an authentic sample of D-glucose phenylosazone (lit.[31] 204–205° uncor.).

(b) **Benzimidazole Derivative.**—An amount of hydrolyzate (filtered from the aglycon and neutralized with bicarbonate) estimated to contain 1.0 g. of hexose was evaporated to 50 cc. and oxidized with bromine, in portions[32]; one week was required for completing the reaction (negative test for reducing sugars, after removal of the bromine). The solution was concentrated to 5 cc. in vacuum and treated with 0.66 g. of *o*-phenylenediamine in acid medium.[33] After cuprammonium salt treatment and removal of the copper, a product was obtained which, after crystallization from water, gave off-white needles, m.p. 216–217.5° (lit.[33] 215° uncor.), yield 50 mg. A mixed m.p. with an authentic specimen of D-glucobenzimidazole prepared similarly from methyl α-D-glucoside showed no depression.

1-O-(β-D-Glucopyranosyl)-picropodophyllin Tetraacetate.—The glucoside (1.0 g.) was refluxed with 20 cc. of acetic anhydride and 0.5 g. of anhydrous sodium acetate for 2 hours. After cooling, and decomposing the excess acetic anhydride with water, an oil which slowly turned crystalline, was obtained; yield 1.16 g. (90%). Crystallization from 1:2 chloroform–methanol gave fine needles, m.p. 269–270.2°, yield 1.03 g. (79%), $[\alpha]^{20}D$ −5.2° (*c* 0.5, chloroform).

Anal. Calcd. for $C_{36}H_{40}O_{17}$: C, 58.1; H, 5.4; 3 OCH_3, 12.5; 4 $COCH_3$, 23.1. Found: C, 58.0; H, 5.4; OCH_3, 12.3; $COCH_3$, 23.2.

BETHESDA, MD.

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[31] E. Fischer, *Ber.*, **17**, 579 (1884).

[32] C. S. Hudson and H. S. Isbell, *J. Research Nat. Bur. Standards*, **3**, 58 (1929).

[33] S. Moore and K. P. Link, *J. Biol. Chem.*, **133**, 302 (1940).

[CONTRIBUTION FROM THE CENTRAL RESEARCH DEPARTMENT, MONSANTO CHEMICAL COMPANY]

Bicyclic Dihydropyrans by the Diels–Alder Reaction

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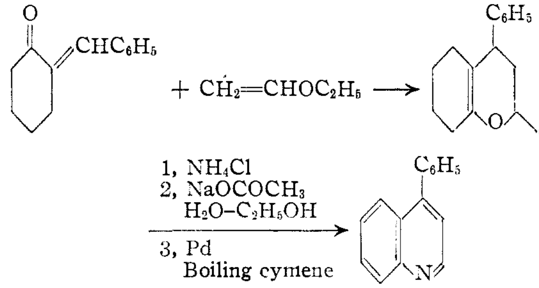
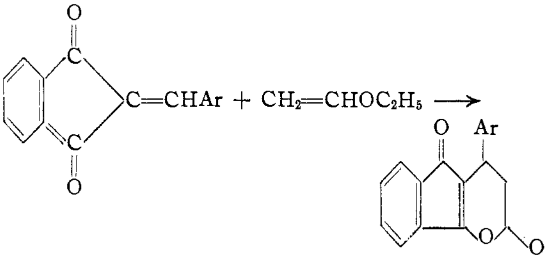
The synthesis of dihydropyrans by the Diels–Alder addition of vinyl ethers to α,β-unsaturated carbonyl compounds has been extended to the preparation of bi- and tricyclic dihydropyrans.

The successful preparation of dihydropyrans by using α,β-unsaturated carbonyl compounds as the diene component in the Diels–Alder reaction[1] has been extended to the synthesis of bicyclic dihydropyrans. When 2-benzylidenecyclopentanone, 2-benzylidenecyclohexanone, 2-piperonylidenecyclohexanone and 2-veratrylidenecyclohexanone were treated with ethyl vinyl ether, the corresponding 2-ethoxy-4-aryl-5,6-tri- or tetramethylene-3,4-dihydro-2H-pyrans were obtained in 22–52% yields.



These structures have been postulated by analogy with the similar monocyclic compounds and from the fact that treatment of 2-ethoxy-3,4,5,6,7,8-hexahydro-4-phenyl-2H-benzopyran with ammonium chloride and then with sodium acetate in aqueous ethanol followed by dehydrogenation of the product with palladium in boiling *p*-cymene yielded tar from which a picrate was isolated which melted at the same point as that recorded for 4-phenylquinoline.

With 2-piperonylidene-1,3-indandione and 2-veratrylidene-1,3-indandione, ethyl vinyl ether yielded compounds believed to be the corresponding 1-aryl-3-ethoxy-1,2,3,4-tetrahydro-4-oxa-9-fluorenones in 43–49% yields.



Under basic conditions the 1-(3,4-dimethoxyphenyl)-3-ethoxy-1,2,3,4-tetrahydro-4-oxa-9-fluorenone yielded a monoxime. Since these conditions would not favor the hydrolysis of the dihydropyran ring, the formation of a monoxime indicates the utilization of one carbonyl group in the Diels–Alder type reaction.

Experimental

Arylidene Ketones.—The method used was similar to that of Vorländer and Kunze.[2] The preparation of 2-benzylidenecyclohexanone is presented as an example of the procedure.

A mixture of 4.16 l. of water, 18.0 g. of sodium hydroxide, 88.0 g. (0.90 mole) of cyclohexanone and 32.0 g. (0.31 mole) of benzaldehyde was stirred at room temperature for 12 hours. Acetic acid (25 cc.) was added to neutralize the sodium hydroxide, and the mixture was extracted three times with benzene. The benzene solution was washed with water, filtered, and distilled to give 22.0 g. (39% yield) of 2-benzylidenecyclohexanone, b.p. 165–171° at 9 mm. Crystallization from aqueous ethanol gave a product melting at 51–53°.

In the preparation of 2-piperonylidene-1,3-indandione and 2-veratrylidene-1,3-indandione, neutralization of the reaction mixtures with acetic acid resulted in the separation of solid products. These products were removed by filtration, recrystallized from xylene and washed with hexane.

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[1] (a) R. I. Longley, Jr., and W. S. Emerson, THIS JOURNAL, **72**, 3079 (1950); (b) W. E. Parham and H. E. Holmquist, *ibid.*, **73**, 913 (1951); (c) C. W. Smith, D. G. Norton and S. A. Ballard, *ibid.*, **73**, 5267 (1951).

[2] D. Vorländer and K. Kunze, *Ber.*, **59**, 2078 (1926).

TABLE I: ARYLIDENE KETONES

Aldehyde	Ketone	Moles of aldehyde	Moles of ketone	NaOH in water %	NaOH in water l.	Time, hr.	Product	B.p., °C.	B.p., Mm.	M.p., °C.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Benzaldehyde	Cyclohexanone	0.31	0.90	0.43	4.16	12	2-Benzylidenecyclohexanone	165–171	9	51–53[a]	39				
Benzaldehyde	Cyclopentanone	.62	1.30	.83	4.32	8.5	2-Benzylidenecyclopentanone	170–177	12	69–71[b]	74	83.8	83.5	6.98	7.08
Piperonal	Cyclohexanone	.89	2.25	.92	4.36	24	2-Piperonylidenecyclohexanone	190–238	10	87–88[c]	22	73.0	73.4	6.09	6.05
Veratraldehyde	Cyclohexanone	.69	1.80	.83	4.32	24	2-Veratrylidenecyclohexanone	202–260	10	83–85	52	73.2	73.4	7.32	7.47
Piperonal	1,3-Indandione	.51	0.34	.48	4.18	14.5	2-Piperonylidene-1,3-indandione			201–202.5	83	73.4	73.3	3.60	3.74
Veratraldehyde	1,3-Indandione	.51	0.33	.48	4.18	8	2-Veratrylidene-1,3-indandione			204–205	86	73.5	73.7	4.80	5.05

[a] G. Vavon and J. M. Conia, *Compt. rend.*, **234**, 526 (1952), give 56.5°. [b] *Ibid.*, m.p. 71–72°. [c] *Ibid.*, m.p. 88–89°.

TABLE II: BICYCLIC DIHYDROPYRANS

α,β-Unsaturated carbonyl compound	Moles of ketone	Moles of EtVi ether	Temp., °C.	Time. hr.	Product	M.p., °C.	B.p., °C.	B.p., Mm.	Yield. %	$n^{25}D$	Carbon, % Calcd.	Carbon, % Found	Hydrogen. % Calcd.	Hydrogen. % Found
2-Benzylidenecyclopentanone	0.41	0.83	181	16	2-Ethoxy-3,4-dihydro-4-phenyl-5,6-trimethylene-2H-pyran		162–168	2	38	1.5798	78.7	79.1	8.25	8.04
2-Benzylidenecyclohexanone	.55	.69	210	28	2-Ethoxy-3,4,5,6,7,8-hexahydro-4-phenyl-2H-benzopyran		160–162	4	52	1.5346	79.1	79.1	8.58	8.61
2-Piperonylidenecyclohexanone	.25	.83	195	16	2-Ethoxy-3,4,5,6,7,8-hexahydro-4- { -methylenedioxy-		174–184	3	22	1.5538	71.5	71.6	7.33	7.25
2-Veratrylidenecyclohexanone	.30	.83	190	16	(3,4-[ ]-phenyl)-2H-benzopyran { -dimethoxy-		211–216	1	40	1.5499	71.7	72.1	8.17	8.06
2-Piperonylidene-1,3-indandione	.28	.35	150	15.5	1-(3,4-[ ]-phenyl)-3-ethoxy-1,2,- { -methylenedioxy-	130–132			49		72.0	72.1	5.18	5.09
2-Veratrylidene-1,3-indandione	.28	.43	150	15.5	3,4-tetrahydro-4-oxa-9-fluorenone { -dimethoxy-	122–124			43		72.1	71.9	6.05	5.92

Table I summarizes the reaction conditions, physical properties of the products, yields and analytical results.

Bicyclic Dihydropyrans.—The reaction of 2-veratrylidenecyclohexanone with ethyl vinyl ether is presented to illustrate the procedure used. 2-Veratrylidenecyclohexanone, 73.0 g. (0.30 mole), 60.0 g. (0.83 mole) of ethyl vinyl ether and 0.1 g. of hydroquinone were placed in a 300-cc. stainless-steel, rocking autoclave. The autoclave was flushed with nitrogen and then heated at 190° for 16 hours. Distillation of the reaction mixture gave 37.5 g. (40% yield) of 2-ethoxy-3,4,5,6,7,8-hexahydro-4-(3,4-dimethoxyphenyl)-2H-benzopyran, b.p. 211–216° at 1 mm., $n^{25}D$ 1.5499. Table II summarizes the reaction conditions, physical properties of the products, yields, and analytical results in these preparations.

4-Phenylquinoline Picrate.—A mixture of 3.0 g. of 2-ethoxy-3,4,5,6,7,8-hexahydro-4-phenyl-2H-benzopyran, 3.0 g. of ammonium chloride, 20 cc. of ethanol and 10 cc. of water was boiled for 5 minutes until clear. After the addition of 10 cc. of water and 5.5 g. of anhydrous sodium acetate the mixture was boiled another 0.5 hour. It was cooled, diluted with water and extracted three times with *p*-cymene. This solution was heated with 2 g. of 5% palladium-on-charcoal over a two-hour period from 125 to 210° by removing solvent as gas was evolved. Upon cooling, the solution was diluted with benzene, filtered and the filtrate evaporated to dryness. As much as possible of the resulting tar was dissolved in ethanol. The solution was added to a solution of picric acid in ethanol. The picrate which precipitated was separated by filtration and recrystallized from a mixture of benzene and ethanol to yield 0.6 g., m.p. 218–220°. An analytical sample was recrystallized twice from benzene and ethanol, m.p. 224–226°.

Anal. Calcd. for $C_{21}H_{14}O_7N_4$: C, 58.0; H, 3.23; N, 12.9. Found: C, 58.3; H, 3.33; N, 13.1.

In another, similar experiment 2.5 g. of 2-ethoxy-3,4,5,6,7,8-hexahydro-4-phenyl-2H-benzopyran yielded 0.2 g. of picrate, m.p. 221–222°. The recorded melting point of 4-phenylquinoline picrate is 224°.[3]

Oxime of 1-(3,4-Dimethoxyphenyl)-3-ethoxy-1,2,3,4-tetrahydro-4-oxa-9-fluorenone.—The procedure was that of Shriner and Fuson.[4] One gram of the ketone was warmed at reflux with 1.0 g. of hydroxylamine hydrochloride, 5 ml. of pyridine, and 5 ml. of absolute ethanol for one hour and forty-five minutes. The pyridine and ethanol were then allowed to evaporate at room temperature, and the residue was washed by trituration with 5 ml. of cold water. Recrystallization of the product twice from aqueous ethanol gave a greenish-yellow solid, m.p. 185–186°.

Anal. Calcd. for $C_{22}H_{23}O_5N$: C, 69.3; H, 6.08; N, 3.67. Found: C, 68.9; H, 6.08; N, 3.70.

DAYTON, OHIO

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[3] W. Koenigs and F. Meimberg, *Ber.*, **28**, 1038 (1895).

[4] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 2nd Edition, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 167.