[Contribution from the Department of Chemistry of Arizona State College]

SYNTHESIS OF SOME *tert*-BUTYLBENZENES RELATED TO SYNTHESIS OF ASYMMETRIC NITRO MUSKS[1]

E. E. BURGOYNE, T. G. KLOSE,[2] AND D. K. WATSON[3]

Received June 20, 1955

Carpenter and Easter (1) have reported the synthesis of 4-bromo-5-*tert*-butyl-*m*-xylene (I) by means of a Sandmeyer reaction from 4-amino-5-*tert*-butyl-*m*-xylene (II) which was obtained in five reactions from *sym*-*tert*-butyl-*m*-xylene (III). We were unable to prepare I this way, but did prepare it in four reactions from III by de-amination of 2-amino-4-bromo-5-*tert*-butyl-*m*-xylene (IV), a new compound characterized by preparation of 3-bromo-4-*tert*-butyl-2,6-dimethylacetanilide (IX) (Flow Sheet A). Although Carpenter and Easter (1) were not successful in preparing 4-bromo-5-*tert*-butyl-2,6-dinitro-*m*-xylene (V) by direct nitration of I, we were successful in doing this as well as preparing V by the method used by Carpenter and Easter (1) involving nitration of 2-nitro-4-bromo-5-*tert*-butyl-*m*-xylene (VI), precursor of IV.

We prepared II from 4-nitro-5-*tert*-butyl-*m*-xylene (VII) prepared directly from III, instead of through 2-nitro-5-*tert*-butyl-*m*-xylene (VIII) as Carpenter and Easter (1) did. Nitration of III gave us a mixture from which was obtained a 35% yield of VII and a 63% yield of VIII.

Schlotter and Clark (2) have called attention to the adversion of the *tert*-butyl group to entry in a position *ortho* to a methyl group in the benzene nucleus. Our experience would confirm this. However, we were successful in synthesizing in low yield a compound in which a *tert*-butyl group was *ortho* to a methyl group.

Bromination of *para*-xylene (X) gave 2-bromo-*p*-xylene (XI), which with a Grignard reaction gave a 5.2% yield of 2-*tert*-butyl-*p*-xylene (XII) (Flow Sheet B).

EXPERIMENTAL

FLOW SHEET A

4-Nitro-5-tert-butyl-m-xylene (VII) *and 2-nitro-5-tert-butyl-m-xylene* (VIII). The following synthesis is based upon that described by Powell and Johnson (3). In a 2-l., three-necked, round-bottom flask equipped with a mechanical stirrer, dropping-funnel, thermometer, and reflux condenser were placed 324 g. (2 moles) of *sym*-*tert*-butyl-*m*-xylene (III) and 360 g. of acetic anhydride. The flask and contents were cooled in an ice-salt bath below 10°. A cold solution of 186 g. (3 moles) of fuming nitric acid in 120 g. of glacial acetic acid and 120 g. of acetic anhydride was added slowly with stirring over a period of 1.7 hours, at a temperature slightly below 15°. The mixture was stirred at about 15° for ½ hour more and then for two hours at room temperature. The mixture then was warmed for ten minutes on the steam-bath at 50° with shaking. Then it was cooled to 30° in an ice-bath and poured slowly

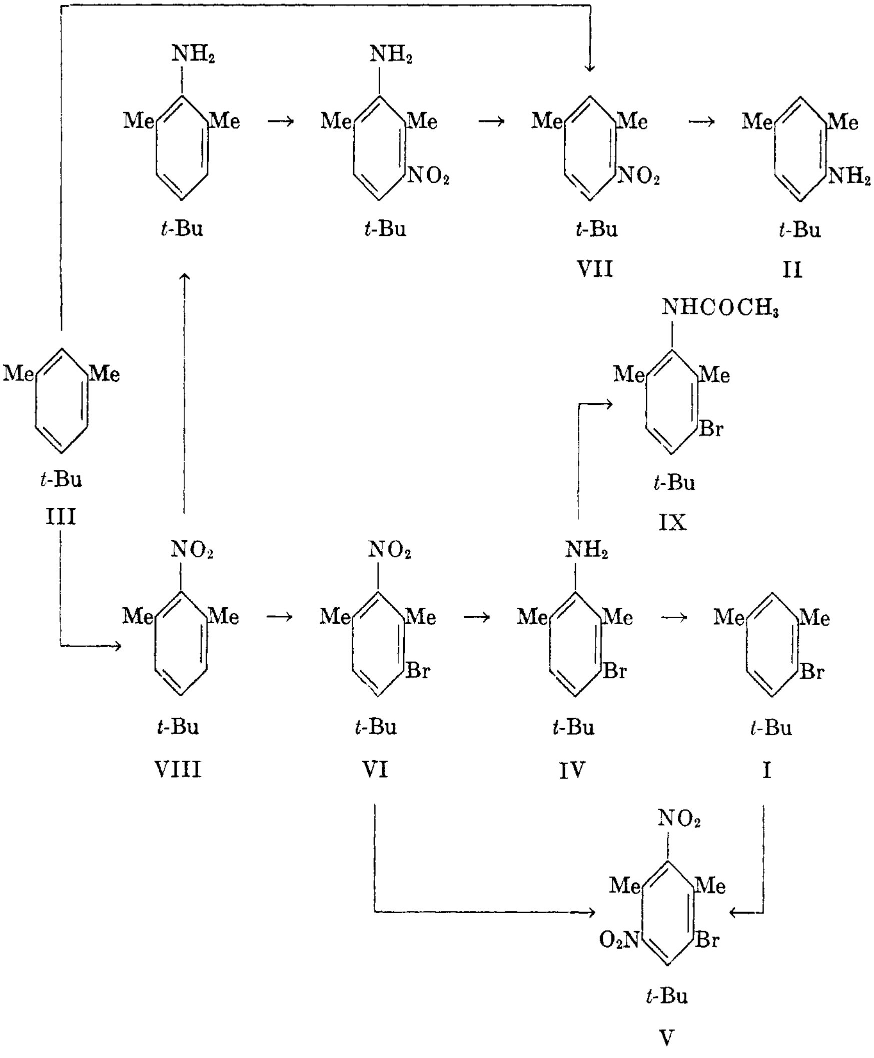
---

[1] Supported by a Cottrell Grant from the Research Corporation, 1949–1950 and 1953–1954.

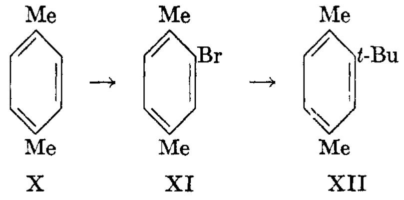
[2] Deceased November 30, 1950.

[3] Present address: Tripp Research Corporation, Dallas, Texas.

FLOW SHEET A



FLOW SHEET B



with stirring into three liters of ice-water and allowed to stand for two hours. The crystals were collected and washed with eight 100-ml. portions of water. The crystals were dissolved in 1200 ml. of boiling methanol and cooled with final cooling in a refrigerator overnight. The crystals were removed by filtration and were recrystallized from 1000 ml. of methanol. There was obtained 260 g. (62.8%) of colorless needle-like crystals of VIII, m.p. 83–85°. Fuson, *et al.*, (4) reported the melting point of this symmetrical isomer as 85°. From the mother liquors an additional 5.0 g. of VIII was obtained after further cooling. The methanol was removed from the mother liquor by distillation and the residual oil was vacuum-distilled to yield 146.5 g. (35.6%) of VII, b.p. 109–111° (4 mm.), n_D^{24} 1.5139. Carpenter and Easter (1) gave the following constants: b.p. 101° (2.5 mm.), n_D^{20} 1.5140.

2-Nitro-4-bromo-5-tert-butyl-m-xylene (VI). In the usual 2-liter apparatus, equipped with a gas-absorption trap were placed 103.5 g. (0.5 mole) of VIII, 500 ml. of carbon tetrachloride, and 2.0 g. of iron powder. To the vigorously stirred mixture was added at room temperature over a period of two hours, 80.0 g. (0.5 mole) of bromine dissolved in 50 ml. of carbon tetrachloride. Stirring at room temperature was continued for 24 hours. Then 200 ml. of saturated sodium bisulfite solution was added to the vigorously stirred mixture. Water-soluble substances then were extracted by washing with three 200-ml. portions of water, one 200-ml. portion of 5% hydrochloric acid, and three 200-ml. portions of water. The organic solution was dried over calcium chloride, filtered, and the carbon tetrachloride was removed by distillation. The residue was crystallized from 250 ml. of methanol to yield 112.8 g. (89.6%) of VI, m.p. 70–74°. Carpenter and Easter (1) found VI to have a melting point of 75–76°.

2-Amino-4-bromo-5-tert-butyl-m-xylene (IV). In a two-liter Florence flask equipped with a reflux condenser were placed 215.3 g. (0.753 mole) of VI, 215.3 g. of iron filings, 11 ml. of conc'd hydrochloric acid, and 1000 ml. of water. The mixture was refluxed on a hot plate for 40 hours. The reaction was made alkaline by the addition of a solution of 60 g. of sodium hydroxide in 200 ml. of water. The hot alkaline mixture was filtered with suction. The filter cake was washed with three 100-ml. portions of ether. These ethereal washings were used for the first extraction of the filtrate. The filtrate then was extracted with three additional 100-ml. portions of ether. The ethereal extracts were combined, washed once with a 200-ml. portion of water, and then dried over magnesium sulfate. The ether was removed by distillation and the residue was distilled to give 135.4 g. (70.3%) of IV, as a light yellow oil, b.p. 138–141° (3 mm.), n_D^{33} 1.5603, d_{25}^{25} 1.293, M_D (calc'd) 65.19, M_D (obs.) 64.50. This we believe to be a new compound.

3-Bromo-4-tert-butyl-2,6-dimethylacetanilide (IX). The characterization of IV was accomplished by the method of Shriner and Fuson (6) by refluxing one gram of the amine for 5 minutes with 10 ml. of acetic anhydride. Dissolving the resulting white syrup in petroleum ether and allowing the solvent to evaporate slowly caused the separation of white plates. Recrystallization from 95% ethyl alcohol yielded about one gram of IX melting at 148–150°.

Anal. Calc'd for $C_{14}H_{20}BrNO$: C, 56.38; H, 6.76.
Found: C, 56.54; H, 6.93.

4-Bromo-5-tert-butyl-m-xylene (I). A suspension of 29.3 g. (0.1 mole) of the hydrochloride of IV in 120 ml. of water and 15 ml. of conc'd hydrochloric acid was diazotized by the method of Fieser and Heymann (5) at a temperature of 5–6° by the addition of 7 g. of sodium nitrite in 30 ml. of water. During a period of ten minutes the clear diazonium solution was added in small portions to an ice-cold solution of sodium stannite prepared from 40 g. of stannous chloride, 50 g. of sodium hydroxide, and 260 ml. of water. After standing for one hour at room temperature, the mixture was steam-distilled and about 900 ml. of distillate was collected. The yellow oil was separated and the water layer was extracted with three 50-ml. portions of ether which then were combined with the oil and the whole dried over calcium chloride. The ether was removed by distillation and the residue was distilled to yield 7.5 g. (31.1%) of I, b.p. 75–82° (3 mm.), $n_D^{27.4}$ 1.5355. The product was dissolved in 15 ml. of hot 95% alcohol. Upon cooling, colorless crystals were obtained, m.p. 37–37.5°. Carpenter and Easter (1) found I to possess b.p. 92–93° (3.5 mm.) and m.p. 34.5°.

Anal. Calc'd for $C_{12}H_{17}Br$: C, 59.75; H, 7.05.
Found: C, 59.74; H, 6.92.

4-Amino-5-tert-butyl-m-xylene (II). In a 200-ml. flask equipped with a reflux condenser was placed a mixture of 160 g. (0.773 mole) of VII, 765 ml. of water, 191 g. of iron filings, and 13 ml. of concentrated hydrochloric acid. The mixture was heated with refluxing for 24 hours. Then it was made strongly acid with concentrated hydrochloric acid, and steam-distilled. After 700 ml. of distillate was collected (including about 13 g. of some insoluble material), the solution was made basic by the slow addition of sodium hydroxide pellets, the hot mixture was filtered with suction, and the filtrate was cooled. The organic layer was separated and the water layer was extracted with six 100-ml. portions of ether. The ether extracts were combined with the organic layer, dried over magnesium sulfate, and the ether was removed by distillation. The residual matter was distilled to yield 93 g. (67.9%) of II, b.p. 97–100° (3 mm.) n_D^{25} 1.5267, d_{25}^{25} 0.9762; M_D (obs.), 55.8; M_D (calc'd), 57.4. Carpenter and Easter (1) found II to distill at 97° (3.5 mm.).

4-Bromo-5-tert-butyl-2,6-dinitro-m-xylene (V). One gram of I was added slowly to 25 ml. of fuming nitric acid while keeping the temperature below 10°. The mixture was kept between 5° and 10° for 30 minutes, then at room temperature (25°) for 30 minutes, and finally it was warmed on a water-bath for 15 minutes. The mixture then was cooled, poured into ice-water, and the organic material was extracted with a total of about 50 ml. of ether used in small portions. The ether was removed by evaporation and the residue was crystallized from 95% ethyl alcohol. A solid product was obtained which had m.p. 88–90°, and so the solid material was put through the above nitration process a second time. Crystals of V then were obtained with a musk odor and a m.p. 67–69°. Carpenter and Easter (1) report V to melt at 67–68°.

In a 100-ml. beaker was placed 30 ml. of fuming nitric acid and 2.0 g. of VI was slowly added at 25°. The mixture was allowed to stand for 30 minutes at 25°, then it was heated on the steam-bath for ten minutes. Then it was cooled, poured into 300 ml. of ice-water, and the organic material was extracted with two 25-ml. portions of ether. The ether was removed by evaporation, and the residue was dissolved in 50 ml. of hot 95% alcohol. Upon cooling, colorless needle-like crystals formed. These were recrystallized from 95% alcohol to yield 2.0 g. of almost colorless needle-like crystals of V with a musk odor, m.p. 66–67°. Carpenter and Easter (1) report V to melt at 67–68°.

FLOW SHEET B

2-Bromo-p-xylene (XI). In the usual 2 liter apparatus was placed 318 g. (3 moles) of *p*-xylene (X) in 250 ml. of carbon tetrachloride. Then 6 g. of 40-mesh iron filings was added. The flask was immersed in ice-water, and 480 g. (3 moles) of bromine in 150 ml. of carbon tetrachloride was added slowly with stirring over a period of 8½ hours. The flask was covered with a cloth during this operation to exclude light. The mixture was allowed to stand 16 hours; then it was washed consecutively with 500 ml. of saturated solution of sodium bisulfite, 250 ml. of water, 250 ml. of 10% sodium hydroxide, and twice with 250 ml. of water. After drying the solution over calcium chloride, the carbon tetrachloride was removed by distillation and the residue was submitted to fractional distillation. The fraction b.p. 107–110° (40 mm.), amounted to 303 g. (54%) of XI, colorless liquid, n_D^{20} 1.5473.

2-tert-Butyl-p-xylene (XII). In the usual 2 liter apparatus was placed 25.0 g. (1.03 moles) of Grignard magnesium turnings covered with about 100 ml. of dry ether. A small crystal of iodine was added. Then 20 ml. of a solution of 190 g. (1.03 moles) of XI in 400 ml. of dry ether was added. One milliliter of methyl iodide was added. The remainder of the solution was run in over a period of two hours with gentle stirring. The mixture was heated to refluxing with a 60-watt lamp bulb for an additional 22 hours. The mixture was cooled to room temperature and 97.4 g. (1.04 moles) of *tert*-butyl chloride was slowly added with stirring over a period of 1½ hours. The mixture then was heated to refluxing and stirred for five hours while a total of 50 g. of additional *tert*-butyl chloride was added. A saturated solution of ammonium chloride followed by 100 ml. of concentrated hydrochloric acid was added and the mixture was allowed to stand for several hours. The ether solution was separated, washed with water, a 5% solution of sodium hydroxide, water, and a 10% solution of sodium thiosulfate, and twice more with water. After drying over calcium chloride the ether was removed by evaporation and the residue was fractionally distilled. There was obtained 8.4 g. (5.2%) of XII, b.p. 213–217° (735 mm.), $n_D^{28.5}$ 1.5003, $d_{29.5}^{29.5}$ 0.8757, M_D (obs.), 54.4; M_D (calc'd), 54.0.

Anal. Calc'd for $C_{12}H_{18}$: C, 88.89; H, 11.11.
Found: C, 88.32; H, 10.87.

SUMMARY

1. A new route has been devised for the synthesis of 4-bromo-5-*tert*-butyl-*m*-xylene.
2. A new compound, 2-amino-4-bromo-5-*tert*-butyl-*m*-xylene, has been prepared in the course of this route and has been characterized by the preparation of the amide, 3-bromo-4-*tert*-butyl-2,6-dimethylacetanilide.
3. A new hydrocarbon, 2-*tert*-butyl-*p*-xylene, has been prepared.

TEMPE, ARIZONA

REFERENCES

(1) CARPENTER AND EASTER, *J. Org. Chem.*, **19**, 77 (1954).
(2) SCHLOTTER AND CLARK, *J. Am. Chem. Soc.*, **75**, 361 (1953).
(3) POWELL AND JOHNSON, *Org. Syntheses*, Coll. Vol. II, p. 449 (1943).
(4) FUSON, *et al.*, *J. Org. Chem.*, **12**, 587 (1947).
(5) FIESER AND HEYMANN, *J. Am. Chem. Soc.*, **64**, 380 (1942).
(6) SHRINER AND FUSON, *Identification of Organic Compounds*, John Wiley and Sons, New York, 1948.

NOTICE TO AUTHORS

On and after September 1, 1955, the Journal will accept *Notes*; the Journal will accept *Communications to the Editor* received on or after November 1, 1955 for publication in Volume 21. See revised Notice to Authors for details.

Effective with Volume 21, the Journal will use a double column format with a page size approximately 6½" by 9". Authors should consider this in connection with graph sizes, and table compositions.