magnetization is then detected in $t2$ while using broadband ${}^{13}C$ decoupling with GARP.[13] During the detection period, the $\uparrow$ and $\downarrow$ ensembles of the H^{β} spins (corresponding again to the two spin states of H^{α}) precess with a frequency difference of ${}^{3}J(H^{\alpha}-H^{\beta})$. The E.COSY-like pattern results from a correlation of the $\uparrow$ and $\downarrow$ ensembles of the C^{α} during $t1$ with the corresponding $\uparrow$ and $\downarrow$ ensembles of H^{β} during $t2$. A similar process acting on the magnetization which begins on C^{β} gives rise to E.COSY-like structure in the $\omega 1 = C^{\beta}$, $\omega 2 = H^{\alpha}$ cross peak.

In conclusion, 2D $C(\omega 1)$–C-selective–$H(\omega 2)$ spectroscopy is a simple approach for determining ${}^{1}H$ homonuclear coupling constants in ${}^{13}C$-enriched molecules. In principle, the experiment can also be used to measure homonuclear coupling constants of ${}^{13}C$-enriched ligands bound to proteins. It represents one of an expanding group of multidimensional NMR methods[15] for obtaining extensive sets of homo- and heteronuclear vicinal coupling constants in polypeptides and proteins.

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Note Added in Proof. Since submitting this paper for publication, we have found that this pulse sequence can be used for determining ${}^{3}J(H^{\alpha}-H^{\beta})$ coupling constants in a small ${}^{13}C$-enriched protein and in long amino acid side chains. We have also developed modified 2D and 3D versions which utilize initial polarization transfer from ${}^{1}H$ to ${}^{13}C$ to enhance the sensitivity of the experiment (Emerson and Montelione, manuscript in preparation).

Registry No. Ala, 56-41-7; Thr, 72-19-5; Val, 72-18-4; Ile, 73-32-5.

Hydrogen Isotope Effect and Traveling Waves in a Halogen-Free Chemical Oscillatory System

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Chemical oscillators and periodic spatial propagation of reaction fronts have received increasing attention.[2-15] A detailed examination of complex chemical reaction systems in their oscillating mode may indeed lead to valuable new mechanistic insights into the nature of the selectivity-determining interplay of diffusional and chemical events.

In 1983, Jensen reported oscillations during the Co(II)-catalyzed air oxidation of benzaldehyde in aqueous acetic acid in the presence of bromide ion.[16] Since then, many attempts have been made to describe the complex chemistry of this system.[17-22] Thus far, three different mechanistic models have been proposed[17,19,21] and used to simulate the oscillatory behavior of the Jensen system by computation.[19,20,22]

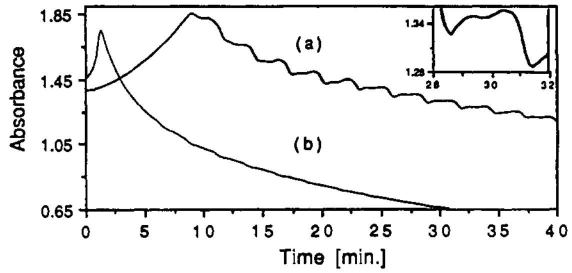

Figure 1. Oscillations in absorbance of Co(III) at 620 nm in a closed system at 60 °C, initially containing [Co(III)] = 8.0×10^{-3} M, [Co(II)] = 2.5×10^{-3} M, and [PhCRO] = 0.15 M. The total volume of the reaction mixture in the cell is 3.2 mL: (a) PhCDO; (b) PhCHO; inset, enlargement of the segment of absorbance curve a between 28 and 32 min.

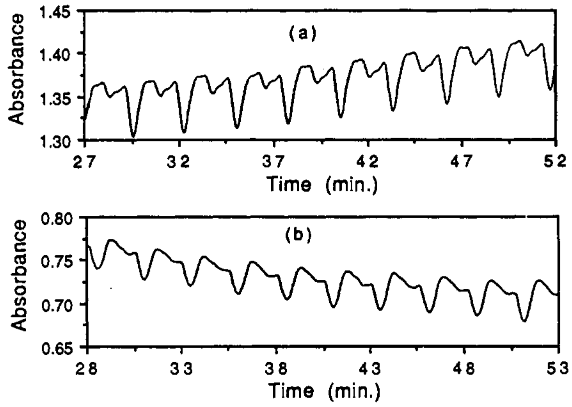

Figure 2. Oscillations in absorbance of Co(III) at 620 nm in an open system at 60 °C, initially containing [Co(III)] = 8.0×10^{-3} M, [Co(II)] = 2.5×10^{-3} M, and [PhCRO] = 0.15 M: (a) PhCDO; (b) PhCHO.

The recent studies[22,23] prompt us to report here the discovery of an oscillatory system which exhibits the following periodic and mechanistic features: (i) The system is based on the autoxidation of benzaldehyde; however, unlike the Jensen oscillator, it is entirely halogen-free. (ii) Our chemical oscillator reveals a considerable kinetic hydrogen isotope effect, which is particularly fascinating. We are able to demonstrate for the first time that an oscillatory behavior can be modulated by taking advantage of an isotope effect. (iii) The present oscillatory system exhibits its chemical periodicity not only in time but also in space: self-generated chemical waves propagating through the motionless reaction mixture have been observed. Although it has already been demonstrated[22,23] that a single propagating reaction front of Co(III) could be initiated in a similar system, we do not recall having yet seen any experimental report on periodically self-generating reaction waves in the autoxidation of benzaldehyde.

The fact that all of these features are displayed in the same system makes the present oscillator particularly attractive for

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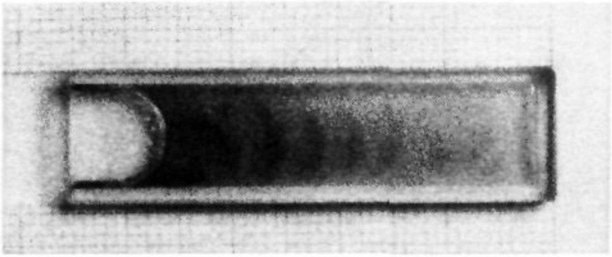

Figure 3. Typical set of traveling waves (dark regions) in an open cell with 2-mm path length, which is placed horizontally on a thermostated plate (65 ± 1 °C). Initial reactant concentrations: [PhCHO] = 0.15 M; [Co(III)] = 0.0020 M; [Co(II)] = 0.0065 M. The photograph was taken 1 h after mixing the reactants. Green waves of Co(III) emerge periodically from the region near the gas–liquid interface, where oxygen from air is absorbed, and propagate through the solution toward the closed end of the cell. Wave velocity: 2.0–2.5 mm/min. Cell length: 4.5 cm.

detailed mechanistic studies. In addition, the hydrogen isotope effect may provide a valuable tool for testing mechanistic models.

Our chemical oscillator consists of benzaldehyde (PhCRO, R = H or D), Co(III),[24] Co(II), and elemental oxygen. The reaction takes place at 60 °C in an acetic acid medium, either in a closed, thermostated 1-cm square spectrophotometer cell where oxygen may be taken up from the remaining head-space gas volume (closed system) or in an open cell where oxygen from the air may be absorbed at the liquid surface of the motionless reaction mixture (open system). The final oxidation product is benzoic acid. The oscillating behavior is recorded with a UV/VIS spectrophotometer (Shimadzu UV-260) by measuring the absorbance of Co(III) at 620 nm.

Figure 1a shows the typical oscillatory pattern of the closed and unstirred reaction system containing PhCDO. After the concentration of Co(III) has reached a maximum, a spontaneous oscillation sets in with a characteristic frequency of 6.0×10^{-3} s^{-1}. Due to the limited amount of oxygen in the closed system, the oscillations are highly damped. It is interesting to note that, if PhCDO is replaced by PhCHO and the other conditions are unchanged, the oscillating behavior is hardly noticeable (Figure 1b).

When the oxidation is carried out in an open system and at sufficiently low conversion, an almost sustained oscillatory behavior is observed for PhCDO as well as for PhCHO, with characteristic oscillation frequencies for the given reaction conditions of 6.0×10^{-3} and 6.7×10^{-3} s^{-1}, respectively (Figure 2).

In the closed as well as in the open reaction systems, the average Co(III) concentration during oscillation is much higher in the case of PhCDO than in the case of PhCHO. Furthermore, it is noteworthy that after allowing for an appropriate induction period, the average concentration of Co(III) in the open system slightly increases or decreases with time, depending on whether the deuterated (Figure 2a) or the nondeuterated (Figure 2b) benzaldehyde is oxidized. The hydrogen isotope effect is further confirmed by a competitive reaction experiment in which the ratio of the oxidation rates of PhCHO and PhCDO was determined to be 3.8.

The spatial periodicity in our system manifests itself not by a single reaction front,[23] but rather by periodically self-generating waves. Figure 3 shows a typical set of such traveling waves. Under the conditions given, self-generated waves are propagating at the velocity of about 2–2.5 mm/min. The nature of these waves and the hydrogen isotope effect in the wave propagation are under investigation and will be reported elsewhere.

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(24) The Co(III) complex used in our system was prepared by O_2 oxidation of $Co(AcO)_2$ in AcOH in the presence of methyl ethyl ketone. The cobalt complexes were then isolated and dried after removing the solvent under vacuum. The total cobalt content was determined by atomic absorption spectroscopy. The concentration of Co(III) was measured spectrophotometrically.[21]

Model for a Platinated DNA Triplex: Watson–Crick and Metal-Modified Hoogsteen Pairing[†]

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Nucleobase triples between adenine (A) and two thymines (T) or between guanine (G), neutral cytosine (C) and protonated cytosine (CH^+) combine Watson–Crick and Hoogsteen base pairing patterns (Figure 1).[2] Formation of such base triples occurs naturally in DNA (H-DNA[3]) or spontaneously (disproportionation) in RNA[4] and represents the basis for numerous site-specific manipulations of DNA which include cleavage,[5-7] nonenzymatic oligonucleotide ligation,[8] and sequence-specific alkylation,[9] for example. Oligonucleotide specificity could feasibly be applied to regulate or inhibit transcription of DNA to RNA, thereby providing a rationale for treatment of viral diseases.[10]

Similarly, the principle of Watson–Crick base pairing and duplex formation between mRNA and a synthetic oligonucleotide is the basis of antisense oligonucleotide chemistry and its possible therapeutic uses.[10]

Both approaches face major challenges as far as future clinical applications are concerned, e.g., (i) the question of oligonucleotide transport into cells, (ii) the danger of enzymatic degradation of the oligonucleotide, or (iii) the problem of persistent fixation of the oligonucleotide to the target sequence. There are many efforts to overcome these inherent problems.[10] As to item iii, attempts have been made to increase the oligonucleotide affinity by various methods such as manipulations of its charge,[11] via linked intercalators,[12] through photocross-linking,[13] or covalent bond formation, e.g., alkylation[14] or cross-linking via Pt(II).[15]

[†] Dedicated to Prof. B. Rosenberg on the occasion of his 65th birthday.

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