does not imply approval or recommendation of the product by the U.S. Department of Agriculture to the exclusion of others that may be suitable.

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New Sweetening Agents: *N'*-Formyl- and *N'*-Acetylkynurenine

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N'-Formyl- (**6**) and *N'*-acetylkynurenine (**7**) are approximately 35 times sweeter than sucrose. The kynurenine derivatives elicit a sweet taste sensation immediately on contact with the taste buds. The sweetness of the acetyl derivative is linearly comparable to sucrose in concentrations up to 2.5 mg/ml. A sweetness comparison of sucrose and the formyl analog is linear to 1.6 mg/ml. An off-flavor at higher levels of **6** may account for the lack of comparability to **7** and sucrose at higher concentrations. A new synthesis for DL-kynurenine is described.

The need for a low or noncaloric sweetener needs no reiteration. A compound which is a normal metabolite and is sweet may offer potential in this area. Several amino acids as well as several dipeptides containing aromatic groups are known to be sweet (Yamaguchi *et al.*, 1970a,b). Yamaguchi *et al.* (1970a,b) have reported D-tryptophan to be 25 to 50 times sweeter than sucrose. L-Tryptophan (Solms *et al.*, 1965) exhibits a bitter flavor half as intense as caffeine. Mazur *et al.* (1969, 1970) have reported various dipeptides and aspartic acid amides to be sweet.

Kynurenine, a tryptophan metabolite, and various derivatives of kynurenine have been synthesized previously from tryptophan (Dagliesh, 1952; Knox and Mehler, 1950). Our studies were undertaken to evaluate the sweetness of kynurenine derivatives and to devise syntheses for kynurenine and related artificial sweeteners from inexpensive starting materials.

EXPERIMENTAL SECTION

Evaluation of Sweetness. A five-member panel compared the sweetness of five samples of kynurenine solutions of varying concentrations to a sucrose solution of a given concentration. The panelists ranked the sweetness of the kynurenine solutions equivalent to the sucrose solution. Results in Table I are expressed in milligrams of kynurenine derivative judged to produce equivalent sweetness.

Synthetic Experiments. A synthetic route to kynurenine (**5**) is outlined in Figure 1. *o*-Chloroaniline (Eastman) was converted to a Grignard reagent at 85° (Spencer and Stokes, 1908). The reaction flask was then cooled in crushed solid carbon dioxide while 5% maleic anhydride in tetrahydrofuran was added dropwise, as described by Newman and Smith (1948). The intermediate product (**4**) was not isolated but put into a Paar bomb, which was then evacuated and charged with ammonia. The mixture was kept under 14 lb of pressure for 16 hr. Kynurenine was then precipitated as described by Auerbach and Knox (1957).

Anal. Calcd for $C_{10}H_{12}N_2O_3$ (mol wt 208.22): C, 57.68; H, 5.81; N, 13.46. Found: C, 58.27; H, 5.95; N, 13.44.

N'-Acetylkynurenine was made as follows. One gram of kynurenine was dissolved in 15 ml of 90% acetic acid. Acetic anhydride (30 ml) was then added and the reaction mixture was stirred for 2 hr. Adding diethyl ether precipitated the product. The yield was 60% after recrystallization from 90% acetic acid with ether (mp = 189°). *N'*-Formylkynurenine was synthesized according to Dagliesh (1952).

RESULTS AND DISCUSSION

The elemental analyses as well as spectroscopic and nuclear magnetic resonance (nmr) data support the structure for the synthetic kynurenine. The ultraviolet spectrum of the synthetic compound shows three peaks which correspond to the literature values (Knox and Mehler, 1950) for kynurenine (**4**): λ 360 (ε 4500), 257 nm (ε 7500), 230 nm (ε 18,900). The 100 Hz nmr spectra of synthetic and commercial kynurenines are shown in Figure 2. Both ultraviolet and nmr spectra of commercial and synthetic kynurenines are

Table I. Comparison of Sweetness of Sucrose and *N'*-Formyl- and *N'*-Acetylkynurenine

	Sweetness[a,b]	
Sucrose, %	*N'*-Formylkynurenine	*N'*-Acetylkynurenine
2.5	0.7	0.6
5.0	1.5	1.4
10.0	3.0	3.0

[a] Milligrams of kynurenine derivative equivalent to sucrose standard. [b] Based on 25 judgments at each of seven levels of kynurenine derivative for each sucrose level. Each figure is the average concentration where 50% of the judges said a level of sweetener was sweeter than the sucrose concentration.

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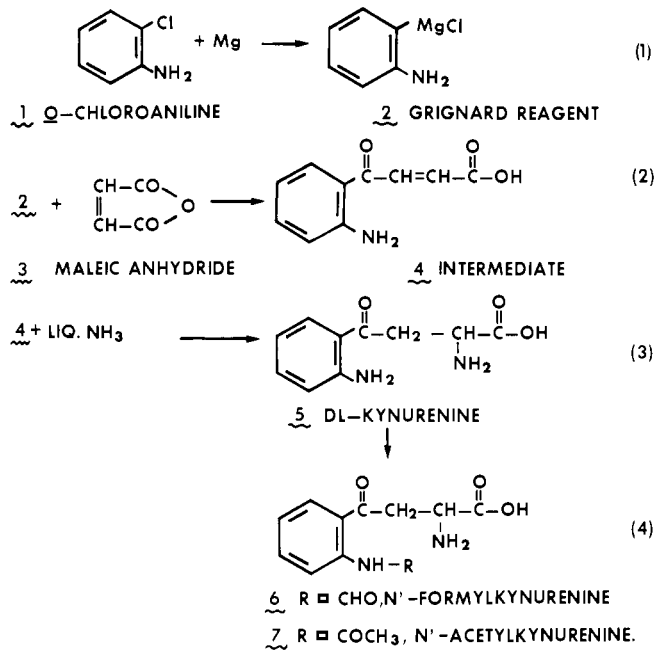

Figure 1. Synthesis of DL-kynurenine and its derivatives.

identical. Ultraviolet absorption maxima of *N'*-formyl- and *N'*-acetylkynurenines are: 321 (ϵ 3750) and 260 nm (ϵ 10,980).

The formyl- and acetylkynurenines are sweet in contrast to the synthetic and commercial kynurenines, which are not sweet. Data in Table I show that both derivatives are

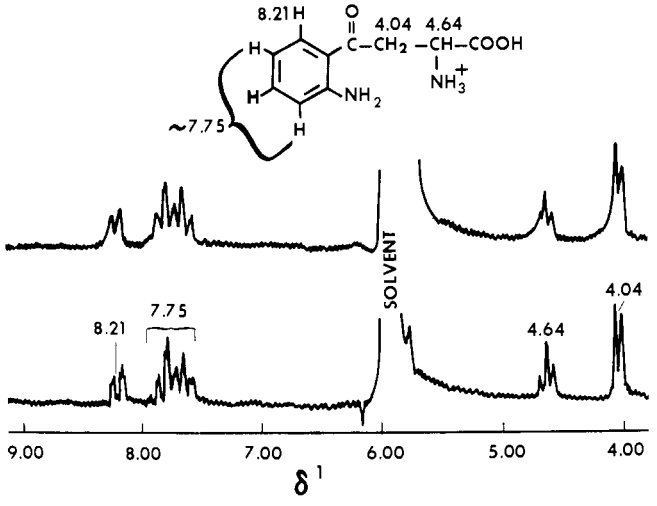

Figure 2. Comparison of nuclear magnetic resonance spectra in D_2O of synthetic (upper plot) and commercial (lower plot) DL-kynurenines.

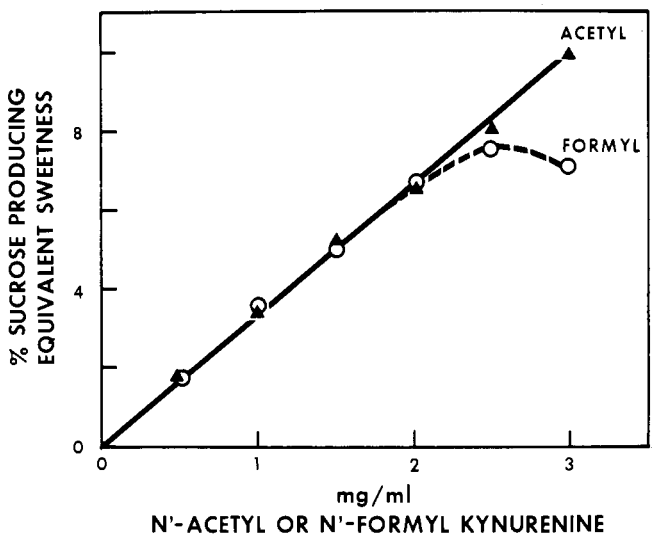

Figure 3. Sweetness of kynurenine derivatives compared to sucrose.

about 35 times sweeter than sucrose. Noteworthy is the fact that kynurenine derivatives elicit a sweet taste immediately on contact with the tongue.

Figure 3 demonstrates that the sweetness ratio with reference to sucrose is constant for *N'*-acetylkynurenine up to 3 mg/ml (equivalent to 10% sucrose). The *N'*-formyl derivative is relatively less sweet at concentrations above 2.5 mg/ml, possibly because of an off-flavor observed at these high levels. Such an off-flavor is not observed with the *N'*-acetylkynurenine. Since our synthetic products are racemic mixtures, it is possible that, as with tryptophan, only one component is sweet while the other may modify the taste.

In conclusion, we have shown that *N'*-formyl- and acetylkynurenines are potentially useful as artificial sweeteners. These compounds have not, however, been tested for safety or approved for use in foods.

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