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NITRO MUSKS. II. *tert*-AMYL HOMOLOGS OF THE COMMERCIAL MUSKS

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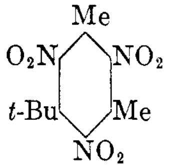
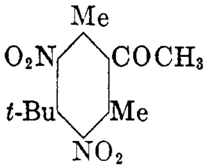
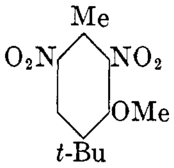
Of all the nitro musks synthesized since Baur (1) first prepared trinitro-*m*-*tert*-butyltoluene in 1888, only five are in commercial use today: Musk Xylene (2), Musk Ketone (3, 4, 5), Musk Ambrette (6, 7), Musk Tibetene[1] (5, 8), and Moskene[1] (9):



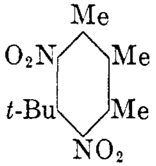
I. Musk Xylene



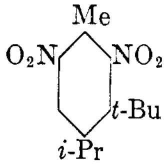
II. Musk Ketone



III. Musk Ambrette



IV. Musk Tibetene



V. Moskene

The present paper describes the *tert*-amyl homologs of four of these musks—that of Musk Ambrette was reported in Paper I of this series (10)—in which the *tert*-butyl group has been replaced by *tert*-amyl. All have musk odors of the same nuance as those of their prototypes, and in but slightly diminished intensity. In the following table are listed the melting points of the *tert*-butyl and *tert*-amyl derivatives:

TYPE	I	II	III	IV	V
tert-Bu M.P., °C	114	136.5	85	136.5	133
tert-Am M.P., °C	68	67.5	44	73	116

EXPERIMENTAL

Musk Xylene Homolog. The yield of this product is much more dependent upon the purity of the *m*-xylene used than is the case in the preparation of Musk Xylene itself. *tert*-Amyl chloride (120 g.) was added during 1 hour with agitation to a mixture of 476 g. of *m*-xylene (c.p. −48°) and 2 g. of aluminum chloride at 10°. Agitation was continued 2 hours further at 20°, the aluminum chloride was washed out with water, and the oil layer agitated for 5 min. at 65° with 100 g. of 5% sodium hydroxide, washed to neutrality, and distilled.

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[1] Reg. U. S. Patent Office.

There was obtained, in addition to 330 g. of recovered *m*-xylene, 200 g. of *sym-tert*-amyl-*m*-xylene, b.p. 78–79°/3 mm., c.p. 3.5°, m.p. 5.5°. If the usual 95% *m*-xylene obtained by the sulfonation of *m*-*p*-xylene be used in the above preparation, a product is obtained having c.p. about −30° and m.p. about −12° which is very difficult to purify. Nitration of this impure material yields a mixture which is also difficult to separate.

To a mixed acid composed of 24.5 g. of 93% sulfuric acid, 47 g. of 20% oleum, and 38 g. of 98% nitric acid, there was added with agitation during 15 min., 28 g. of *sym-tert*-amyl-*m*-xylene, keeping the temperature at 65°. Oleum (20%, 28 g.) was then added and the temperature gradually raised to 110° during one-half hr. The mixture was cooled to room temperature, quenched on ice, the thick oil taken up in benzene, washed with 5% sodium hydroxide until the washes were light-colored (3 washes), then with water to neutrality, and the solvent removed. A pale yellow oil (49 g.) remained which crystallized on short standing. It was taken up in 440 g. of naphtha and the turbid solution filtered, removing 1.5 g. of powder of m.p. 180–181°, which was probably 2,4,6-trinitro-*m*-xylene [reported (11) m.p. 182°]. The solvent was removed and the crystals recrystallized from 100 g. of ethanol, yielding 39 g. of 1,3,5-trinitro-2,4-dimethyl-6-*tert*-amylbenzene as brilliant, pale yellow plates, m.p. 68°, having a musk odor similar to that of Musk Xylene and of comparable strength.

Anal. Calc'd for $C_{13}H_{17}N_3O_6$: C, 50.14; H, 5.51; N, 13.50.

Found: C, 50.33; H, 5.48; N, 13.73.

Musk Ketone Homolog. A mixture of 132 g. of *sym-tert*-amyl-*m*-xylene (see above) and 80 g. of acetic anhydride was added with agitation to a mixture of 200 g. of aluminum chloride and 275 g. of ethylene dichloride during ¾ hour at −10°. Agitation was continued one-half hour further at −10° and the solution quenched on ice. It was washed to neutrality with water, the solvent distilled off, and the remainder distilled *in vacuo*. There was obtained, in addition to 50 g. of recovered *tert*-amyl-*m*-xylene, 83 g. of 2,6-dimethyl-4-*tert*-amylacetophenone as a colorless oil, b.p. 118°/2.5 mm., c.p. 10.5°, m.p. 12.5°, having a mild aromatic odor similar to that of its lower *tert*-butyl homolog.

The ketone (48 g.) was added with vigorous agitation to 235 g. of 98% nitric acid during 50 min. at −12°; 23 g. of 93% sulfuric acid was then added, agitation continued 20 min. further at −12°, and the solution quenched on ice. The pale yellow oil was taken up in benzene, washed with 5% sodium hydroxide until the washes were light-colored (3 washes), then to neutrality with water, and the solvent removed. The 68 g. of crude product thus obtained remained liquid for 3 weeks before it congealed. Three crystallizations from methanol yielded 17 g. of 3,5-dinitro-2,6-dimethyl-4-*tert*-amylacetophenone as small, practically colorless needles, m.p. 67.5°, having a musk odor similar in character and strength to that of Musk Ketone.

Anal. Calc'd for $C_{15}H_{20}N_2O_5$: C, 58.41; H, 6.54; N, 9.09.

Found: C, 58.39; H, 6.57; N, 9.11.

Musk Tibetene Homolog. A mixture of 352 g. of *sym-tert*-amyl-*m*-xylene (see above), 20 g. of paraformaldehyde, and 130 g. of 31% hydrochloric acid was warmed to 60° and then, with vigorous agitation, 275 g. of 72% sulfuric acid was added during 2 hours at 60–70°. The temperature was gradually raised to 80° during the next 2 hours and held at 80° for 3 hours, all the while maintaining vigorous agitation. After cooling, the oil layer was separated, washed once with water, dried over sodium carbonate, and distilled. There was obtained, in addition to 280 g. of recovered *tert*-amyl-*m*-xylene, 72 g. of 2,6-dimethyl-4-*tert*-amylbenzyl chloride as a colorless oil of mild odor having b.p. 117°/2 mm., c.p. 20°, m.p. 22°.

The chloride (72 g.) was added during 1 hour to a refluxing, vigorously agitated mixture of 30 g. of zinc dust and 67 g. of water. After 5 hours' refluxing, the oil layer was chlorine-free. The mixture was steam-distilled and the oil distilled *in vacuo*; 46 g. of *sym-tert*-amylhemimellitene was obtained as a colorless oil, b.p. 83°/1.5 mm., c.p. −14°, m.p. −12°, having a mild odor similar to that of its *tert*-butyl homolog.

The *tert*-amylhemimellitene (38 g.) was added, with vigorous agitation, to a mixture of 29 g. of 98% nitric acid and 116 g. of 93% sulfuric acid during 1 hour at 20°. Sulfuric acid

(93%, 70 g.) was then added and the temperature gradually raised to 60° during one-half hour. The mixture was cooled to room temperature, quenched on ice, the crystals taken up in benzene and washed with 5% sodium hydroxide until the washes were light-colored (3 washes), then to neutrality with water. The solvent was removed and the remaining 54 g. of crude product was crystallized three times from methanol to yield 31 g. of 1,3-dinitro-2-*tert*-amyl-4,5,6-trimethylbenzene as pale yellow, compact prisms, m.p. 73°, having a musk odor similar to that of Musk Tibetene.

Anal. Calc'd for $C_{14}H_{20}N_2O_4$: C, 59.97; H, 7.19; N, 10.00.
Found: C, 60.18; H, 7.17; N, 10.40.

Moskene Homolog. Sulfuric acid (93%, 1,200 g.) was cooled to 0° and 480 g. of *p*-cymene was added with agitation keeping the temperature at 0°. *tert*-Amyl alcohol (120 g.) was then added during 1 hour, maintaining the temperature at 0°, and stirring continued one-half hour longer. The oil layer was removed, washed with water, then with 5% sodium hydroxide, and finally with water to neutrality and distilled. There was obtained, in addition to 337 g. of recovered *p*-cymene, 95 g. of 3-*tert*-amyl-4-isopropyltoluene, as a colorless oil of mild odor having b.p. 84°/3.5 mm., d_{25}^{25} 0.9020, n_D^{20} 1.5072.

The hydrocarbon (50 g.) was added with agitation to a mixture of 100 g. of 98% nitric acid and 300 g. of 93% sulfuric acid during 25 min. at 25°. Stirring was continued one-half hour further at 25–30° and the mixture quenched on ice. The crystals were taken up in benzene and washed with 5% sodium hydroxide until the washes were light-colored, then to neutrality with water, and the solvent removed. The remaining crude product, 71 g., was crystallized twice from ethanol and three times from methanol to yield 25 g. of 2,6-dinitro-3-*tert*-amyl-4-isopropyltoluene as pale yellow, irregular prisms, m.p. 116°, having a musk odor similar in character and strength to that of Moskene.

Anal. Calc'd for $C_{15}H_{22}N_2O_4$: C, 61.19; H, 7.57; N, 9.56.
Found: C, 60.93; H, 7.00; N, 9.47.

All analyses were performed by Mr. D. Johnston and the staff of the Analytical Laboratory.

SUMMARY

The *tert*-amyl homologs of four of the five commercial nitro musks: Musk Xylene, Musk Ketone, Musk Tibetene, and Moskene have been prepared and found to have musk odors similar in strength and quality to those of their *tert*-butyl prototypes. The *tert*-amyl homolog of the remaining number of the group —Musk Ambrette—was reported in a previous paper of this series.

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