少する結果となり, kation, anion の $\text{HPO}_4^{//}$ 自身に対する電氣的影響が大きい事と合せて, 水素イオンの活量が減少し pH が小となる」のではないかと推定される。

終始懇篤なる御指導を賜つた東大石館教授, 九大百瀬, 塚元両教授に深く感謝し, 理論的指導を賜つた東京教育大飯島教授, 九大松浦教授並びに実験上の便宜を頂いた九大平田, 木本両氏に謝意を表する。なお本実験の一部は科研池田巴津子君の熱心な協力によつたものである。謝意を表する。

九州大学医学部薬学科 (Received June 1, 1951)

Tyunosin Ukita and Makoto Matsumoto: Ethyl α -Acetylsalicyl-acetoacetate

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3-Acetyl-4-hydroxycoumarin (I) has been reportedly synthesized by the following four methods: (1) The condensation of acetylsalicylchloride (II) with ethyl acetoacetate (III) by sodium in dry ether¹⁾; (2) the treatment of 4-hydroxycoumarin with acetic anhydride using boron fluoride as a catalyst and subsequent decomposition of the resultant boron fluoride-complex with ethyl alcohol²⁾; (3) the treatment of disodio derivative of *o*-hydroxy-acetylacetophenone with phosgene³⁾; and (4) the acetylation of 4-hydroxycoumarin with acetyl chloride in pyridine containing a trace of piperidine.³⁾

Anschtütz treated 1 mole of (II) and 3 moles of (III) with 3 moles of sodium in dry ether, and acidified the reaction mixture with hydrochloric acid to obtain (I).

Robertson, et al.²⁾, modified Anschtütz's method by condensation of (II) and ethyl sodioacetoacetate in equimolar quantities in dry ether and a subsequent addition of one more mole of sodium ethoxide without isolating the intermediate ethyl α -acetylsalicyl-acetoacetate (IV).

The authors obtained ethyl α -acetylsalicyl-acetoacetate (IV) by extraction of the ethereal reaction mixture of one mole each of ethyl sodioacetoacetate and acetylsalicylchloride with sodium carbonate solution and followed by acidification with 10% hydrochloric acid.

Ethyl α -acetylsalicyl-acetoacetate (IV) formed colorless prisms, m.p. 54° , which was stable against warm 10% hydrochloric acid, but yielded 3-acetyl-4-hydroxycoumarin by acidification with the same acid after dissolving in 1% caustic alkali or 5% aqueous ammonia.

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Experimental

Ethyl α -acetylsalicyl-acetoacetate (IV) : To 11.5 g of powdered sodium in 450 cc. of dry ether was added 65 g. of ethylacetoacetate under stirring. To the resulting ethyl sodioacetoacetate was added gradually 100 g. of acetylsalicylchloride in one hour, and the mixture was refluxed for further 30 hours under stirring. The reaction mixture was poured into ice-water and extracted successively with 5% sodium bicarbonate and then with 5% sodium carbonate solution. The latter extract was acidified with 10% hydrochloric acid and extracted with ether, the ethereal solution was washed with water, dried and then the ether was removed. The crystals that appeared among residual reddish brown oil were recrystallized from alcohol to colorless prisms, m.p. 54°, which gave red coloration by ferric chloride in alcohol. *Anal.* Calcd. for $\text{C}_{15}\text{H}_{16}\text{O}_6$: C, 61.64; H, 5.52. Found: C, 61.60; H, 5.55.

3-Acetyl-4-hydroxycoumarin (I) : A cooled solution of ethyl α -acetylsalicyl-acetoacetate in 1% sodium hydroxide solution or 5% aqueous ammonia was acidified with 5% hydrochloric acid. The crystals precipitated was recrystallized from alcohol to colorless prisms, m.p. 134°, which was identical with an authentic 3-acetyl-4-hydroxycoumarin prepared by the Anschütz's method.

(Recived June 9, 1951)