stability of the diazonium ion toward ionic decomposition to phenol.

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The Swamping Catalyst Effect in Bromination of Acetophenone

Sir:

We have obtained a 60% yield of *m*-bromoacetophenone, uncontaminated with phenacyl bromide, by the bromination of acetophenone mixed with a large excess of aluminum chloride catalyst. With catalytic quantities of aluminum chloride the bromination of acetophenone yields phenacyl bromide apparently unaccompanied by nuclear substitution products.[1] We attribute this rather dramatic change in orientation of the bromine atom to (a) suppression of "active methylene" activity by complex formation between the carbonyl group and the catalyst[2] and (b) the increase in substitution activity of bromine as it exists in complex formation with the catalyst. The synthesis of *m*-bromoacetophenone was as follows: acetophenone (0.28 mole) was added dropwise to anhydrous aluminum chloride (0.84 mole) contained in a flask equipped with a stirrer, gas outlet, and drying tubes. Bromine (0.28 mole) then was added to the fluid mass at room temperature within 10 minutes. After being stirred an additional hour and becoming semi-solid, the mixture was quenched in a slurry of ice and acid. After the usual extraction, washing, and drying of the oil in ether, the oil was concentrated and stripped from the residue (5.6 g.) by distillation at 2 mm. pressure; yield, 42.7 g. Fractionation of the distillate at 2 mm. yielded crude acetophenone (b.p. 57–94°, 3.4 g., 10%) and *m*-bromoacetophenone (b.p. 94–95°, n_D^{25} 1.5740; m.p. and reported[3] m.p. 7–8°; 33.1 g., 59.4%; *oxime* m.p. and mixture m.p. with an authentic sample 100–101°). Larger amounts of bromine relative to ketone gave a product contaminated with a lachrymatory substance.

Continuing studies of the swamping catalyst effect in substitution behavior of ketones and of other substances will be reported at a later date.

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(1) *Org. Syntheses*, Coll. Vol. II, 480 (1944).

(2) Baddeley, *J. Chem. Soc.*, 232 (1944).

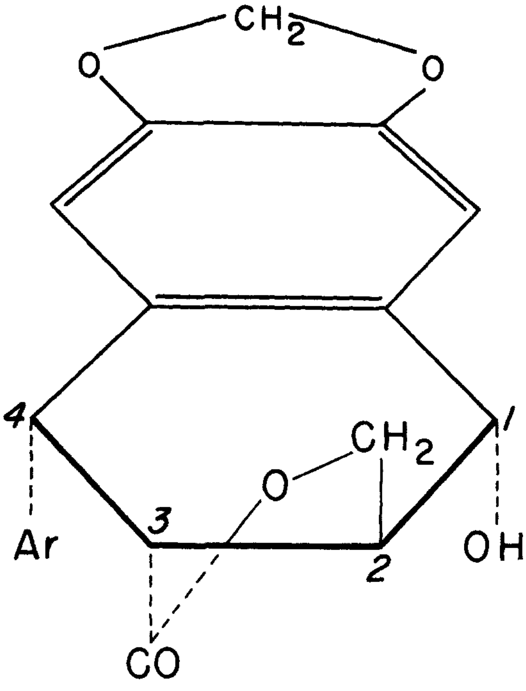
(3) Elson, Gibson, and Johnson, *J. Chem. Soc.*, 1128 (1930).

Components of Podophyllin. XX.[1] The Absolute Configuration of Podophyllotoxin and Related Lignans

Sir:

Since the tumor-damaging potency of podophyllotoxin (I) and related compounds is closely associated with their stereochemistry,[2] a determination of their absolute configuration might shed further light on the mechanism of their action, a question of importance in the search for effective chemotherapeutic agents.

Previous research[3] has demonstrated the *trans*-(1:2)-*trans*(2:3)-*cis*(3:4) arrangement[4] of I and its configurational identity at C_3 with (−)-guaiaretic acid dimethyl ether[5] (II).[6] We now wish to report the stereochemical correlation of II with a natural α-amino acid; this *ipso facto* proves the absolute configuration of I.



Ar = *3,4,5*-$(MeO)_3C_6H_2$
I

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(1) Paper XIX, Schrecker, Trail, and Hartwell, *J. Org. Chem.*, **21**, 292 (1956).

(2) Hartwell, Schrecker, and Leiter, *Proc. Am. Assoc. Cancer Research*, **1** (No. 2), 19 (1954).

(3) Schrecker and Hartwell, *J. Am. Chem. Soc.*, **75**, 5916 (1953); **77**, 432 (1955).

(4) The numbering of I was chosen to conform with the one appropriate for the majority of lignans.

(5) Schroeter, Lichtenstadt, and Ireneu, *Ber.*, **51**, 1587 (1918).

(6) Formulas conform to the Fischer convention and represent absolute configurations; *cf.* W. Klyne, "*Progress in Stereochemistry*," Academic Press Inc., New York, 1954, p. 178; W. Klyne in Braude and Nachod "*Determination of Organic Structures by Physical Methods*," Academic Press Inc., New York, 1955, p. 74.