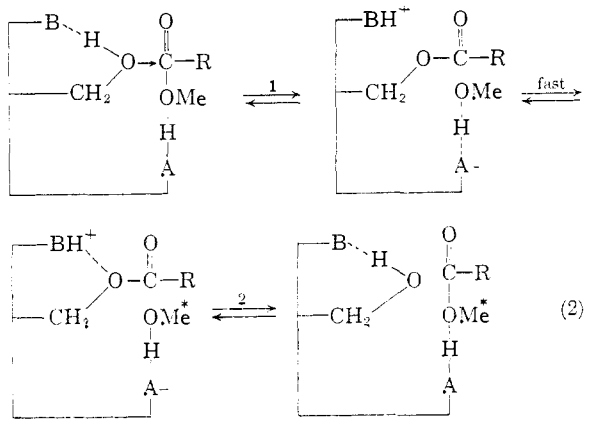
Deuterium oxide causes two effects in the deacylation of cinnamoyl-α-chymotrypsin (Curve B): the apparent pK_a is 7.7 in D_2O; and the rate constant at any pH(pD) is 2.5 fold more in H_2O than in D_2O. The shift in the pK_a of the catalytically important group in D_2O is expected.[7] A substantial decrease in rate in D_2O also is found in the acylation of chymotrypsin using p-nitrophenyl trimethylacetate and in the hydrolysis of the specific substrate, N-acetyl-L-tryptophan methyl ester (k^H/k^D = 2.83).[8] These isotope effects cannot be attributable to a pathway involving nucleophilic catalysis alone, which would be expected to exhibit essentially no D_2O isotope effect.[7,9,10] The deuterium oxide and pH results are consistent with a mechanism involving general basic catalysis by a group of pK_a 7.1, or a mechanism involving nucleophilic catalysis together with general acid catalysis by a species of pK_a above 12.5. In either case k^H/k^D would reflect a slow proton transfer and be approximately 2–3.[6,11]

Acylation and deacylation are mechanistically similar: they exhibit similar pH dependencies,[3] deuterium isotope effects and effects of structure on reactivity.[12] Let us assume that acylation and deacylation correctly describe the catalytic process, and that the α-chymotrypsin-catalyzed isotopic exchange reaction[2] proceeds through the same steps as the hydrolysis reaction (Eq. 1). Then it follows that the "acylation" and "deacylation" steps (1 and 2) of the isotopic exchange must be identical. (Step 1 = step −2, but since RCOEn

$$\underset{\text{MeOH}}{\overset{1}{\rightleftharpoons}} \qquad \underset{\text{MeOH*}}{\overset{2}{\rightleftharpoons}} \qquad (1)$$

is also an alkyl ester, step 1 = step 2). A mechanism meeting these requirements must employ at least two simultaneous catalytic functions such as general acidic and general basic catalysis (Eq. 2).[13] In acylation B and HA will be operative while in deacylation the kinetically equivalent combination of BH^+ and A^- will be operative. It is suggested that this form of catalysis be called "conjugate" catalysis for a base and its conjugate acid are operative in the two catalytic steps, as are an acid and its conjugate base.[14]

Catalysis by a lone general base[6] (*e.g.*, in Eq. 2) would fit the kinetic results but would violate the chemical symmetry required by the exchange



(2)

reaction A lone general base would remove a proton from the attacking alcohol in step 1 (but not in step 2) and its conjugate acid (BH^+) would donate a proton to the alkoxyl group of the ester in step 2 (but not in step 1), whereas in this exchange chemical symmetry requires that exactly the same processes take place in both halves of the over-all exchange reaction. Therefore it must be concluded that a single kind of catalysis (either acid, base or nucleophile) is not sufficient and that one must postulate a scheme such as eq. 2.

If extrapolation to the hydrolytic system is allowed (substitution of H_2O for MeOH in the deacylation step) the *enzymatic participants* in acylation and deacylation must still bear the same relationship to one another, requiring that a general base (or nucleophile) and a general acid again be involved.

(7) The shift of 0.6 ± 0.1 pK unit is within the experimental error of the predicted shift of 0.56 pK unit for a group of pK_a 7; R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p. 188.

(8) J. F. Thompson, *Arch. Biochem. Biophys.*, **90**, 1 (1960), reports k^H/k^D = 2.5 for the fumarase-catalyzed conversion of fumarate to malate.

(9) Unpublished observations of M. L. Bender and M. C. Neveu.

(10) D_2O stabilizes the helical form of ribonuclease, relative to its uncoiled form; J. Hermans and H. A. Scheraga, *Biochim. et Biophys. Acta*, **36**, 534 (1959).

(11) B. Zerner and M. L. Bender, *J. Am. Chem. Soc.*, **83**, in press (1961); Y. Pocker, *Proc. Chem. Soc.*, 17 (1960); A. R. Butler and V. Gold, *ibid.*, 15 (1960).

(12) Unpublished observations of G. A. Hamilton and K. Nakamura.

(13) This treatment assumes no tetracovalent intermediates such as $RC(OH)(OR)_2$.

(14) A referee has suggested that in addition to an enzymatic group, HA could be a water molecule.

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ORGANIC DISULFIDES AND RELATED SUBSTANCES. III. ONE-STEP PREPARATION OF SULFINIC ESTERS FROM LEAD TETRAACETATE AND DISULFIDES OR THIOLS[1]

Sir:

We wish to report a novel means of preparing sulfinic esters by oxidizing disulfides with lead tetraacetate (I) in chloroform–methanol, probably according to the equation

$$\underset{}{RSSR} + \underset{\text{I}}{3Pb(OAc)_4} + 4CH_3OH \longrightarrow 2RS(O)OCH_3 + 3Pb(OAc)_2 + 4AcOH + 2AcOCH_3$$

Thiols also can be used, since the agent I oxidizes them to disulfides.[2] In view of the stability and ready availability of disulfides and thiols, the present process should make sulfinic esters much

(1) Research supported by the Office of Ordnance Research, U. S. Army. Presented at the Southeastern Regional Meeting of the American Chemical Society, Birmingham, Ala., Nov. 3–5, 1960. Part II, D. E. Pearson, D. Caine and L. Field, *J. Org. Chem.*, **25**, 867 (1960).

(2) L. Field and J. E. Lawson, *J. Am. Chem. Soc.*, **80**, 838 (1958).

TABLE I

SULFINIC ESTERS PREPARED

No.	RS(O)OCH₃	Procedure	Total product: Yield, %	Conversion, %	$n^{25}D$ (m.p., °C.)	Carbon, %: Calcd.	Carbon, %: Found	Hydrogen, %: Calcd.	Hydrogen, %: Found	Sulfur, %: Calcd.	Sulfur, %: Found
II	Phenyl	A	79	47	1.5434–7	53.82	53.57	5.16	5.37	20.53	20.74
		A′	62	38	1.5428–30						
III	Phenyl[a]	A[a]	87	61	1.5246–8	58.67	58.44	6.57	6.62	17.40	17.20
IV	Phenyl[b]	A[b]	80	38	1.5214–22	58.67	58.23	6.57	6.69	17.40	17.36
V	*p*-Tolyl	B[c]	73	73	1.5405–8	56.45	56.36	5.92	5.92	18.84	18.56
VI	*o*-Tolyl	B′	72	72	1.5421–5	56.45	56.62	5.92	5.66	18.84	18.52
VII	*o*-Methoxycarbonylphenyl	B[d]	30	11[d]	1.5511–55	50.46	49.18[d]	4.71	4.91	14.97	15.38
VIII	2-Naphthyl	B[e]	33	33	(43–44)	64.05	64.13	4.89	4.95	15.55	15.65
IX	2-Benzothiazolyl	A	61	61	(72–74.5)	45.05	45.13	3.31	3.58	30.07	30.26
X	Pentyl	C	35	35	1.4450–2	47.97	48.21	9.39	9.51	21.34	21.62

[a] 1-Propyl ester; an equimolar amount of 1-propanol was substituted for methanol. [b] 2-Propyl ester; an equimolar amount of 2-propanol was substituted for methanol. [c] Kept at 25° instead of at reflux between the two additions of I. [d] Crude VII extracted into warm pentane, then methanol, then distilled (the viscous liquid decomposed partly on distillation and evolved SO_2). [e] Crude VIII was extracted into pentane; chilling gave first tar, then VIII.

more readily accessible than syntheses hitherto available.[3]

Nine esters prepared thus far, shown in Table I, include aromatic, heterocyclic and aliphatic types.[4] 1-Propyl and 2-propyl esters (III, IV) were prepared by using the appropriate alcohols instead of methanol (the methyl esters themselves presumably are alternative sources of other esters *via* transesterification[5]).

That electronegative groups inhibit the oxidation was suggested by the reduced yield with the *o*-methoxycarbonyl sulfinate VII. This indication was confirmed by recovery of 92 and 78%, respectively, of *o*- and *p*-nitrophenyl disulfide when oxidation of these disulfides was attempted.[6] Steric hindrance seems to be less deleterious than electron withdrawal, since results were comparable in the preparation of the *p*- and *o*-toluenesulfinic esters (V and VI).

In Procedure A, disulfide (0.075 mole) was stirred under reflux in chloroform–methanol (140 ml. of each), and I (0.30–0.34 mole) in chloroform (600 ml.) was added over 8.5–12 hr. Heating was continued for *ca.* 12 hr. The mixture was cooled, treated with water (100 ml.) and filtered. The chloroform layer was washed free of lead salts with water and dried ($MgSO_4$). After removal of solvent, products were purified by recrystallization or distillation (21–47 cm. spinning-band columns). In Procedure B, for improved conversions, the disulfide was used in chloroform (140–440 ml.)–methanol (60–75 ml.) with I (0.33 mole) in chloroform (600 ml.), but after the heating period (10–24 hr.) the addition of I and heating (12 hr.) were repeated. In Procedure A′ and B′, 0.15 mole of thiol in chloroform (50–100 ml.) first was oxidized to disulfide by addition to I (0.093 mole) in chloroform (500 ml.) during *ca.* 1 hr. at *ca.* 25°; Procedure A or B then was followed. Procedure C differs from A in that the I was added during 2 hr. and distillation was from potassium carbonate.

Evidence that the products are sulfinic esters includes: (a) elementary analysis; (b) strong infrared absorption at 1099–1150 cm.$^{-1}$ and 909–991 cm.$^{-1}$; absorption at 1126–1136 cm.$^{-1}$ and 960 cm.$^{-1}$ is reportedly characteristic[7]; (c) identity of the infrared spectra of II, V and VIII with published spectra[8] and agreement for II, V, and VIII in other reported properties; (d) sap. equiv. of 153 for II (calcd. 156) and of 142–158 for X (calcd., 150); the sulfinate salts produced were converted to phenyl and pentyl 2,4-dinitrophenyl sulfone; (e) consumption of 103% of expectation of potassium permanganate by X, assuming that 3 moles of X reacts with 2 of permanganate, and isolation of methyl 1-pentanesulfonate in 53% yield.

(3) *Cf.* "Methoden der Organischen Chemie (Houben–Weyl)," E. Müller, Ed., Vol. 9, 4th ed., G. Thieme Verlag, Stuttgart, 1955, p. 297 (M. Quaedvlieg), 338–340 (F. Muth).

(4) Further work is necessary before the reaction is considered adequately developed for alkanesulfinates such as X. Variations of Procedure C gave products with $n^{25}D$ and infrared spectra similar to those of X, but poor analyses suggested difficultly separable impurities.

(5) *Cf.* H. Phillips, *J. Chem. Soc.*, **127**, 2552 (1925).

(6) Infrared spectra indicated trace formation of methyl *p*-nitrobenzenesulfinate.

(7) S. Detoni and D. Hadži, *J. Chem. Soc.*, 3163 (1955).

(8) Cards 1061–1063, respectively, in the collection published by Butterworths, London, or Verlag Chemie, Weinheim (Dec., 1956). The spectrum of our II lacked bands at 1370 and 1185 cm.$^{-1}$; these evidently resulted in the reported spectrum from methyl benzenesulfonate, which absorbs strongly at these points.

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CYCLOPENTADIENYL-3-CYCLOPENTENYLNICKEL(II)

Sir:

Nickel carbonyl and cyclopentadiene react to form the red crystalline diamagnetic complex.[1] $C_{10}H_{12}Ni$, for which Structure I has been assigned. It has been reported[2] that this same complex can be prepared more conveniently by reducing dicyclopentadienylnickel with sodium amalgam in ethanol. We wish to propose the alternative structure, II, for the $C_{10}H_{12}Ni$ complex which is in better accord with our experimental data. Structure II indicates that during the reduction of dicyclopentadienylnickel only one of the cyclopentadienyl rings is reduced to a cyclopentenyl grouping and the

(1) E. O. Fischer and H. Werner, *Ber.*, **92**, 1423 (1959).

(2) A. H. Filbey, J. C. Wollensak and K. A. Keblys, Abstracts of Papers Presented at the 138th Meeting of the American Chemical Society, New York, N. Y., September 1960, p. 54-P.