

Reactions in the Diene Series : Condensation of Isoprene with Aniline and Phenol.

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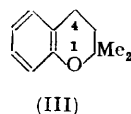
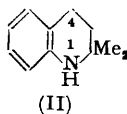
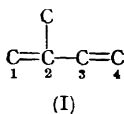
Condensation of isoprene with aniline gives 1 : 2 : 3 : 4-tetrahydro-2 : 2- and -4 : 4-dimethylquinoline, with a third, unidentified, base. After reaction with phenol only 2 : 2-dimethylchroman was identified.

ISOPRENE and aniline (1 mol. each), with a trace of iodine at 150—160°, give a mixture of basic and non-basic products. From the former by fractionation and picrate formation two isomeric secondary bases have been separated which gave quinaldine and lepidine respectively, after dehydrogenation. That the former (formed in much the greater amount is 1 : 2 : 3 : 4-tetrahydro-2 : 2-dimethylquinoline (II) is shown by its conversion into 1 : 2 : 3 : 4-tetrahydro-1 : 2 : 2-trimethylquinoline (Freund and Richard, *Ber.*, 1909, **42**, 1112). The other secondary base is doubtless 1 : 2 : 3 : 4-tetrahydro-4 : 4-dimethylquinoline. It too has been methylated but 1 : 2 : 3 : 4-tetrahydro-1 : 4 : 4-trimethylquinoline does not appear to have been described previously. Thus aniline condenses in the two possible ways, with C₍₂₎ and C₍₄₎ of isoprene [see (I)].

A third, isomeric base was separated as a greenish picrate in insufficient amount for further investigation. The colour of the picrate, however, appears to show that condensation has not taken place on C₍₁₎ and C₍₃₎ of isoprene to give a reduced quinoline, but rather at positions 1 : 2 or 3 : 4, to give a dihydroindole, or possibly at positions 1 : 4 to give a reduced seven-membered ring base.

Claisen (*Ber.*, 1921, **54**, 200) reported that condensing isoprene with phenol yields 2 : 2-dimethylchroman (III). We have repeated this and also isolated the chroman (III), the

structure of which is proved by its dehydrogenation to 6 : 6-dimethyl-1 : 2-benzopyran which on ozonolysis gives salicylaldehyde (Shriner and Sharp, *J. Org. Chem.*, 1939, **4**, 575). In the condensation of but-2-enyl bromide and trimethylquinol Karrer (*Helv. Chim. Acta*, 1939, **22**, 1287) obtained a chroman-coumaran mixture but so far no coumaran has been isolated from the reaction of isoprene with phenol.



In efforts to open the ether ring of the chroman (III) by acid we were unsuccessful, but treatment with acetic anhydride and zinc chloride gave a ketone and an acid. The former suggested a Friedel-Crafts acylation to give a 6- or 8-acetyl derivative of the chroman (III), and the properties of the acid suggests the introduction of the $-\text{CH}_2\cdot\text{CO}_2\text{H}$ group into the chroman. To settle the structure of the ketone condensation of *o*- and *p*-hydroxyacetophenone with isoprene was examined. In the former case only a trace of cyclic product was obtained, but in the latter a crystalline product resulted which differed from the ketone described above. Further the Willgerodt reaction on 6-acetyl-2 : 2-dimethylchroman gave a crystalline acid different from that obtained in the zinc chloride-acetic anhydride reaction which appears, therefore, to be the 8-acetyl derivative.

EXPERIMENTAL

Condensation of Isoprene with Aniline.—Isoprene (5 g.), aniline (7 g.), and a crystal of iodine were heated at 150–160° in a sealed tube for 8 hr. Extraction of the mixture with hydrochloric acid and subsequent basification and fractionation (2 mm.) gave fractions: (2 g.) b. p. 40–54°; (0.2 g.) b. p. 54–90°; (1.5 g.) b. p. 92–100°; (1.5 g.) thick viscous product b. p. up to 170°; residue (1.2 g.). The first fraction was recovered aniline. The third fraction (1 g.) in ether was added to ethereal picric acid (1.5 g.); after $\frac{1}{2}$ hr. the picrate (*A*) was collected and dried (1.6 g.), and the mother-liquor concentrated; yellow crystals (*B*) (0.2 g.) separated overnight. The mother-liquors from two such experiments were further concentrated and left for 24 hr.; green prisms (*C*) separated, with more of the picrate (*B*).

Picrate (A) was recrystallised from alcohol, giving prisms, m. p. 152° (Found: C, 52.3; H, 4.7. $\text{C}_{17}\text{H}_{18}\text{O}_7\text{N}_4$ requires C, 52.3; H, 4.6%). Treatment with ammonia gave 1 : 2 : 3 : 4-tetrahydro-2 : 2-dimethylquinoline, b. p. 95–98°/2 mm. (Found: C, 81.6; H, 9.5. $\text{C}_{11}\text{H}_{15}\text{N}$ requires C, 81.9; H, 9.3%). With nitrous acid it formed a *nitronitroso-derivative*, m. p. 159° (Found: C, 55.8; H, 5.7. $\text{C}_{11}\text{H}_{13}\text{O}_3\text{N}_3$ requires C, 56.2; H, 5.5%). On dehydrogenation with selenium at 300° a base was obtained whose picrate melted at 194–195° alone or mixed with quinaldine picrate (Found: C, 51.8; H, 3.5. Calc. for $\text{C}_{16}\text{H}_{12}\text{O}_7\text{N}_4$: C, 51.6; H, 3.2%).

The base (0.2 g.) from picrate (*A*) was heated at 100° for 12 hr. with methyl iodide (1.5 c.c.). On cooling, 1 : 2 : 3 : 4-tetrahydro-1 : 2 : 2-trimethylquinoline *hydriodide* separated. This recrystallised from alcohol ether as prisms, m. p. 167° (Found: C, 48.1; H, 6.3. $\text{C}_{12}\text{H}_{17}\text{N}\cdot\text{HI}$ requires C, 47.5; H, 6.0%). When this was heated with potassium hydroxide a base distilled which gave a picrate, m. p. 178–179° (lit., m. p. 178°) (Found: C, 53.6; H, 5.3. Calc. for $\text{C}_{18}\text{H}_{20}\text{O}_7\text{N}_4$: C, 53.5; H, 4.9%).

Picrate (B) formed yellow prisms, m. p. 115° (Found: C, 52.6; H, 4.9%), and treatment with ammonia liberated a base, b. p. 98°/2 mm. (Found: C, 82.3; H, 9.5%), which gave the Liebermann reaction. On dehydrogenation with selenium a base was obtained whose picrate melted at 212–213° alone or mixed with lepidine picrate (Found: C, 51.8; H, 3.5%). 1 : 2 : 3 : 4-Tetrahydro-1 : 4 : 4-trimethylquinoline was formed *via* the *hydriodide*, plates, m. p. 243–244° (Found: C, 48.1; H, 6.4%), and gave a *picrate*, m. p. 165° (Found: C, 53.2; H, 4.7%).

Picrate (C) formed greenish needles (from methanol), m. p. 165° (Found: C, 52.1; H, 4.6%).

Condensation of Isoprene with Phenol.—Isoprene (1 mol.), phenol (1 mol.), and a trace of iodine were heated in a sealed tube. The best yield (15%) of neutral steam-distilled product was obtained at 150°. This was fractionated; 24% of the product distilled at 82–92°/2 mm., showed no unsaturation, and was analysed as 2 : 2-dimethylchroman (Found: C, 81.6; H, 8.9. Calc. for $\text{C}_{11}\text{H}_{14}\text{O}$: C, 81.5; H, 8.6%).

The chroman (3.5 g.), *N*-bromosuccinimide (4.1 g.), and benzoyl peroxide (0.17 g.) were

refluxed in carbon tetrachloride (15 c.c.) with stirring for 4 hr. The cold mixture was filtered, the solvent removed, and the residue heated in benzene (20 c.c.) with sodium ethoxide on the water-bath for 3 hr. After addition of water the benzene layer was separated and distilled, giving a fraction, b. p. 76—80°/2 mm., n_D^{20} 1.546 (lit., b. p. 79—80°/2 mm., n_D^{20} 1.549). Ozonolysis gave salicylaldehyde whose 2 : 4-dinitrophenylhydrazone had m. p. and mixed m. p. 252°.

Action of Acetic Anhydride and Zinc Chloride on the Chroman (III).—2 : 2-Dimethylchroman (0.6 g.), acetic anhydride (15 c.c.), and zinc chloride (1 g.) were heated in a sealed tube in the water-bath for 12 hr. The excess of anhydride was decomposed by water, the mixture extracted with ether, the ether removed, and the residue distilled at 180—190°/0.1 mm. to give a solid. This was separated by sodium hydrogen carbonate solution to give a *ketone*, needles, m. p. 75° (from light petroleum) (Found : C, 76.3; H, 8.2. $C_{13}H_{16}O_2$ requires C, 76.5; H, 7.8%), and an *acid*, prisms, m. p. 181—182° (from light petroleum) (Found : C, 70.5; H, 7.5. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%). The ketone gives a 2 : 4-dinitrophenylhydrazone, m. p. 255°, and the acid a *methyl ester*, m. p. 87° (Found : C, 71.5; H, 7.8%; *M*, 225. $C_{14}H_{18}O_3$ requires C, 71.8; H, 7.7%; *M*, 234).

6-Acetyl-2 : 2-dimethylchroman.—Isoprene (3 g.), *p*-hydroxyacetophenone (3.2 g.), and a crystal of iodine were heated at 150° for 6 hr. The mixture was made alkaline and steam-distilled. The distillate solidified and gave the *6-acetyl derivative* as prisms, m. p. 90° (1.2 g.), from light petroleum (Found : C, 76.8; H, 8.2. $C_{13}H_{16}O_2$ requires C, 76.5; H, 7.8%). It forms a 2 : 4-dinitrophenylhydrazone, m. p. 244° (Found : C, 59.6; H, 5.5. $C_{16}H_{20}O_5N_4$ requires C, 59.4; H, 5.2%).

Willgerodt Reaction on 6-Acetyl-2 : 2-dimethylchroman.—The chroman (0.13 g.), sulphur (0.18 g.), pyridine (0.4 c.c.), and ammonia solution (0.3 c.c.; *d* 0.88) were heated at 120° for 5 hr. The dried product was refluxed for 4 hr. with 10% aqueous sodium hydroxide (5 c.c.), then diluted and filtered and the filtrate acidified with hydrochloric acid. The resulting *acid* formed prisms, m. p. 165° (50 mg.), from light petroleum, depressed on admixture with the acid of m. p. 181—182° (Found : C, 70.5; H, 7.2. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%).