Crystalline structure rather than particle size thus dictates the binding energy of surface sites.

Aminoacids are adsorbed at the quartz surface [5] but when the process occurs from aqueous solution their interaction energy is competitive with water itself. In the case of proline, however, a specific interaction with quartz was observed: in that case the heat released upon contact with quartz was 30 times higher than on amorphous silica and the interaction lasted many hours indicating an activated process, possibly the oxidation to hydroxyproline specifically catalyzed by the quartz surface.

All these findings may be regarded as a first step in the investigation of the particular reactivity of crystalline SiO_2 within the cells.

1 J. Summerton and S. Hoenig, *Exper. Mol. Pathol, 26,* 113–128 (1977).
2 Ralph K. Iler 'The Chemistry of Silica', Wiley, New York (1979) pp. 770–775.
3 F. Kozin, B. Millstein, G. Mandel and N. Mandel, *J. Coll. and Int. Sci., 88,* 326–337 (1982).
4 V. Bolis, B. Fubini and G. Venturello, in 'Journées de Calorimétrie et Analyse Thermique', Genève 29–30 March 1982, vol. XIII, II.4.23.
5 W. A. Bonner, P. R. Kavasmaneck, F. S. Martin and J. J. Flores, *Science, 186,* 143 (1974).

V23

Divalent Metal Ions in the Pharmacodynamics of Morphine-like Opiates

ELENA GAGGELLI, IDA BARNI COMPARINI and MARIA PIA PICCHI

Department of Chemistry, University of Siena, Pian dei Mantellini 44, 53100 Siena, Italy

Paramagnetic Mn(II) ions were used to sample the interaction of morphine-like opiates with divalent metal ions, which are known, especially Ca^{++}, to be involved in the mechanisms of drug dependence and tolerance.

The motional correlation time of the opiate molecule in aqueous solution was determined by selective proton irradiation methods ($\tau_c = 7 \times 10^{-10}$ sec at 22 °C) and a preferred *cis* conformation of H_5 and H_6 protons was inferred.

The water proton relaxation rates at different metal to ligand ratios were used to evaluate the equilibrium constant ($K_{ass} = 10^{-2}\ M^{-1}$) by assuming a dipolar only interaction with T_{1p}^{-1} modulated by rotational tumbling of the complex (see figure).

The temperature dependence of T_{1p}^{-1} was measured (Table I) in the range 25–60 °C: it turned out that H_1, H_2, H_5, H_7 and H_8 proton relaxation rates were in the fast exchange region, while the $-NCH_3$ protons were undergoing slow exchange from the metal coordination sphere.

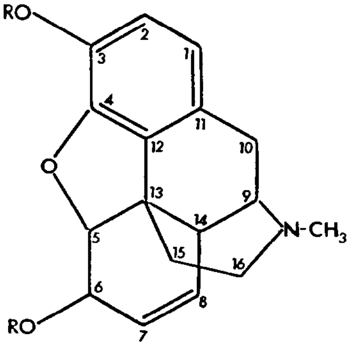

TABLE I. Temperature Dependence of T_{1p}^{-1} of Morphine Protons. [Morphine] = 0.05 *M*, [Mn^{++}] = 0.1 m*M*, pD = 7.

1000/*T* (K^{-1})	T_{1p}^{-1} (sec^{-1})	
	H_5	$-NCH_3$
3.00	0.10	0.24
3.10	0.22	0.13
3.20	0.37	0.05
3.25	0.42	0.04
3.30	0.50	0.07
3.35	0.56	0.12

As a consequence, metal–proton distances could be calculated for almost all the protons considered and it was shown that simultaneous binding to the two -OH groups was consistent with the similar measured magnitudes of the Mn–H_1, Mn–H_2, Mn–H_7 and Mn–H_8 vectors (r is in the range 3.01–3.16 Å). H_5 was found to be the nearest proton to the metal ion ($r = 2.84$ Å).

The temperature dependence of T_{1p}^{-1} of the $-NCH_3$ methyl protons was taken to evaluate the thermodynamic functions for the exchange process from the metal coordination sphere ($k_{off} = 2.25 \times 10^4\ sec^{-1}$, $\Delta H^{\ddagger} = 14.1$ kcal/mol, $\Delta S^{\ddagger} = 7.2$ e.u.).

The structural and kinetic information was used to suggest that interaction with divalent metal ions is characterized, for morphine-like opiates, by an almost exclusively enthalpic barrier due to binding to charged OH groups. Such interaction can be relevant either in modulating the interaction of divalent metal ions with external groups in membranes or in affecting the receptor–opiate interaction modes.