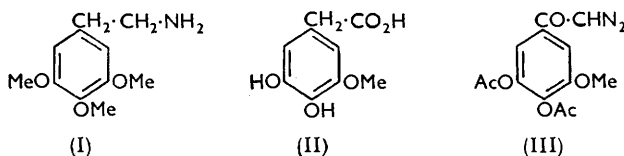


525. *Synthesis of 3:4-Dihydroxy-5-methoxyphenylacetic Acid, a Metabolite of Mescaline in Man.*

By JOHN HARLEY-MASON and A. H. LAIRD.

WE have described¹ earlier the isolation, from the urine of human volunteers dosed with mescaline (I), of small quantities of a metabolite, the glutamine conjugate of 3:4-dihydroxy-5-methoxyphenylacetic acid (II).



The synthesis of this acid is now described. An Arndt-Eistert reaction was performed on 3:4-diacetoxy-5-methoxybenzoyldiazomethane² (III) by using silver oxide in ethanol, leading to ethyl 3:4-diacetoxy-5-methoxyphenylacetate. Alkaline hydrolysis of this with complete exclusion of oxygen gave the required acid.

Experimental.—3:4-Dihydroxy-5-methoxyphenylacetic acid. A solution of 3:4-diacetoxy-5-methoxybenzoyldiazomethane (3 g.) in ethanol (50 c.c.) was heated at 60° and silver oxide (10 mg.) was added. The mixture was kept at 60° for 5 hr. with occasional stirring, while nitrogen was slowly evolved. After filtration, the solvent was removed and the residual oil was distilled at 165° (bath)/10⁻³ mm., giving ethyl 3:4-diacetoxy-5-methoxyphenylacetate as a very viscous oil (Found: C, 57.9; H, 5.6. C₁₅H₁₈O₇, requires C, 58.1; H, 5.8%). This ester (1 g.) was treated with previously boiled out aqueous sodium hydroxide (5%; 60 c.c.) in a sealed vessel under nitrogen. After 24 hr. at room temperature (occasional shaking), the mixture was acidified and extracted with ethyl acetate (4 × 50 c.c.). After removal of the solvent, the residue was distilled at 135°/10⁻³ mm., giving a colourless gum which crystallised after 3 months. Recrystallisation from ethyl acetate–light petroleum gave 3:4-dihydroxy-5-methoxyphenylacetic acid as needles, m. p. 132–134° (Found: C, 54.4; H, 5.3. C₉H₁₀O₅, requires C, 54.5; H, 5.0%).

One of us (A. H. L.) thanks the Department of Scientific and Industrial Research for a Maintenance Grant.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE.

[Received, February 24th, 1959.]

¹ Harley-Mason, Laird, and Smythies, *Confinia Neurologica*, 1958, **18**, 152.

² Bradley, Robinson, and Schwartzenbach, *J.*, 1930, 814.

526. *Monocalcium Aluminate Hydrate in the System CaO–Al₂O₃–H₂O at 21°.*

By A. PERCIVAL and H. F. W. TAYLOR.

PREVIOUS studies on the system CaO–Al₂O₃–H₂O at or near 21° (see, *e.g.*, refs. 1 and 2) have established stable or metastable solubility curves for the hydrated calcium aluminates 3CaO, Al₂O₃, 6H₂O, 2CaO, Al₂O₃, 8H₂O, and 4CaO, Al₂O₃, 19H₂O, but not for CaO, Al₂O₃, 10H₂O. Recent work at 1°³ and 5°⁴ shows that a metastable curve can be obtained for CaO, Al₂O₃, 10H₂O at these temperatures; from experiments in which it was treated with

¹ Wells, Clarke, and McMurdie, *J. Res. Nat. Bur. Stand.*, 1943, **30**, 367.

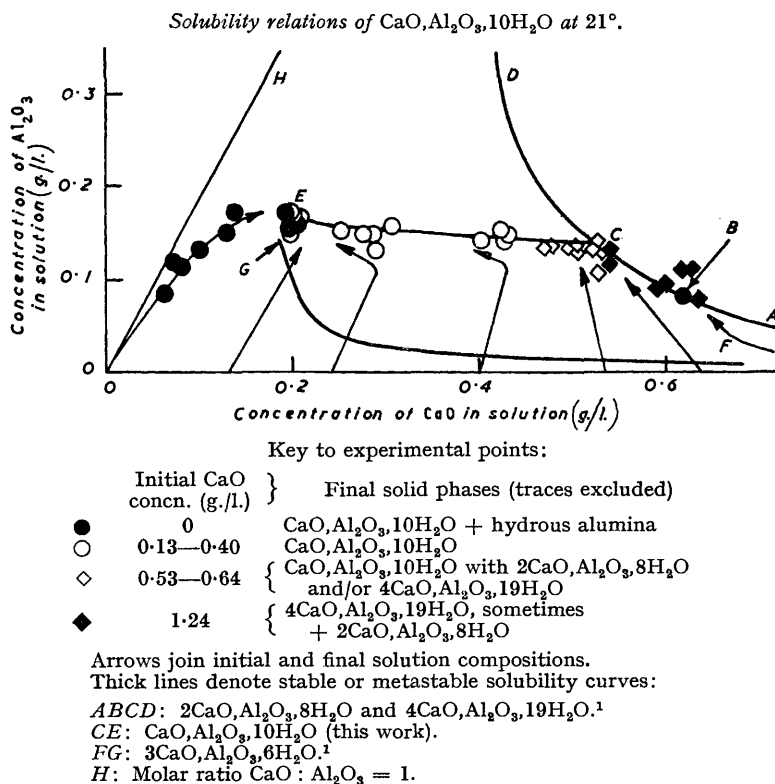
² D'Ans and Eick, *Zement-Kalk-Gips*, 1953, **6**, 197.

³ Carlson, *J. Res. Nat. Bur. Stand.*, 1958, **61**, 1.

⁴ Buttler and Taylor, *J.*, 1958, 2103.

water or lime solutions, one has now been obtained for it at 21°. It was not found possible to define the curve from experiments starting with supersaturated solutions, or to obtain any curve at 50°.

Experimental.—Procedures were similar to those used at 5°, weighed amounts (0.3—1.3 g.) of $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ being treated with water or lime solutions (*ca.* 400 ml.) whose initial concentrations varied from zero to saturation. The suspensions were contained in screw-stoppered Polythene bottles with PVC gaskets, and shaken at $21^\circ \pm 0.1^\circ$ for times usually between 2 days and 4 months. A range of times was studied for each set of initial conditions. After the suspensions had been filtered, the solutions were analyzed for CaO and Al_2O_3 . The solids



were equilibrated over saturated calcium chloride and then examined by *X*-ray powder diffraction. Some were also examined optically for traces of $3\text{CaO}, \text{Al}_2\text{O}_3, 6\text{H}_2\text{O}$. Rigorous precautions were taken to minimize contamination by carbon dioxide. Similar experiments were also made at 50°; precipitation at 21° from supersaturated calcium aluminate solutions was also studied by methods similar to those employed at 5°.⁴

Results.—The Figure gives the main results at 21°. On treatment with water, $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ is partly decomposed giving hydrous alumina (badly crystallized bayerite or gibbsite). The concentrations of lime and alumina in solution rise rather slowly, and become constant near point *E* in 30—40 days. With lime solutions containing initially 0.1—0.4 g. of $\text{CaO}/\text{l.}$, dissolution is approximately congruent, and within a few days the solution compositions reach values on the curve *CE* that are steady for one or more weeks. With longer times the solution compositions move to the left along this curve. $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ persists as the sole, or by far the major phase, for at least 4 months, the longest time studied. With lime solutions containing initially 0.5—0.6 g. of $\text{CaO}/\text{l.}$, dissolution is again incongruent. Partial decomposition occurs, giving $2\text{CaO}, \text{Al}_2\text{O}_3, 8\text{H}_2\text{O}$, or $4\text{CaO}, \text{Al}_2\text{O}_3, 19\text{H}_2\text{O}$, or both; the solution composition becomes almost steady within a few days near *C*. With more concentrated

lime solutions, $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ is usually completely decomposed within a few days. $4\text{CaO}, \text{Al}_2\text{O}_3, 19\text{H}_2\text{O}$, and sometimes also $2\text{CaO}, \text{Al}_2\text{O}_3, 8\text{H}_2\text{O}$, are formed, and the solution compositions lie on or near curve ABC . In none of the above experiments was $3\text{CaO}, \text{Al}_2\text{O}_3, 6\text{H}_2\text{O}$ found in the products, either optically or by X-rays. Traces of $3\text{CaO}, \text{Al}_2\text{O}_3, \text{CaCO}_3, 12\text{H}_2\text{O}$ were sometimes found, but only when the initial CaO concentration exceeded 0.2 g./l.

Supersaturated calcium aluminate solutions with $\text{CaO} : \text{Al}_2\text{O}_3$ molar ratios of 1.01—1.05, and initial CaO concentrations of 0.45—0.88 g./l., were also left to precipitate at 21°. $2\text{CaO}, \text{Al}_2\text{O}_3, 8\text{H}_2\text{O}$ was always formed. The more concentrated solutions gave $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ as well, but only as a transitory product which soon decomposed giving more $2\text{CaO}, \text{Al}_2\text{O}_3, 8\text{H}_2\text{O}$. The solution compositions (not shown in the Figure) in general lay on or to the left of curve CD . When $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ was treated at 50° with water or lime solutions containing up to 0.35 g. of CaO /l., the Al_2O_3 concentrations rose within a few days to unreproducible values around 0.3—0.4 g./l., later falling. The CaO concentrations quickly attained relatively steady values around 0.2—0.45 g./l. The $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ began to decompose within a few days, and after about a week hydrous alumina or $3\text{CaO}, \text{Al}_2\text{O}_3, 6\text{H}_2\text{O}$ was usually the main solid phase.

Discussion.—The present results show that a metastable solubility curve (CE) can be obtained for $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ at 21°, but not at 50°. It is bounded at one end by the indefinite triple point E for $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$, solution, and a form of hydrous alumina. At the other end, C is the triple point for $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$, $2\text{CaO}, \text{Al}_2\text{O}_3, 8\text{H}_2\text{O}$, and solution. $ABCD$ is the metastable solubility curve for $2\text{CaO}, \text{Al}_2\text{O}_3, 8\text{H}_2\text{O}$ and $4\text{CaO}, \text{Al}_2\text{O}_3, 19\text{H}_2\text{O}$.¹ The position of the triple point for these two phases and solution is hard to establish, but recent work⁵ places it near B ; for this reason, point C was stated above to involve $2\text{CaO}, \text{Al}_2\text{O}_3, 8\text{H}_2\text{O}$ and not $4\text{CaO}, \text{Al}_2\text{O}_3, 19\text{H}_2\text{O}$. The present results provide incidental confirmation of part of the curve for $4\text{CaO}, \text{Al}_2\text{O}_3, 19\text{H}_2\text{O}$. Earlier workers did not obtain a metastable curve for $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ at or near 21° because they made no suitable experiments starting from this compound. Most of the earlier work was done by starting from supersaturated solutions, and the present results show that a curve for $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ cannot be thus obtained at 21°.

The slow, leftward movement of solution compositions along CE can be attributed to gradual formation of the more basic compounds $4\text{CaO}, \text{Al}_2\text{O}_3, 19\text{H}_2\text{O}$ and $3\text{CaO}, \text{Al}_2\text{O}_3, \text{CaCO}_3, 12\text{H}_2\text{O}$. Slight decomposition of $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$, whether or not caused by contamination by carbon dioxide, thus seems not to affect the definition of its metastable solubility curve.

$\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ is not a stable phase in the system $\text{CaO}-\text{Al}_2\text{O}_3-\text{H}_2\text{O}$ at any temperature, but at 1° or 5° it is very persistent, and a metastable solubility curve can be obtained from either under- or super-saturation. At 21° it is less persistent, and the curve can only be reached from undersaturation. When $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ is formed from highly supersaturated solutions, the crystals seem to be very small or imperfect at first,⁴ and in suspensions at 21° they disappear to give other phases before they have reached a less reactive condition. At 50°, even crystals which have been previously grown and isolated are unstable in aqueous suspension, and it seems impossible to determine a metastable solubility curve by either method.

At 5°, the triple point for $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$, hydrous alumina, and solution lies to the left of the solubility curve for $3\text{CaO}, \text{Al}_2\text{O}_3, 6\text{H}_2\text{O}$ and there is no appreciable tendency for $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ to react with water or dilute lime solutions to give $3\text{CaO}, \text{Al}_2\text{O}_3, 6\text{H}_2\text{O}$.⁴ At 21°, the triple point lies slightly to the right of that curve (Figure), and $\text{CaO}, \text{Al}_2\text{O}_3, 10\text{H}_2\text{O}$ must therefore tend to react with water or dilute lime solutions to give $3\text{CaO}, \text{Al}_2\text{O}_3, 6\text{H}_2\text{O}$. In practice, this change seems to be slow, and was not observed under our conditions.

We thank the Lafarge Aluminous Cement Company Ltd. (London) for generous financial support.