-11,5-(epoxymethano)dibenzo[*b*,*e*][1,4]thiazepine (**3**) was formed following the Pummerer Rearrangement of 7-(trifluoromethyl)dibenzo[*b*,*e*][1,4]-thiazepine-5(11*H*)carboxaldehyde 10-oxide (**1**), when the work-up involved the use of diethyl ether that contained ethanol as a normal ingredient, *i.e.*, the grade of that solvent employed in anesthesia.

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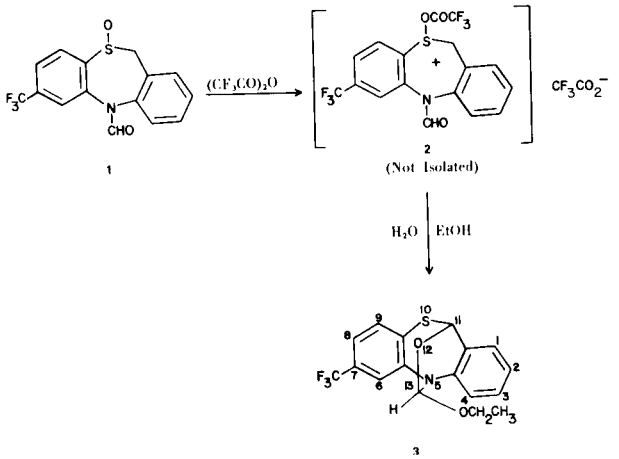
The reaction whereby a sulfoxide bearing at least one α-hydrogen undergoes intramolecular oxidation-reduction and yields a sulfide with an oxygen containing substituent in the α-position is known as the Pummerer Rearrangement (1). The reagent frequently used to initiate this reaction is acetic anhydride. When that reactant was employed with 7-(trifluoromethyl)dibenzo[*b*,*e*][1,4]thiazepine-5-(11*H*)carboxaldehyde 10-oxide (**1**) (2), no reaction occurred; reaction occurred readily, however, with trifluoroacetic anhydride (3). Work-up, prior to isolation of the product, involved extraction with commercially available anesthetic grade diethyl ether that contained as a normal component *ca.* 2.3% of ethanol along with *ca.* 0.7% of water. Those circumstances led, unexpectedly, to the formation of the novel 5,11-bridged tetracycle **3**, presumably *via* secondary reactions involving the intermediate **2** (4).



1 2 (Not Isolated) 3

The structure of **3** was readily deduced. The molecular ion at mass 353 was the second most abundant fragment in the mass spectrum; the most abundant species was the ion of mass 45, arising, presumably, from a loss of an ethoxyl group. The ir spectrum revealed the absence of HO, NH, or carbonyl absorption. The pmr spectrum showed the anticipated singlets of the two tertiary protons at positions-11 and -13, as well as the characteristic chemical shifts of the CH_3CH_2 protons; the spectrum was not altered after equilibration with deuterium oxide (4).

The mechanism of the Pummerer Rearrangement has yet to be clarified (1); in the same sense, it is not presently understood how **2**, presumably was converted in several steps to **3**, a cyclic acetal of a formamide derivative.

EXPERIMENTAL

The ir, pmr, and mass spectral determinations were carried out by members of the Analytical Department of this Institute and the author expresses his thanks for their assistance; the instruments employed have been described in earlier papers. Melting points were determined in an electrically heated oil bath and are uncorrected.

13-Ethoxy-7-(trifluoromethyl)-11*H*-11,5-(epoxymethano)dibenzo-[*b*,*e*][1,4]thiazepine (**3**).

To a stirred suspension of 1.63 g. (0.005 mole) of 7-(trifluoromethyl)dibenzo[*b*,*e*][1,4]thiazepine-5(11*H*)carboxaldehyde 10-oxide (**1**) in 25 ml. of anhydrous benzene was added 1.05 g. (0.005 mole) of trifluoroacetic anhydride, dropwise. An exothermic reaction occurred and a solution formed. The mixture was kept at ambient temperature for 48 hours until tlc (silica gel-chloroform) showed the absence of **1**. The solution was concentrated *in vacuo*, to give an oil. The latter was dissolved in 100 ml. of Squibb anesthetic grade ether. That solution was stirred for 3 hours with a solution of 1.0 g. of sodium bicarbonate in 10 ml. of water and the ether layer was separated, washed with 10 ml. of saturated aqueous sodium chloride solution, dried, and concentrated *in vacuo*. The residual solid, 1.68 g., was recrystallized from 40 ml. of cyclohexane to give 0.76 g. (43% yield) of **3**, m.p. 136-138° dec.; R_f (one spot), 0.83 (cyclohexane), 0.66 (cyclohexane: chloroform - 9:3); ir (potassium bromide): ν 1590(m), 1580(m), 1570(m), 1490(s), 1480(m), 1455(w), 1430(s) cm^{-1}; pmr (deuteriochloroform): δ 1.35 [t (J = 12 Hz), 3H, OCH_2CH_3], 3.60-4.20 (m, 2H, OCH_2CH_3), 5.53 (s, 1H, C*H* at position-13), 7.00-7.66 (m, 7H, 7 Ar-*H*).

Anal. Calcd. for $C_{17}H_{14}F_3NO_2S$: C, 57.78; H, 3.99; N, 3.97; S, 9.08; F, 16.13; M^+, 353. Found: C, 57.74; H, 4.10; N, 4.04; S, 8.92; F, 16.44; M^+, 353.

REFERENCES AND NOTES

(1) For a review of this Rearrangement, *cf.*, T. Durst, in "Advances in Organic Chemistry, Methods and Results", Interscience Publishers, New York, N.Y., Vol. 6, 1969, pp. 356-365.

(2) For the preparation of this intermediate, *cf.*, H. L. Yale, B. Beer, J. Pluscec, and E. R. Spitzmiller, *J. Med. Chem.*, **13**, 713 (1970).

(3) R. Tanikaga, Y. Yabuki, and A. Kaji, *Tetrahedron Letters*, 2257 (1976), have reported that trifluoroacetic anhydride was superior to acetic anhydride in effecting the Pummerer Rearrangement.

(4) While the mechanism of the Pummerer Rearrangement has not been elucidated, there is general agreement that the first reaction product is probably an acetoxysulfonium salt like **2**