Tetrahedron Vol. 40, No. 24, pp. 5275 to 5279, 1984
Printed in the U.S.A.

0040-4020/84 \$3.00 + .00
Pergamon Press Ltd.

A QUESTION CONCERNING THE p*K* RANGE WITHIN WHICH AN ORGANIC FREE RADICAL EXHIBITS NORMAL RADICAL BEHAVIOUR. THE CASE OF GALVINOXYL

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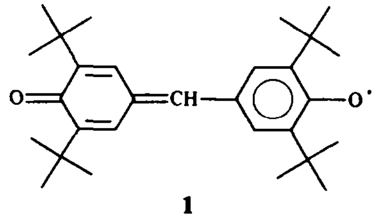
(*Received in UK* 31 *January* 1984)

Abstract—Galvinoxyl ($G^{\cdot}$) reacts with a series of substituted acetic acids and forms hydrogalvinoxyl (GH) as the sole product. The kinetic data conform with a Brønsted type analysis. Hydrogalvinoxyl may dissociate to the relevant cation G^+, in a process which appears to be a *thermal hydride ejection*. In addition GH exhibits thermochromism with the following parameters: $\Delta H = -17.0 \pm 0.8$ kcal mol^{-1} and at 298 K, $K_e = 1.16\ (\pm 0.28) \times 10^{-5}$ M^{-1}, $\Delta S = -79.0 \pm 8.0$ cal K^{-1} mol^{-1}. The behaviour of $G^{\cdot}$ at various acidities is described.

Some time ago one of us[1] proposed the term "amphielectronic ionization" for the conversion of a stable free radical $R^{\cdot}$ to the respective anion and cation by a *thermal* single electron transfer reaction with nucleophilic and electrophilic reagents, respectively (Eq. (1)).

$$R^+ \xleftarrow{\text{Electrophiles}} R^{\cdot} \xrightarrow{\text{Nucleophiles}} R^- \qquad (1)$$

Given that a condensed medium or reagent can have an electrophilicity or nucleophilicity ranging from that of superacids to that of superbases (*ca.* 100 p*K* units), it appears reasonable to ask: What is the p*K* range within which a given radical exhibits *normal* radical behaviour? This question becomes important if one bears in mind that outside this p*K* range the radical will be transformed into an anion or cation.[1-3] To understand the factors influencing this phenomenon we initiated a study of the reaction of Galvinoxyl (**1**), a stable free radical with basic and acidic reagents of varying strength. This paper deals with the reaction between **1** and a series of substituted acetic acids.



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Galvinoxyl[4] in the presence of an acid such as CF_3CO_2H undergoes "bleaching" which can be followed spectrophotometrically with time (curve 4, Fig. 1). A similar behaviour is exhibited by **1** with other substituted acetic acids, e.g. CH_2ClCO_2H (curve 1) or $CHCl_2CO_2H$ (curve 2, Fig. 1). It is apparent from Fig. 1 that the reaction rate depends on the strength of the acid. Thus, bleaching of **1** is much slower with CH_2ClCO_2H than with CF_3CO_2H, despite the fact that the initial concentration of the former acid was much higher; see the relevant caption and compare the p*K* values of the two acids, 2.81 and −0.26, respectively. A plot of 1/(absorbance) versus time is linear up to 3 half-lives (Fig. 2) albeit the initial concentrations of **1** and the acid were not equal. From such plots the second order rate constants were extracted, which, after normalization with respect to the initial concentration of the acid, gave values of k_3 which are summarized in Table 1, along with other relevant data.

The dependence of the rate of bleaching on the strength of the acid is shown to be of the Brønsted type. Figure 3 shows a plot of log k_3 versus p*K*, which is acceptably linear. The least-squares line is given by $\log k_3 = 4.88 - 1.29(pK)$ ($r = 0.998$). Perhaps, an indication of the soundness of our kinetic

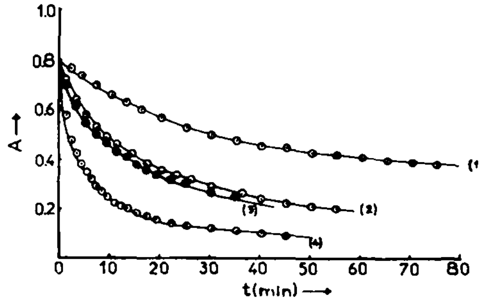


Fig. 1. Decay of the absorption due to $G^{\cdot}$ ($\lambda_{max} = 428$ nm) with time. (1) $[CH_2ClCO_2H]_0 = 2.5 \times 10^{-1}$ M; (2) $[CHCl_2CO_2H]_0 = 2.5 \times 10^{-2}$ M; (3) $[CCl_3CO_2H]_0 = 1.5 \times 10^{-3}$ M; (4) $[CF_3CO_2H]_0 = 5.0 \times 10^{-4}$ M. In all cases $[G^{\cdot}]_0 = 5.0 \times 10^{-5}$ M, Solvent: $ClCH_2CH_2Cl$, temp. 23°.

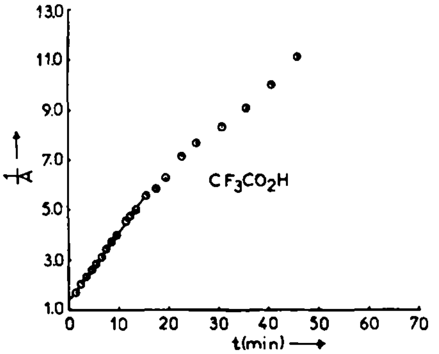


Fig. 2. Representative plot of 1/(absorbance) at 428 nm vs time.

analysis could be obtained from the observation that a plot of the logarithm of the "normalized" (with respect to the initial concentration of the acid) initial slopes versus p*K* is linear with a slope of −1.25, compared to −1.29 of the log k_3 vs p*K* plot. From the regression equation we estimate the p*K* of the acid in which **1** can survive for a long time. This pK^w is estimated to be 6.4 and it is based on the assumption that any acid reacting with **1** more slowly than acetic acid by two orders of magnitude can be considered practically inert toward **1**.

When the concentration of acid with a p*K* equal to or below a certain limit is increased beyond a "threshold" concentration, the characteristic absorption due to the relevant cation (G^+) appears with $\lambda_{max} = 520$ nm.[5] It must be stressed that the formation of G^+ is observed even with strict exclusion of oxygen from the system. Figure 4 represents a sort of spectrophotometric titration of **1** against CF_3CO_2H, where the absorbance due to G^+ is plotted against the acid concentration. The initial slopes of such plots are given in the last column of Table 1, for the acids capable of producing cation G^+. These initial slopes, $(\Delta A/\Delta C)_i$, are plotted in Fig. 5 against p*K*. The plot indicates that the above-mentioned limit of p*K* for the appearance of G^+ should be *ca.* 2.6. It is felt that this conclusion is valid for reaction media having dielectric constants comparable with that of 1,2-dichloroethane. In fact we observed that formic acid (p*K* = 3.75) in 1,2-dichloroethane 10–90 v/v% fails to produce any G^+, but G^+ can be produced from **1** in neat formic acid. The dielectric constants of 1,2-dichloroethane and formic acid are 10.65 and 58.5, respectively.[6]

Figure 6 shows the spectral changes caused by the addition of acid to **1**. We note that it takes only 0.21 M of CF_3CO_2H in order to produce more G^+ molecules than the ones produced by 2.1 M $CHCl_2CO_2H$ (compare curves 6 and 7). This effect is expressed in a quantitative manner by the $(\Delta A/\Delta C)_i$ initial slopes (see Fig. 4 and Table 1). This implies that the weaker the acid the larger the number of acid molecules needed in order to stabilize the cation G^+.

Another fact to be noted is the occurrence of an isosbestic point in Fig. 6. This indicates that there is a proportionality between the number of G^+ molecules and the number of molecules of its precursor.[7] It may then be concluded that **1** behaves somewhat like an ordinary indicator. It therefore appears reasonable to hope that by using this type of "indicator" we may be able to construct a scale of *single electron electrophilicity or nucleophilicity.*

Another practical outcome of this work is that it allows one to prescribe conditions under which oxidation of **2** could lead to one of the possible products, *sc.* $G^\cdot$ (**1**), G^+, or the precursor of G^+. Thus, by employing a "neutral" solvent one can get **1**, whereas, in an acid medium with a p*K* greater than 2.6, oxidation should lead to the precursor of G^+. Finally, the oxidation of **2** in a strongly acidic medium will produce directly the cation G^+. In fact, these predictions are confirmed experimentally. For example, in order to determine the molar extinction coefficient of G^+ we oxidized **2** with manganese dioxide in 50–50 v/v% CF_3CO_2H–$ClCH_2CH_2Cl$. The extinction coefficient at 520 nm was then found to be 130,000, compared to 134,000 derived from the data of Fig. 4.

Table 1.

Acid	$\frac{(\Delta A/\Delta t)_i}{[C]_0}$ [a]	k_3 [b]	pK_a [c]	$(\Delta A/\Delta C)_i$ [d]
CH_3CO_2H	1.89×10^{-6}	4.057×10^{-2}	4.76	—
CH_2BrCO_2H	2.85×10^{-4}	15.21	2.90	—
CH_2ClCO_2H	8.70×10^{-4}	30.38	2.81	—
CH_2FCO_2H	7.55×10^{-4}	31.63	2.57	0.04
$CH_2(CN)CO_2H$	1.90×10^{-3}	113.67	2.47	—
$CHCl_2CO_2H$	2.67×10^{-2}	978.00	1.30	0.32
CCl_3CO_2H	5.00×10^{-1}	18,114.00	0.52	1.78
CF_3CO_2H	3.33	162,636.00	−0.26	4.16
$PhCH_2CO_2H$	—	7.74	4.31	
HCO_2H	—	13.74	3.75	

[a] "Normalized" initial slopes, Fig. 1.

[b] In M^{-2} sec^{-1} at 23°C.

[c] The p*K* values were taken from the compilations of J. W. Emsley, J. Feeney and L. H. Sutcliffe; *High Resolution Nuclear Magnetic Resonance Spectroscopy*, Vol. 1, p. 520. Pergamon Press, Oxford (1965); A. Albert and E. P. Serjeant, Chapman and Hall, London, p. 84 (1971).

[d] Initial slopes, see, e.g. Fig. 4.

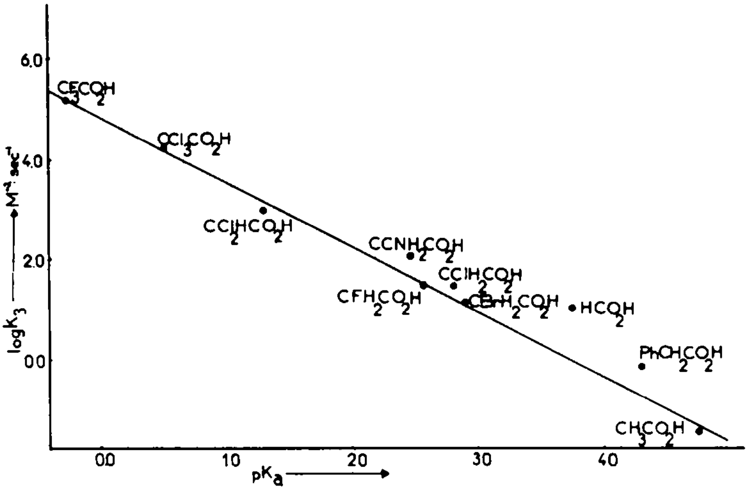
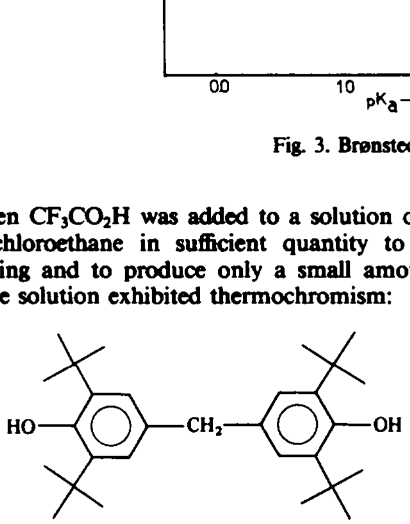


Fig. 3. Brønsted-type plot of the data in Table 1.

When CF_3CO_2H was added to a solution of **1** in 1,2-dichloroethane in sufficient quantity to cause bleaching and to produce only a small amount of G^+, the solution exhibited thermochromism:



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by lowering the temperature of the solution the absorbance at 520 nm was increased. The phenomenon was perfectly reversible and the cycle could be repeated several times. From the data in Fig. 7 a ΔH^0 of −17.0 ± 0.8 kcal mol^{-1} was derived, and at 298 K $K_e = 1.16\ (\pm 0.28) \times 10^{-5}\ M^{-1}$, $\Delta S = -79.0 \pm 8.0$ cal K^{-1} mol^{-1}.

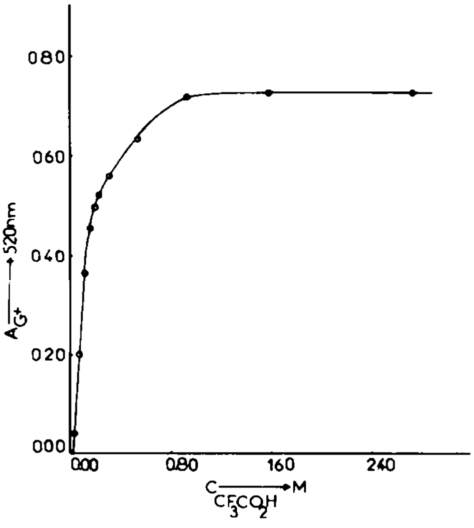


Fig. 4. Extent of cation G^+ formation as a function of the concentration of added CF_3CO_2H.

We were able to characterize the reaction products. We isolated from a mixture of **1** and acetic acid, after completion of bleaching, compound **3**, i.e. hydrogalvinoxyl GH. The spectral data of this compound were identical to those of an authentic sample prepared by two different routes, namely, (a) by hydroquinone reduction of **1**[8] and (b) according to Eq. (2).

$$G^{\cdot} \xrightarrow[THF]{Bu^tOLi} G^-Li^+ \xrightarrow{H_2O} GH \qquad (2)$$

Hydrogalvinoxyl appears to be the sole reaction product, on the basis of NMR analysis of the entire reaction mixture from **1** and acetic acid. On the basis of the chemical and the kinetic evidence we propose Scheme I, which, it is felt, explains the experimental facts.

$$G^{\cdot} + H^+ \underset{Fast}{\overset{K_e}{\rightleftharpoons}} GH^{\cdot +} \qquad (i)$$

$$GH^{\cdot +} + G^{\cdot} \xrightarrow{slow} GH + G^+ \qquad (ii)$$

$$G^+ \xrightarrow[fast]{H^- \text{ abstraction}} GH \qquad (iii)$$

Scheme I.

We assume a fast and reversible step (i) in which **1** is protonated and forms a sort of radical cation, with

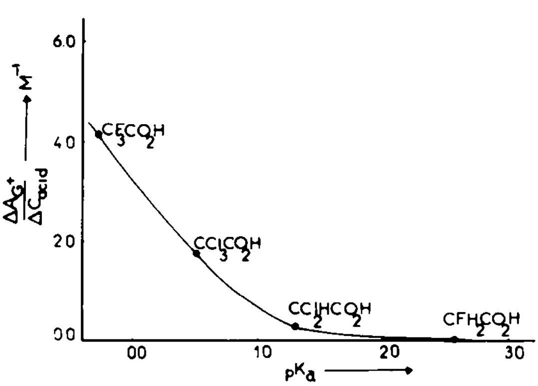


Fig. 5. Initial slopes, from plots such as in Fig. 4, plotted against the pK value of the acid.

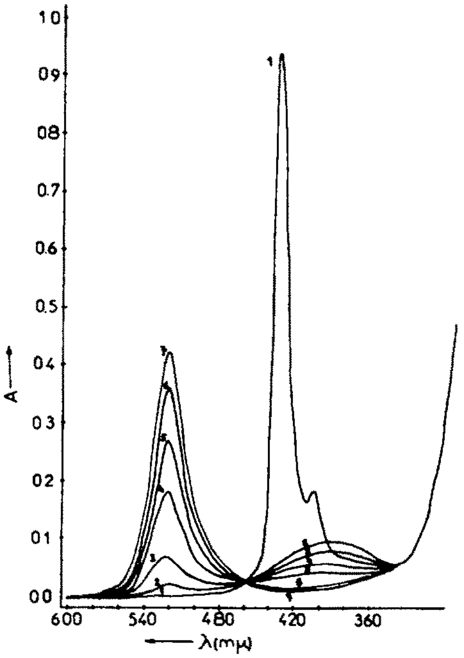


Fig. 6. Spectral changes upon the addition of acid to a solution of $G^{\cdot}$ in 1,2-dichloroethane: 2–6 $CHCl_2CO_2H$ (2, 0.148 M; 3, 0.293 M; 4, 0.663 M; 5, 1.052 M; 6, 2.077 M) 7 CF_3CO_2H, 0.219 M.

K_e very small.[9] This step is followed by the rate-controlling one in which the "radical cation" $GH^{\cdot +}$ reacts with **1** and gives products.

Cation G^+ is stable only in the presence of a concentration equal to or larger than a threshold of an acid with pK < 2.6. In kinetic runs the initial acid concentration was kept below the threshold. Under these conditions G^+ is unstable, or in other words reactive, and it seems reasonable to expect that it can decay by a hydride-abstraction process (step (iii)). Scheme I leads to the rate expression of Eq. (3), according to which the

$$-d[G^{\cdot}]/dt = k_3[\text{Acid}][G^{\cdot}]^2 \qquad (3)$$

kinetic data were analysed.

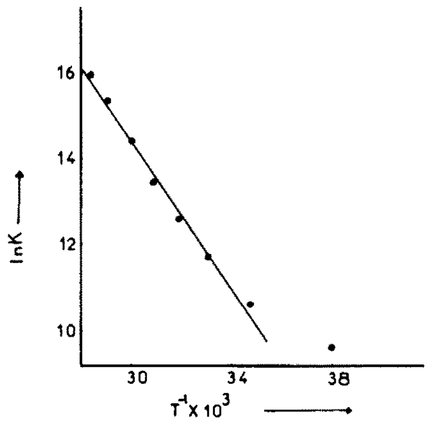
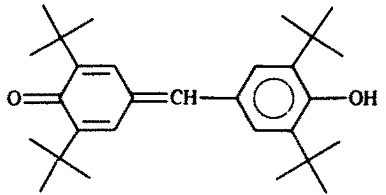


Fig. 7. Logarithm of dissociation constant of GH plotted against the inverse of temperature.

Perhaps the most difficult to explain is the formation of the cation from its presursor, namely hydrogalvinoxyl. We have found that hydrogalvinoxyl prepared according to the literature,[8] or according to Eq. (2) when dissolved in a 50–50 v/v% mixture of CF_3CO_2H and 1,2-dichloroethane and under the strict exclusion of oxygen, ionizes to the relevant cation G^+. We believe that one is forced to consider a thermal "hydride-ejection", Eq. (4). Although this explanation is without precedent, it could be considered the formal analog of thermal electron ejection.

$$GH \xrightarrow[\text{Medium}]{\text{Electrophilic}} G^+ + H^- \qquad (4)$$

One could argue further in favour of Eq. (4) by referring to the principle of microscopic reversibility.[10] Indeed, Eq. (4) is the reverse reaction of step (iii) (Scheme I).



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Considering now the thermochromism data, it appears that the negative dependence on temperature as well as the very large negative value of entropy could mean that the cation G^+ is stabilized by ordering either of solvent molecules or, more probably, of "free acid" molecules around the ion pair. This appears to corroborate with the initial slopes $(\Delta A/\Delta C)_i$; see Table 1 and relevant discussion.

Concluding remarks. We have determined a set of pK values in the acidic region which are characteristic of galvinoxyl. Namely, the stable free radical retains its properties at pK's above 6.4 and up to the still unknown pK limit in the basic region. At the pK range 6.4–2.6 it is transformed to hydrogalvinoxyl, whereas, at the pK range 2.6–*ca.* 0 hydrogalvinoxyl coexists with the cation G^+. Below p$K \simeq 0$, hydrogalvinoxyl dissociates completely to G^+. Consequently, the latter value constitutes the lower limit of pK for the amphielectronic ionization of galvinoxyl. It is felt that for every organic radical there is an analogous set of pK values which are characteristic of the particular free radical. Finally, the relevance of the present work to technological matters such as the function of antioxidants in the presence of electrophilic reagents should not be overlooked.

Acknowledgement—We thank Professor Andreas A. Zavitsas for comments in the manuscript.

EXPERIMENTAL

NMR and IR spectra were recorded on a Varian FT 80A NMR spectrometer and a Beckman IR-33 spectrophotometer, respectively. Kinetic measurements were made with a Perkin-Elmer 356 spectrophotometer, and thermochromism was studied with a PYE UNICAM UV-VIS spectrophotometer equiped with UNICAM SP 8005 programme controller. 1,2-Dichloroethane was purified by drying over calcium chloride followed by double distillation. Galvinoxyl was prepared according to the literature[11] and it was found[12] to be 96% pure. All but one of the carboxylic acids used in this study were commercial products 99% pure and were used as received. Bromoacetic acid was prepared according to the literature.[13] We found that the use of a catalytic amount of

Table 2.

Temp. K	Absorbance (520 nm)
263.4	0.423
287.7	0.311
302.5	0.211
313.8	0.145
324.0	0.100
333.0	0.065
344.0	0.041
352.0	0.030

PCl_3 shortens markedly the reaction time between bromine and acetic acid. The bromoacetic acid was distilled twice before use.

The rate of disappearance of **1** in the presence of acid was followed spectrophotometrically at its $\lambda_{max} = 428$ nm at 23 ± 1°. The reaction medium was 1,2-dichloroethane and cuvettes of 1 mm path length were used. Exclusion of air from the reaction system was found to be unnecessary. The pseudo-second order rate constants were extracted from the linear segment of 1/(absorbance) vs time plots by numerical analysis of the data. The apparent second order rate constants were divided by the initial concentration of the acid to give k_3s which are listed in Table 1.

Thermochromism

A solution being initially 4.50×10^{-5} M in **1** and 5.24×10^{-2} M in CF_3CO_2H, exhibited the absorbances summarized in Table 2, at the indicated temperatures. The data were analysed on the basis of $\epsilon(520) = 134{,}000$, which was derived from the data in Fig. 4.

Reaction of galvinoxyl and hydrogalvinoxyl with trifluoroacetic acid under exclusion of oxygen

To a carefully degassed solution of CF_3CO_2H in 1,2-dichloroethane, 50–50 v/v%, was added solid **1** under argon. The characteristic colour of G^+ appeared instantly, thus precluding the possibility that G^+ is produced by "autoxidation". Identical results were obtained when hydrogalvinoxyl was added to the CF_3CO_2H–$ClCH_2CH_2Cl$ mixture.

Preparation of hydrogalvinoxyl (**3**)

To a solution of lithium sec-butoxide in toluene, prepared from sec-butanol (0.092 mL, *ca.* 1 mmol), butyllithium in benzene (0.6 mL, 1.70 M, 1.02 mmol), and toluene (8 mL), was added a solution of **1** (0.2 g) in 14 mL of anhydrous, peroxide-free THF. The characteristic colouration of G^- appeared instantly. The mixture was stirred under argon for 14 h and then quenched with dilute acetic acid. The product was taken up in methylene chloride, the organic layer was separated, washed with water, dried over $MgSO_4$, and evaporated to constant weight after removal of drying agent. NMR analysis of the product indicated almost pure hydrogalvinoxyl: $\delta(CDCl_3)$: 1.40 (d, 36H, 4 Bu^t); 5.50 (s, 1H, OH); 6.75–7.88 (m, with peaks at 6.97, 7.11, 7.21, 7.31 and 7.57, 5H, olefinic + aromatic).

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