gesättigt und mit einer Lösung von 1.5 g 4-Cyano-α-picolin in 30 ccm Alkohol nach Kindler³⁾ unter Eintropfen derselben Lösung katalytisch hydriert. H_2-Aufnahme: ca. 600 ccm. Die vom Katalysator abfiltrierte Lösung wurde im Vakuum zum Trocknen verdampft und der Rückstand aus Methanol umkristallisiert. Nadeln vom Zers. Pkt. 274°. Die Ausbeute: 1.6 g (65% d. Theorie). $C_7H_{10}N_2 \cdot 2HCl$ —Ber.: C, 43.1; H, 6.1; N, 14.3. Gef.: C, 43.26; H, 5.82; N, 13.82.

Pikrat: Nadeln aus Methanol, Schmp. 195～196°. $C_7H_{10}N_2 \cdot (C_6H_3N_3O_7)_2$—Ber.: C, 39.0; H, 2.7; N, 19.2. Gef.: C, 39.35; H, 2.14; N, 18.93.

Benzoat: Nadeln aus Benzol, Schmp. 81～83°.

ii) 1 g 4-Cyano-α-picolin wurde in 10 ccm Alkohol gelöst. Diese Lösung wurde unter Eintropfen zu einer Suspension von Pd-Kohle (aus 1 g aktiver Kohle und 20 ccm 1%iger Palladiumchlorid-Lösung bereitet) in 30 ccm mit 10 Tropfen 30%iger Salzsäure angesauertem Alkohol katalytisch hydriert. Die Reaktionsmischung wurde vom Katalysator abfiltriert und analogerweise wie bei (i) aufgearbeitet. Nadeln vom Zers. Pkt. 218～220°. Die Ausbeute: 1.3 g (77.3% d. Theorie). $C_{14}H_{17}N_3 \cdot 3HCl$ —Ber.: C, 49.9; H, 5.9. Gef.: C, 49.40; H, 6.41.

Zusammenfassung

Ausgehend von α-Picolin wurden 4-Nitro- und 4-Brom-α-picolin dargestellt. Durch Erhitzen von 4-Brom-α-picolin mit Kuprocyanid wurde 4-Cyano-α-picolin hergestellt. Die katalytische Reduktion des letzteren führt zu 4-Aminomethyl-α-picolin bzw. Bis-(4-α-picolylmethyl)-amin je nach der Reduktionsbedingung.

(Eingegangen am 19. April 1954)

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[3] Arch. Pharm., 769, 74.

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38. **Shigehiko Sugasawa, Niro Yoshida, and Masanao Terashima**: Some Reactions of 6-Formylsafrole. II.¹⁾

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In the previous paper¹⁾ we described the synthesis of 6-formylsafrole and some of its reactions. Some additional reactions of this aldehyde will be reported in this paper.

The aldehyde condensed readily with nitromethane either by Rosenmund or Knoevenagel method, forming 6-β-nitrovinylsafrole (II) in fair yields.

By crossed Canizzaro reaction²⁾ there was obtained 6-hydroxymethylsafrole (IIIa), which was proved to be indentical with the authentic specimen prepared from 6-chloromethylsafrole (V) via acetoxymethyl derivative (VI). By Canizzaro reaction, however, 6-hydroxymethylisosafrole (IIIb) and the corresponding acid (IVb) were produced, due to the isomerization of allyl side chain during the reaction under alkaline condition.

Grignard reaction applied upon this aldehyde yielded the anticipated secondary carbinols (V), which suffered dehydration on being treated with phenyl isocyanate, when R is methyl or butyl (or probably any primary or secondary alkyl), but in the case of R=phenyl, the corresponding phenylurethane was obtained.

Our attempts to synthesize 1-*tert*-akyl-1,2,3,4-tetrahydroisoquinolines by applying Sugasawa and Fujisawa's method³⁾ upon (VI: R=*tert*-alkyl or phenyl) have so far failed

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[1] Sugasawa, Yoshida: This Bulletin, 1, 281 (1953).

[2] Davidson, Bogert: J. Am. Chem. Soc., 57, 905 (1935).

[3] This Bulletin, 1, 82 (1953).

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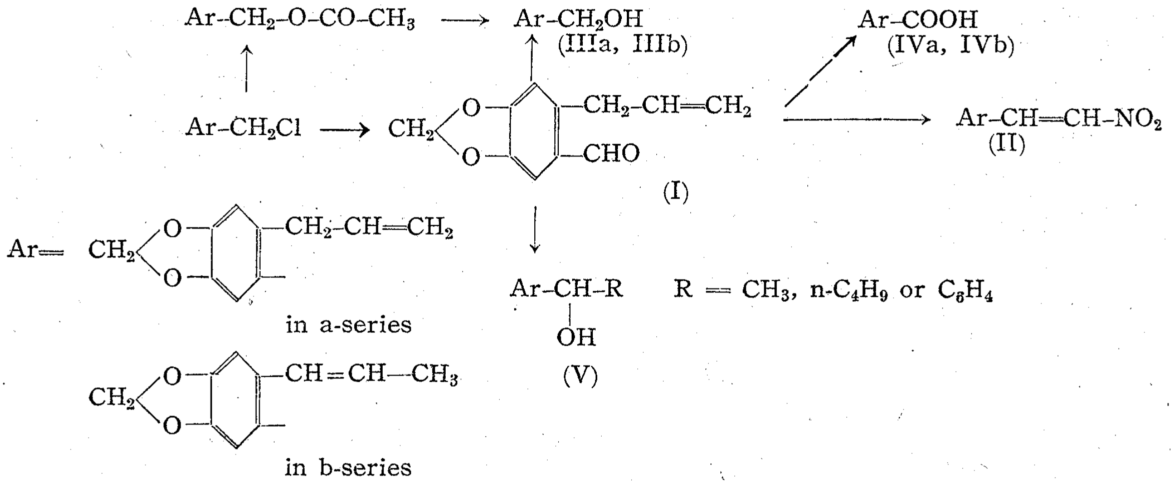
owing to the difficulty with which the bromination of this unsaturated carbinol is attended.



The authors' thanks are due to the members of the analysis room of this Institute for the microanalytical data.

Experimental

6-β-Nitrovinylsafrole (II)—1) By the Rosenmund Method: A solution of 6-formylsafrole (1 g.) and nitromethane (0.35 g.) in absolute alcohol (16 cc.) was added dropwise with methanolic sodium hydroxide solution (0.7 g. NaOH in 0.7 cc. CH_3OH) with stirring, giving a yellowish solution, which gradually changed to brown. After standing 1 hr. at room temperature (ca. 15°) the whole was poured into ice-cold 10% hydrochloric acid, precipitating a yellow solid, which was collected on a filter, washed, and purified from alcohol, forming brilliant yellow needles of m.p. 104°. Yield, 0.95 g. or 77%. *Anal.* Calcd. for $C_{12}H_{11}O_4N$: C, 61.8; H, 4.7; N, 6.0. Found: C, 61.4; H, 4.3; N, 6.2.

2) By the Knoevenagel Method: The aldehyde (1 g.), nitromethane (0.35 g.), methylamine hydrochloride (0.088 g.), and anhydrous sodium carbonate (0.014 g.) were mixed in absolute alcohol (1.3 cc.) and the whole was kept standing in an ice-chest with occasional shaking. After 8 days the crystalline solid formed was collected on a filter, washed with water, and purified from alcohol, giving the same compound as above. Yield, 0.85 g. or 69.5%.

Crossed Canizzaro Reaction—The aldehyde (0.5 g.) in methanol (0.5 cc.) was mixed with formaldehyde solution (0.3 cc.). To this was added aqueous caustic soda solution (0.4 g. NaOH in 0.5 cc. H_2O) with cooling. The mixture was warmed at 63～65° for 0.5 hr. and then at 85° for 7 minutes. On cooling, the reaction mixture was diluted with water and extracted with benzene, which was washed, dried, and evaporated, leaving a yellowish liquid (IIIa), which solidified on cooling and melted at 47°. Yield, 0.29 g. or 58%. This was identified as 6-hydroxymethylsafrole (IIIa) by comparison with an authentic specimen prepared as follows.

6-Chloromethylsafrole was treated with anhydrous sodium acetate in boiling acetic acid, yielding 6-acetoxysafrole, which on being treated with boling 10% sulfuric acid gave 6-hydroxysafrole, m.p. 48.5°, identical with the one obtained above.

The phenylurethane of (IIIa) forms needles from methanol and melts at 78°. *Anal.* Calcd. for $C_{18}H_{17}O_4N$: C, 69.4; H, 5.5; N, 4.5. Found: C, 69.6; H, 5.55; N, 4.6.

6-Carboxysafrole (IVa)—A solution of the aldehyde (1 g.) in alcohol was mixed with a saturated aqueous solution of silver nitrate (1.8 g.) and to this mixture was then added an aqueous solution of caustic soda (0.65 g. NaOH in 32 cc. H_2O) during 1 hr. with stirring. The whole was then left standing for 48 hrs. at room temperature, filtered, and the filtrate was extracted with benzene to remove the unreacted aldehyde. The aqueous layer was then acidified with hydrochloric acid, separating a pale yellow solid, which was collected on a filter, washed, and purified from methanol, forming pale yellow plates of m.p. 128～129°. *Anal.* Calcd. for $C_{11}H_{10}O_4$: C, 64.05, H, 4.9. Found: C, 63.2; H, 4.8.

Canizzaro Reaction—The aldehyde (2 g.) was mixed with a saturated aqueous solution of potassium hydroxide (2 g.) and to this was added some methanol to make a homogeneous solution.

After being heated on a boiling water bath for 3 hrs., the reaction mixture was diluted with water and then repeatedly extracted with ether. The combined ethereal solution was thoroughly washed with water, dried, and evaporated. The residual yellowish-brown oil solidified on cooling, giving needle-shaped crystals of m.p. 67°. Yield, 0.75 g. (37.5%). Gives crystalline phenylurethane of m.p. 120°. *Anal.* Calcd. for $C_{18}H_{17}O_4N$: C, 69.4; H, 5.5; N, 4.5. Found: C, 69.3; H, 5.55; N, 4.7.

This alcohol is not identical with the one obtained by the crossed Canizzaro reaction, so it is probably 6-hydroxymethylisosafrole (IIIb).

On being acidified with hydrochloric acid, the aqueous layer gave a faint yellow solid, 6-carboxyisosafrole (IVb), which forms faint yellow plates of m.p. 192°. Yield, 1 g. or 45.5%. *Anal.* Calcd. for $C_{11}H_{10}O_4$: C, 64.05; H, 4.9. Found: C, 63.8; H, 4.9.

Grignard Reaction—Phenylmagnesium bromide was prepared in ether as usual from bromobenzene (9.2 g., 4 moles) to which the ethereal solution of the aldehyde (4 g., 1 mole) was added with stirring and cooling. After 2 to 3 hrs.' heating, the mixture was cooled and then decomposed with ice-cold dilute hydrochloric acid and extracted repeatedly with ether which was washed, dried, and evaporated. The residual yellowish brown oil was distilled *in vacuo*, giving very viscous, yellow oil of b.p$_1$ 185~190°. Yield, 68.2% based on the aldehyde used. This compound is phenyl-2-allyl-4,5-methylenedioxyphenylcarbinol (V) as is shown by the analytical data of the phenylurethane derived from it.

Phenylurethane: Colorless needles, m.p. 136~136.5°. *Anal.* Calcd. for $C_{24}H_{21}O_4N$: C, 74.4; H, 5.5; N, 3.6. Found: C, 73.7; H, 5.8; N, 3.9.

The corresponding methyl- and butyl-carbinols were prepared in a similar manner in yields of 92% and 50%, respectively, both forming a yellowish viscous oil. The former boils at 135~140° under 4 mm. and the latter comes over at 155~159° under 6 mm. The attempts to prepare phenylurethane derivatives of these carbinols ended fruitless, only giving intramolecular dehydration products.

Efforts are being made to prepare 1-*tert*-alkyl-1,2,3,4-tetrahydroisoquinolines from the appropriately substituted carbinols.

Summary

In order to examine the aldehydic nature of 6-formylsafrole, this was condensed with nitromethane, giving the expected β-nitrostyrene derivative. This aldehyde also responded normally to Canizzaro and crossed Canizzaro reations, undergoing allyl side-chain isomerization only in the former case. It also behaved normally towards the Grignard reagents, giving the corresponding carbinols in good or fair yields.

(Received May 17, 1954)