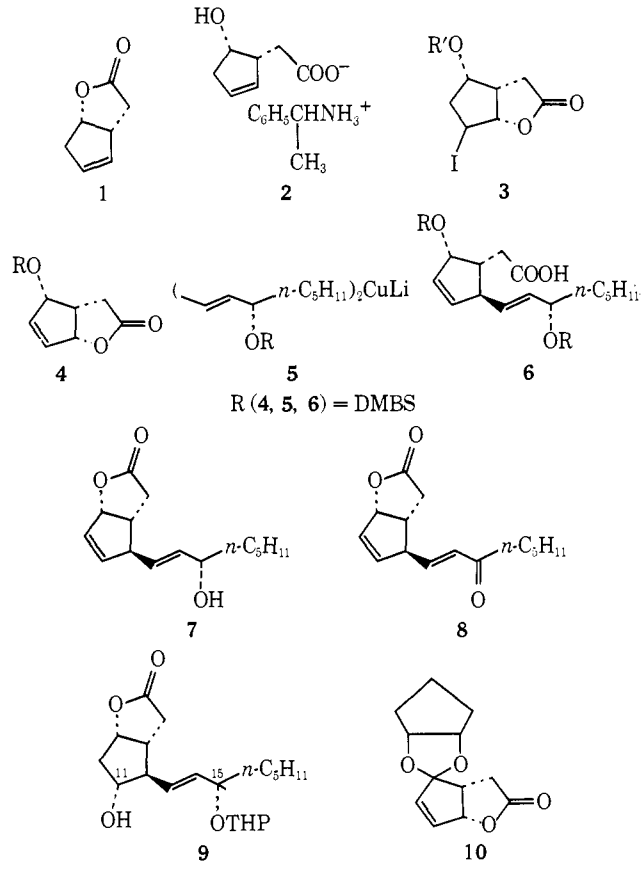
2 in aqueous base (1 equiv) with ether to remove α-methylbenzylamine followed by reaction of the aqueous phase at pH 5 and 20° with 2.5 equiv of iodine afforded the iodolactone **3** (R′ = H)[7a] (85%)[8] as an oil which was treated directly with dimethyl-*tert*-butylsilyl chloride (1.5 equiv) and imidazole (2 equiv) in dimethylformamide[9] at 35° for 22 hr to give the silyl ether **3** (R′ = DMBS),[7] as a colorless oil (85%), $[\alpha]^{18}D$ +28.5° (*c* 1.05 in $CHCl_3$). Exposure of this silyl ether to 1,5-diazabicyclo[4.3.0]non-5-ene[10] (1 equiv) in tetrahydrofuran at 70° for 2 hr under argon led to elimination of HI to form the unsaturated lactone **4**,[7] $[\alpha]^{14}D$ −25.5° (*c* 1.86 in $CHCl_3$), isolated in 94% yield as a colorless liquid.

The unsaturated lactone **4** was treated with an equimolar quantity of the organocopper reagent **5** (*S* configuration, *vide infra*) in ether–pentane (*ca.* 2:1, 7 ml/mmol of **4** total volume) under argon at −78 to −60° for 1 hr, −60 to −40° for 1 hr, and finally at −40 to −20° for 1 hr (reaction complete). The mixture was cooled to −50° and quenched with methanol. The coupling product **6**, obtained from this mixture by partitioning between saturated aqueous ammonium chloride–ether and concentration of the ether phase, was directly converted to the hydroxy lactone **7** by heating with 1:1 acetone–0.2 *M* aqueous hydrochloric acid at 55–60° for 2 hr. Purification was effected by saponification of **7** with 1.5 equiv of lithium hydroxide in 1:1 dimethoxyethane–water at 5°, extraction with ether to remove nonacidic material, acidification to pH 3, and extraction with ethyl acetate. The product contained in the extract underwent clean acid-catalyzed cyclization after several hours at 25° to afford the pure lactone **7**[7,8] (*ca.* 80% yield), $[\alpha]^{18}D$ +252° (*c* 0.2 in $CHCl_3$), as a colorless oil identical in all respects with a specimen of **7** produced by an independent and unambiguous synthetic route.[11] Further, oxidation of **7** using activated manganese dioxide produced the enone **8**[7] which was identical spectroscopically and chromatographically with a sample of **8** synthesized in these laboratories from the known substance **9** by the sequence: **9** → 11-tosylate (TsCl–pyridine) → $\Delta^{10,11}$ olefin (base) → 15-alcohol ($HOAc-H_2O$) → 15-ketone **8** (MnO_2).[12]

Careful chromatographic examination of the mixture produced by reaction of **4** and **5** did not reveal the presence of the coupling product corresponding to S_N2' mode of reaction. In contrast, however, we have observed that reaction of the cuprate **5** with the ketal **10** proceeds to give comparable amounts of S_N2 and S_N2' products. The observed selectivity for S_N2 product in the case of substrate **4** would appear to be a consequence of the bulk of the *tert*-butyldimethylsilyloxy group and a preference for cis stereochemistry in the S_N2' process.[13]

The vinylic copper reagent **5** required for the above described coupling was prepared from the corresponding vinylic lithium reagent along lines previously described,[14] starting from the corresponding vinylic iodide



(obtained essentially by the method of the Syntex group[15]).

The conversion of **7** to prostaglandins which is described elsewhere,[11] taken together with the work described herein, constitutes a synthesis of the major prostaglandins of the second series, PGA_2, PGE_2, and $PGF_{2\alpha}$. This route to prostaglandins is short and simple, completely stereocontrolled, and, as indicated earlier, affords the A prostaglandin directly rather than indirectly. It should be of value in the synthesis of PGA analogs having modified side chains, substances which are currently of great medical interest.[16]

(7) Satisfactory (a) infrared, proton magnetic resonance, and (b) mass spectral data were obtained for this intermediate.
(8) Yield not optimized.
(9) E. J. Corey and A. Venkateswarlu, *J. Amer. Chem. Soc.*, **94**, 6190 (1972).
(10) H. Oediger, F. Möller, and K. Eiter, *Synthesis*, 591 (1972).
(11) E. J. Corey and G. Moinet, *J. Amer. Chem. Soc.*, **95**, 6831 (1973).
(12) The first two steps of this sequence were performed by Dr. Shiro Terashima.
(13) See G. Stork and W. N. White, *J. Amer. Chem. Soc.*, **78**, 4609 (1956).
(14) E. J. Corey and D. J. Beames, *ibid.*, **94**, 7210 1972).
(15) A. F. Kluge, K. G. Untch, and J. H. Fried, *ibid.*, **94**, 7827 (1972). In our work (*S*)-(−)-oct-1-yn-3-ol [J. Fried, C. H. Lin, M. M. Mehra, and P. Dalven, *Ann. N. Y. Acad. Sci.*, **180**, 38 (1971)] was converted to the *tert*-butyldimethylsilyl ether,[9] hydroborated with 9-borabicyclo[3.3.1]-nonane to afford a vinylborane which yielded the vinylic iodide by successive treatment with trimethylamine oxide and iodine.
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Effects of Halogen Substituents on the Intrinsic Acidity of Acetic Acids Determined by Measurements of Gas-Phase Ion Equilibria

Sir:

Recently[1] we reported results for the gas-phase equilibria (1) measured with a pulsed electron beam high-

(1) R. Yamdagni and P. Kebarle, *J. Amer. Chem. Soc.*, **95**, 4050 (1973).

Table I[a]

(a) Directly Measured Equilibria $A_1^- + A_2H = A_1H + A_2^-$

A_1H	A_2H	$-\Delta G°_{600}$	A_1H	A_2H	$-\Delta G°_{600}$
H_2S	CH_3CO_2H	5.0	CH_2ClCO_2H	CH_2BrCO_2H	1.2
CH_2FCO_2H	HCl	1.2	CH_2ClCO_2H	CHF_2CO_2H	5.1
CH_2FCO_2H	CH_2ClCO_2H	2.0	CH_2ClCO_2H	$CHCl_2CO_2H$	7.0[b]
CH_2FCO_2H	CH_2BrCO_2H	3.0	CHF_2CO_2H	$CHCl_2CO_2H$	1.8[c]
CH_2FCO_2H	CHF_2CO_2H	7.2	CHF_2CO_2H	CF_3CO_2H	7.2

	(b) Acidity of AH[g]		(c) Proton Transfer from AH to $CH_3CO_2^-$	
AH	D(A–H) − EA(A)	EA(A)	$-\Delta G°_{gas}$	$-\Delta G°_{aqua}$[f]
CH_3CO_2H	31.8[d]	(78.2)[e]	0	0
CH_2FCO_2H	21.0	(89.0)[e]	10.8	3.1
CH_2ClCO_2H	19.0	(91.0)[e]	12.8	2.7
CH_2BrCO_2H	17.9	(92.1)[e]	13.9	2.7
CHF_2CO_2H	13.8	(96.2)[e]	18.0	5.0
$CHCl_2CO_2H$	12.0	(98.0)[e]	19.8	4.9
CF_3CO_2H	6.6	(103.4)[e]	25.2	6.4

[a] All energy values in kcal/mol. [b] Measured at 490°K. [c] Measured at 536°K. [d] R. Yamdagni and P. Kebarle, *J. Amer. Chem. Soc.*, **95**, 4050 (1973). [e] Estimated on basis of D(A–H) = 110 kcal/mol, V. I. Vedeneyev, *et al.*, "Bond Energies, Ionization Potentials and Electron Affinities," E. Arnold Publishers Ltd., London, 1966. [f] From aqueous acid dissociation constants, C. R. Noller, "Chemistry of Organic Compounds," W. B. Saunders Co., Philadelphia, Pa., 1966, p 988. These values were obtained at room temperature. [g] The gas-phase acidity is normally defined as equal to $\Delta G°$ or $\Delta H°$ for the reaction $AH(g) = A^-(g) + H^+(g)$. The $\Delta H°$ equals D(A–H) + I_p(H) − EA(A). The large and constant I_p(H) = 313.6 kcal/mol was omitted from the acidity values given in the table in order to facilitate comparison of the relative changes.

$$A_1^- + A_2H = A_1H + A_2^- \quad (1)$$

pressure ion source mass spectrometer. The compounds AH were mostly aliphatic carboxylic acids. The present work is an extension to fluoro-, chloro-, and bromo-substituted acetic acids.

The directly measured equilibria are shown in Table Ia. The experimental conditions were very similar to those used previously.[1]

The equilibrium constants K_1 were calculated from the known neutral concentrations $[A_1H]$ and $[A_2H]$ admitted to the ion source and the measured ion ratio of the A_2^- and A_1^- signals observed after the equilibrium (1) was established. The $\Delta G°$ values in Table Ia were obtained from the relationship $-RT \ln K_1 = \Delta G°$. The temperature dependence of $\Delta G°$ for proton transfer reactions involving amines like $NH_4^+ + CH_3NH_2 = NH_3 + CH_3NH_3^+$ was examined in an earlier publication[2] which established that $\Delta S°$ was generally not larger than 1–2 eu and thus $\Delta G° \approx \Delta H°$ in the range 30–300°. Small entropy changes are expected in such systems, where essentially only a change of symmetry number occurs. However, for the present compounds, changes of several entropy units are conceivable since barriers to rotation around single bonds[3] might be created or eliminated in reaction 1. Therefore, attempts were made to measure the temperature dependence of K_1. However, the accessible temperature range was restricted by thermal decomposition of the acids above 370° and formation of the AHA^- dimers below 300°. The temperature dependence of K_1 for proton transfer from difluoroacetic acid to the monofluoroacetate ion in the above range gave $\Delta S° \sim 2.5$ eu which corresponds to a difference of 1.5 kcal between $\Delta H°$ and $\Delta G°$ at 330°. It was felt that no accurate entropies can be obtained over such a narrow range and further entropy determinations were postponed until a modification to the apparatus could be made which would allow measurements at lower temperatures and pressures where the rate of formation of AHA^- will be slow but reaction 1 still fast enough for equilibration.

The acids are shown in Table Ib in order of decreasing D(H–A) − EA(A), *i.e.*, in order of increasing gas-phase acidity. These data were obtained by assuming that $\Delta G_1° = \Delta H_1°$ and using the equation $\Delta H_1° = D(A_2\text{–H}) - D(A_1\text{–H}) + EA(A_1) - EA(A_2)$. The known[4] D(H–Cl) − EA(Cl) = 20 and D(HS–H) − EA(SH) = 37.0 kcal/mol[5] together with the acidities determined in the earlier publication[1] were used as reference points.

Examining the numerical values one finds that the introduction of a halogen substituent leads to a large increase of acidity. The well-known acidity increase of haloacetic acids in aqueous solution has been ascribed to the stabilizing influence on the negative charge by the electron-withdrawing halo substituents. (−I inductive effect). The $\Delta G°$ values for proton transfer from acetic acid to haloacetic acids in the gas phase are compared in Table Ic with the corresponding aqueous values which were measured at room temperature. Since we assume that $\Delta G°$ in the gas phase has only small temperature dependence, the comparison of the two sets of data should be meaningful in spite of the temperature difference. The gas-phase $\Delta G°$ changes are seen to be 3.5–5 times larger. Attenuation of substituent effects in aqueous solution has been observed previously by Taft[6] and others[7] and must be due to a solvation decrease for the stabilized ions.

It is interesting to note that the order of the inductive effect of the halo substituents in the gas phase is Br > Cl > F which is reverse of the aqueous order. At present we cannot eliminate the possibility that the reversal is due to halo substituent dependence of rota-

(2) J. P. Briggs, R. Yamdagni, and P. Kebarle, *J. Amer. Chem. Soc.*, **94**, 5128 (1972).

(3) Information on various energy barriers to rotation can be obtained from J. P. Lowe, *Progr. Phys. Org. Chem.*, **6**, 1 (1968).

(4) Selected values of chemical thermodynamic properties, *Nat. Bur. Stand. (U. S.) Tech. Note*, 270-3.

(5) J. A. Kerr, *Chem. Rev.*, **66**, 465 (1966); B. Steiner, *J. Chem. Phys.*, **45**, 5057 (1968).

(6) M. Taagepera, W. G. Henderson, R. T. Brownlee, J. L. Beauchamp, D. Holtz, and R. W. Taft, *J. Amer. Chem. Soc.*, **94**, 1369 (1972).

(7) A. G. Harrison, P. Kebarle, and F. P. Lossing, *J. Amer. Chem. Soc.*, **83**, 777 (1961).

tional barrier entropy changes. However, it is more likely that the reversal is caused by electronic effects. The most probable explanation would be the higher polarizability[8] of the larger halo substituents. The atomic polarizabilities α of F, Cl, and Br are 0.53, 2.61, 3.79 Å^3, respectively.[9] The distance r in the acetate ions between one of the O atoms and the halogen substituent may be estimated to be 2.69, 2.85, and 2.89 Å, respectively. Assuming that one-half electronic charge is on the O atom, one calculates, using the electrostatic equation for potential energy $u = \alpha e^2/2r^4$, the negative energies 0.5, 1.6, and 2.2 kcal/mol, respectively. Somewhat larger energies can be obtained with bond polarizabilities.[10] The energy differences in both cases would seem sufficient, to explain the gas-phase results, *only* if the inductive effect, in the absence of polarization, changes (increases) very little from Br to F. There is some independent evidence that this is so. Thus the aqueous acidity of meta-halo-substituted benzoic acids and phenols does not increase from Br to F as might have been expected but increases from F to Cl ≈ Br then decreases slightly for I. Gas-phase acidities of meta-substituted phenols determined recently by McIver[11] also increase in the order F, Cl, Br. Since the stabilizing effect of the substituents in the gas phase increases in the order F, Cl, Br, the higher aqueous acidity of the fluoroacetic acid must be due to solvent effects. Since the halo atom acquires a small negative charge, one water molecule might be hydrogen bonding to it. This bonding interaction will be weaker for the larger Br atom than the smaller F.

The values of Table Ic show that in general the second halogen atom leads to a smaller increase of acidity than the first. This effect is observed also in solution and is generally expected. An exception is the change between difluoro- and trifluoroacetic acid where the gas-phase acidity difference is the same as that between mono- and difluoro-. We are not certain whether this is a true result or an experimental error.

(8) The effect of polarizability of alkyl groups on gas-phase acidities of alcohols was first suggested by J. I. Brauman and Larry K. Blair, *J. Amer. Chem. Soc.*, **92**, 5986 (1970).

(9) S. Fraga, K. M. Saxena, and B. W. N. Lo, *Atomic Data*, **3**, 323 (1971).

(10) J. D. Hirshfelder, C. F. Curtiss, and R. B. Bird, "Molecular Theory of Gases and Liquids," Wiley, New York, N. Y., 1964, p 947.

(11) R. T. McIver, private communication.

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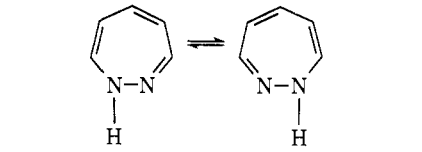
Iron Tricarbonyl Complexes of 1(1*H*),2-Diazepine and Methyl Substituted Derivatives. Novel Fluxional Organometallic Compounds

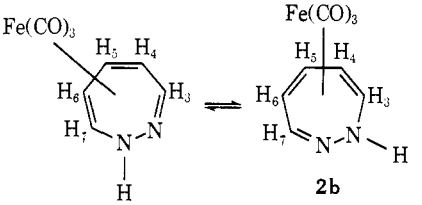
Sir:

The unsubstituted molecule 1(1*H*),2-diazepine has so far escaped synthesis.[1] As a vinylogous analog of pyrazole, 1(1*H*),2-diazepine is a nonaromatic polyene for which N–H tautomerism, represented by structures **1a** → **1b**, is expected.[2]

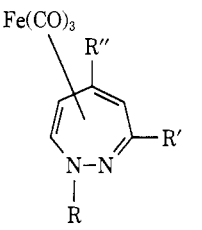
Streith first prepared 1-acylated $Fe(CO)_3$–1(1*H*),2-diazepine complexes.[1b] Our interest in 1,2-diazepines and their complexes[1a,3–5] led us to investigate the trapping of **1** as an iron tricarbonyl analog of *N*-acetyl-1(1*H*),2-diazepine as a first step in studies on the chemistry of the complexed heterocycle. We describe herein the synthesis of 1(1*H*),2-diazepine iron tricarbonyl (**2**) and the methyl substituted derivatives **3a**,**b**, the conversion of **2** to the *N*-benzyl complex **3c**, and a novel type of fluxional behavior of the N–H complexes **2** and **3b** which is a direct



1a **1b**



2a **2b**



3a, R = H; R′ = CH_3; R″ = H
b, R = H; R′ = H; R″ = CH_3
c, R = $CH_2C_6H_5$; R = R′ = H
d, R = $COCH_3$; R′ = R″ = H
e, R = $COOC_2H_5$; R′ = R″ = H
f, R = $COCH_3$; R′ = CH_3; R″ = H
g, R = $COCH_3$; R′ = H; R″ = CH_3

consequence of the tautomeric behavior of the diazepines. Thermodynamic parameters ($\Delta G^{\ddagger}$, $\Delta S^{\ddagger}$) calculated from line-shape analysis of the nmr spectra are of interest in the wider contexts of molecular tautomerism[6] and fluxionality.[7]

Treatment of **3e**[1a] with sodium ethoxide in ethanol (0°, 1 hr) gave, after chromatography on alumina, yellow crystals of **2**[8] (60%): mp 121°; ir (C_6H_{14}) 3275 m (N–H), 2052 (s), 1990 (s), 1976 (s) cm^{-1}. The mass spectrum of **2** showed a parent ion at *m/e* 234 together with ions at *m/e* 206, 178, and 150 from successive loss of three CO groups and at *m/e* 94 due to the diazepine $[C_5H_6N_2]^+$ ion. A Mössbauer spectrum of **2** (δ

(1) For recent summaries of work on 1,2-diazepines see (a) A. Balasubramanian, J. M. McIntosh, and V. Snieckus, *J. Org. Chem.*, **35**, 433 (1970); (b) J. Streith and J. M. Cassal, *Bull. Soc. Chim. Fr.*, 2175 (1969); (c) G. Taurand and J. Streith, *Tetrahedron Lett.*, 3575 (1972); (d) F. D. Popp and A. C. Noble, *Advan. Heterocycl. Chem.*, **8**, 22 (1967).

(2) L. Hunter, *J. Chem. Soc.*, 806 (1945).

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(5) A. J. Carty, D. P. Madden, and T. Birchall, *Inorg. Chem.*, **11**, 1453 (1972).

(6) A. R. Katritzky and J. M. Lagowski, *Advan. Heterocycl. Chem.*, **1**, 312, 341 (1963); **2**, 3, 27 (1963).

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(8) Satisfactory elemental analyses have been obtained for all compounds described herein.