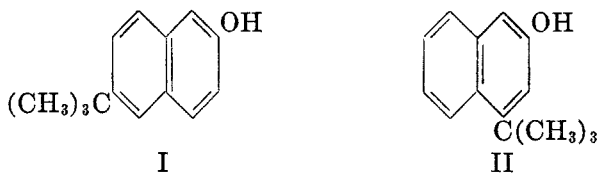


*tert*-BUTYLATION OF  $\beta$ -NAPHTHOL AND 1-CHLORO-2-NAPHTHOL  
NG. PH. BUU-HOÏ, HENRI LE BIHAN, FERNAND BINON, AND PAULIN RAYET

Received April 11, 1950

Although the *tert*-butylation of  $\beta$ -naphthol and its methyl ether has already formed the subject of several publications, as yet there is complete uncertainty in the literature as to the constitution of the reaction products.

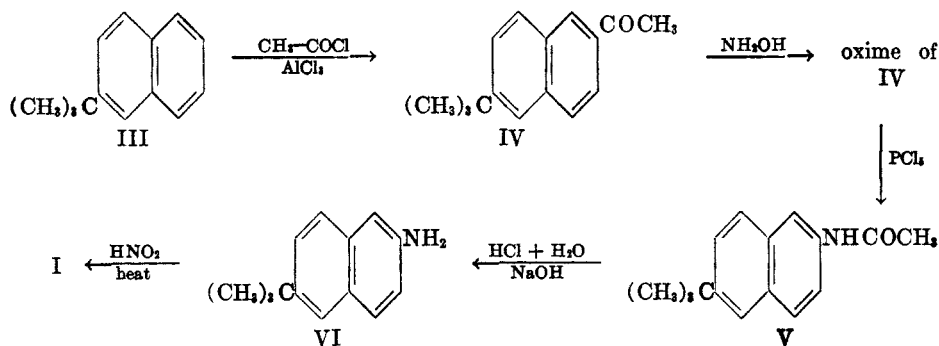
In 1898, Cahen (1) investigated the Friedel-Crafts reaction of neroline with isobutyl bromide in the presence of aluminum chloride, and obtained a butylneroline of which neither the structure of the alkyl group nor its location in the naphthalene ring was discussed. In 1931, Koenigsberger (2) patented the alkylation of  $\beta$ -naphthol by *tert*-butyl chloride and aluminum chloride; this gave a product melting at about 102°, which he termed "4-*tert*-butyl-2-naphthol" without any proof of constitution. A few years later, a *tert*-butyl- $\beta$ -naphthol was mentioned without details in two further patents (3); and in 1935, Tschitschibabin (4) described the alkylation of  $\beta$ -naphthol with *tert*-butyl alcohol in the presence of phosphoric acid and described a *tert*-butyl- $\beta$ -naphthol melting at 113°, whose constitution was also left undecided. These reactions were recently more thoroughly investigated by Contractor, Peters, and Rowe (5), who found that the products described in the patents and by Tschitschibabin were impure samples of a *tert*-butyl- $\beta$ -naphthol melting at 119–120° (*picrate*, m.p. 142°). In the molecule of this compound, the location of the alkyl group at the 1-position was excluded on the ground that azo derivatives were readily obtained with *m*- and *p*-nitrophenyldiazonium salts; the 6-position was discarded because of the non-identity with a *liquid* naphthol obtained from  $\beta$ -*tert*-butyl-naphthalene by sulfonation and subsequent alkaline fusion, and believed to be 6-*tert*-butyl-2-naphthol (I). On these grounds, Contractor, *et al.* assumed the most probable constitution of the compound of m.p. 119–120° to be that of 4-*tert*-butyl-2-naphthol (II).



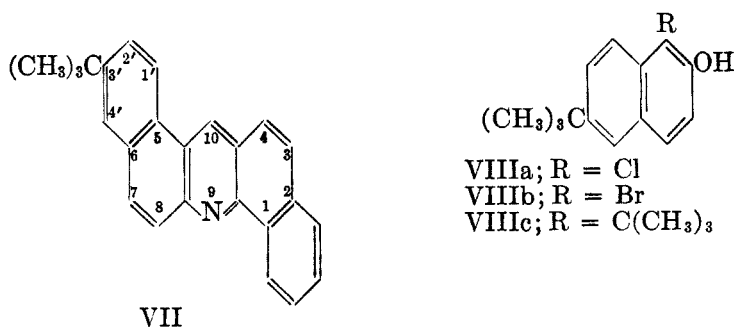
In the course of an investigation into bactericidal and vermifugal drugs, we came to study the same problem. We found that, as well as the procedures already described,  $\beta$ -naphthol was readily *tert*-butylated with isobutyl alcohol or isobutylene. We confirmed the properties found by Contractor, *et al.* for the compound m.p. 119–120°, but the proposed constitution (II) appeared to us improbable since such an alkylation of a phenol at the *meta* position<sup>1</sup> would be

<sup>1</sup> The reported *meta*-ethylation of phenols [*e.g.* Jannasch and Rathjen, *Ber.*, **32**, 2391 (1899)] involved unusual experimental conditions suggesting the intervention of some mechanism (*e.g.* free radicals, Jacobsen's degradation, etc. . .) different from the normal course of a Friedel-Crafts reaction.

unprecedented (6). It would also be surprising, in view of the outstanding reactivity of the 6-position in 2-substituted naphthalenes (7), if  $\beta$ -naphthol were not *tert*-butylated, at least in part, at the 6-position. The fact that all the 6-alkyl-2-naphthols previously described have relatively high melting points, and the evidence that rearrangements frequently accompany the sulfonation of aromatic hydrocarbons bearing ramified alkyl groups (8), led us to suspect that the substance of m.p. 119–120° might well be 6-*tert*-butyl-2-naphthol, and that the liquid isomer which was given the formula (I) might have another structure than that previously assumed. This has now been confirmed by synthesis in the following way: (a)  $\beta$ -*tert*-butylnaphthalene (III) was acetylated with acetyl chloride and aluminum chloride in cold nitrobenzene, a procedure known to bring about 6-substitution (9); (b) Beckmann rearrangement of the oxime of the resulting 6-*tert*-butyl-2-acetonaphthone (IV) gave 6-*tert*-butyl-2-acetaminonaphthalene (V); (c) 6-*tert*-butyl-2-naphthylamine (VI), obtained by acid hydrolysis of (V), was diazotized and the diazo compound decomposed in aqueous medium to 6-*tert*-butyl-2-naphthol (I). The latter was identified with the product obtained directly from  $\beta$ -naphthol, by mixed melting-point determinations upon the



free naphthols, their picrates, and their methyl ethers. A further proof of this identity was supplied by performing an Ullmann-Fettvadjan reaction (10) with samples of the naphthol (I) from these two sources,  $\alpha$ -naphthylamine and paraformaldehyde: in both cases, the same *tert*-butyl-1,2,5,6-dibenzacridine (VII) was obtained.

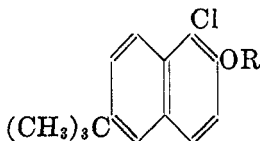


In the molecule of 6-*tert*-butyl-2-naphthol, the 1-position was found to be the most reactive, as chlorination gave a monochloro derivative identical to that obtained by *tert*-butylating 1-chloro-2-naphthol, and which must therefore be

TABLE I  
SUBSTITUTED 2-NAPHTHOLS

NAPHTHOL	M.P., °C.	REFERENCE
6-Methyl-2-naphthol.....	128-129	(12)
6-Ethyl-2-naphthol.....	97-98	(13)
6- <i>tert</i> -Butyl-2-naphthol.....	119-120	
6-Cyclohexyl-2-naphthol.....	161-162	(11)
6- <i>n</i> -Heptyl-2-naphthol.....	96-98	(14)
6- <i>n</i> -Octyl-2-naphthol.....	92-93	(15)
6-Chloro-2-naphthol.....	115	(16)
6-Bromo-2-naphthol.....	127	(17)

TABLE II  
NEW ETHERS OF 6-*tert*-BUTYL-1-CHLORO-2-NAPHTHOL



R	FORMULA	M.P., °C.	ANALYSES	
			Chlorine	
			Calc'd	Found
Methyl.....	C <sub>16</sub> H <sub>17</sub> ClO	115	14.2	14.0
Ethyl.....	C <sub>18</sub> H <sub>19</sub> ClO	80	13.5	13.2
<i>n</i> -Propyl.....	C <sub>19</sub> H <sub>21</sub> ClO	60	12.8	12.7
Isopropyl.....	C <sub>17</sub> H <sub>21</sub> ClO	58	12.8	12.5
Allyl.....	C <sub>17</sub> H <sub>19</sub> ClO	45	12.8	12.5
Isobutyl.....	C <sub>19</sub> H <sub>23</sub> ClO	79	12.2	11.9
Isoamyl.....	C <sub>19</sub> H <sub>25</sub> ClO	60	11.6	11.5
<i>n</i> -Octyl.....	C <sub>22</sub> H <sub>31</sub> ClO	35	10.2	10.0
$\omega$ -Undecenyl.....	C <sub>23</sub> H <sub>35</sub> ClO	b.p. 275-280/16 mm.	9.2	8.9
<i>n</i> -Octadecyl.....	C <sub>22</sub> H <sub>31</sub> ClO	61	7.3	7.0
Benzyl.....	C <sub>21</sub> H <sub>21</sub> ClO	94	10.9	10.8
<i>p</i> -Methylbenzyl.....	C <sub>22</sub> H <sub>23</sub> ClO	110	10.5	10.2
<i>p</i> -Chlorobenzyl.....	C <sub>21</sub> H <sub>20</sub> Cl <sub>2</sub> O	132	9.9	9.7
$\beta$ -Phenylethyl.....	C <sub>22</sub> H <sub>23</sub> ClO	112	10.5	10.7
Hydnocarpyl.....	C <sub>30</sub> H <sub>43</sub> ClO	b.p. 315-320/17 mm.	7.8	7.5

6-*tert*-butyl-1-chloro-2-naphthol (VIIIa) (this was also proof of the reactivity of the 6-position in the molecule of 1-substituted 2-naphthols). Bromination similarly yielded 6-*tert*-butyl-1-bromo-2-naphthol (VIIIb). Further *tert*-butylation of 6-*tert*-butyl-2-naphthol occurred very easily too, yielding 1,6-di-*tert*-

butyl-2-naphthol (VIIIc), a compound which, like many cryptophenols of the same type, was insoluble in aqueous alkali, but whose hydroxyl group could easily be shown by the Tschugaeff-Zerewitinow procedure; the location of a *tert*-butyl group at the 1-position was deduced from the inability of VIIIc to couple with aryldiazonium salts. The fact that there is no O-ether function in this compound was also established by its stability to boiling pyridine hydrochloride. Compound VIIIc is identical with a substance previously described in the literature (6) as the *tert*-butylether of *tert*-butyl- $\beta$ -naphthol m.p. 119–120°, apparently because of its alkali insolubility.

The structures which we assigned to the products from the *tert*-butylation of  $\beta$ -naphthol fall well in line with observations previously made by Alberti (11) upon the cyclohexanation of the same naphthol. The melting point of 6-*tert*-butyl-2-naphthol is also consistent with those of already-known 6-alkyl- and 6-halogeno-2-naphthols as listed in Table I.

6-*tert*-Butyl-1-chloro-2-naphthol was found of practical interest as an anthelmintic against the tape-worm; it also has fungicidal properties against *Fusarium graminearum*. The study of similar compounds is under way.

Table II in the experimental part contains a list of ethers of 6-*tert*-butyl-1-chloro-2-naphthol which we prepared for biological testing in view of Sexton's recent work upon fungistatic properties of  $\beta$ -naphthol ethers (18).

#### EXPERIMENTAL<sup>2</sup>

*tert*-Butylation of  $\beta$ -naphthol. The three procedures reported by Contractor, *et al.* (5) were followed, except that in each instance, the crude alkylation products were vacuum-distilled, and three fractions isolated. Fraction 1 (b.p. <170°/13 mm.) contained mostly the recovered  $\beta$ -naphthol, fraction 2 (b.p. 175–190°/13 mm.) was chiefly the mono-*tert*-butylnaphthol, and fraction 3 (b.p. >190°/13 mm.) corresponded to the di-*tert*-butylnaphthol. In the first two procedures of Contractor, *et al.* (5), *tert*-butyl chloride could be replaced by isobutylene or isobutyl chloride in equivalent amounts, and in the third one, isobutyl alcohol could be used instead of *tert*-butyl alcohol.

6-*tert*-Butyl-2-naphthol (I). The fractions of b.p. 175–190°/13 mm. melted indefinitely at around 80–110° as reported in Koenigsberger's patent (2) and by Tschitschibabin (4), but gave after repeated crystallizations from ligroin, long colorless needles with a naphtholic odor, melting at 118–119° (literature: 119–120°). The orange *picrate* of this compound melted at 143–144° (literature: 142°). The mother-liquors from the purification of (I) contained notable amounts of a product crystallizing from ligroin in silky colorless needles melting at about 86–87° (the *picrate* formed deep orange needles from ethanol, m.p. about 118–120°), having the same composition as (I).

*Anal.* Calc'd for C<sub>14</sub>H<sub>16</sub>O: C, 84.0; H, 8.0.

Found: C, 83.8; H, 8.3.

This is not, however, a pure isomer of (I), as fractional sublimation yielded considerable amounts of the latter; the lower-melting residue (85–86°) could not be freed from traces of (I).

1,6-Di-*tert*-butyl-2-naphthol (VIIIc). The fractions b.p. >190°/13 mm. were repeatedly recrystallized from methanol and ligroin, giving silky colorless needles melting at 138–139° (in accordance with the melting point recorded by Contractor, *et al.* (5) for "4(?)-*tert*-butyl-2-naphthol *tert*-butylether"). The product was insoluble in aqueous sodium hy-

<sup>2</sup> All melting points were taken with a Maquenne-block.

dioxide, nor did it couple with 4-nitrophenyldiazonium chloride, but produced an abundant evolution of methane when added to a solution of methylmagnesium iodide in anisole. Two grams of the substance, refluxed for four hours with redistilled pyridine hydrochloride (15 g.) (a most effective reagent for the splitting of O-ether linkages) were recovered unchanged after treatment with water and crystallization from methanol.

*6-tert-Butyl-2-naphthol methyl ether.* This compound was obtained from the potassium salt of 6-*tert*-butyl-2-naphthol by treatment with methyl sulfate in the usual way. From methanol it formed colorless needles melting at 95°.

*Anal.* Calc'd for  $C_{15}H_{18}O$ : C, 84.1; H, 8.4.

Found: C, 84.0; H, 8.6.

*6-tert-Butyl-1-chloro-2-naphthol* (VIIIa). To a well-stirred mixture of 100 g. (0.56 mole) of 1-chloro-2-naphthol and 5 g. of finely powdered aluminum chloride, 65 g. (0.7 mole) of *tert*-butyl chloride was added, the temperature being kept at about 25°. After the addition, stirring was continued, while the mixture was slowly heated in a water-bath up to 80° and kept at this temperature for one hour. The reaction product was diluted with 150 ml. of ligroin, washed with water, then with an aqueous solution of sodium bicarbonate and again with water. The organic layer was dried over calcium chloride, the solvent removed, and the residue vacuum-distilled (about 170–200°/15 mm.). About half the distillate crystallized on cooling, giving long colorless needles with a sharp odor, which melted at 76° after recrystallization from ligroin.

*Anal.* Calc'd for  $C_{14}H_{15}ClO$ : C, 71.6; H, 6.4.

Found: C, 71.5; H, 6.6.

The same compound was obtained when 6-*tert*-butyl-2-naphthol was treated with the calculated amount of chlorine in acetic acid or carbon disulfide (19) in the usual way.

*6-tert-Butyl-1-bromo-2-naphthol* (VIIIb). A solution of 16.2 g. of bromine in acetic acid (10 ml.) was stirred into a mixture of 6-*tert*-butyl-2-naphthol (20 g.) and acetic acid (50 ml.). The reaction product was poured into water, and the precipitated oil taken up in benzene; the benzene layer was washed with an aqueous solution of sodium bicarbonate and then with water, dried over calcium chloride, the solvent removed, and the residue purified by vacuum-distillation (at about 170–190°/13 mm.). After crystallization from ligroin, long asbestos-like needles melting at 78° were obtained.

*Anal.* Calc'd for  $C_{14}H_{15}BrO$ : C, 60.2; H, 5.4.

Found: C, 60.1; H, 5.7.

*6-tert-Butyl-2-acetonaphthone* (IV). Finely powdered aluminum chloride (120 g., 0.9 mole) was added in small portions to a well-stirred mixture of  $\beta$ -*tert*-butylnaphthalene (20) (150 g.; 0.8 mole), acetyl chloride (72 g.; 0.9 mole), and nitrobenzene (500 ml.). The temperature was kept at around 0° during the addition, and for a further 20 hours. The reaction product was poured onto ice, the nitrobenzene removed by steam-distillation, and the residue taken up in benzene. The benzene solution was washed with dilute sodium hydroxide and then with water, dried over sodium sulfate, the solvent removed, and the residue vacuum-distilled. The portion boiling at 180–210°/15 mm., which solidified on cooling, yielded after recrystallization from methanol 58 g. of colorless prisms melting at 87°.

*Anal.* Calc'd for  $C_{16}H_{18}O$ : C, 84.9; H, 7.9.

Found: C, 84.8; H, 8.0.

The corresponding *oxime* formed colorless needles melting at 168° from methanol.

*Anal.* Calc'd for  $C_{16}H_{19}NO$ : N, 5.8. Found: N, 5.8.

*6-tert-Butyl-2-acetaminonaphthalene* (V). A suspension of 10 g. (0.04 mole) of the foregoing *oxime* in anhydrous ether (100 ml.) was treated at 0° with 13 g. of finely powdered phosphorus pentachloride (0.06 mole). The mixture was kept at 0° for one hour with frequent shaking, and then poured onto cracked ice. The solid product formed after evaporation of the ether was thoroughly washed with sodium carbonate, then with water, dried, and recrystallized from methanol. A 90% yield was obtained of colorless prisms melting at 156°.

*Anal.* Calc'd for  $C_{16}H_{19}NO$ : N, 5.8. Found: N, 5.6.

*6-tert-Butyl-2-naphthylamine* (VI). Hydrolysis of the foregoing *amide* by concentrated hydrochloric acid, followed by basification with sodium hydroxide, yielded a solid *amine* which crystallized from ligroin in almost colorless needles melting at 65–66°, which reddened on exposure to the air.

*Anal.* Calc'd for  $C_{14}H_{17}N$ : N, 7.0. Found: N, 6.8.

This *amine* was further characterized by its *picrate* (which formed yellow prisms from ethanol melting at about 189–191°), and by the reaction product it gave when refluxed for one hour with 2,3-dichloro-1,4-naphthoquinone (21) in ethanol in the presence of sodium acetate. *2-Chloro-3-(6-tert-butyl-2-naphthylamino)-1,4-naphthoquinone* formed long silky dark violet needles melting at 153° from ethanol.

*Anal.* Calc'd for  $C_{24}H_{26}ClNO_2$ : N, 3.5. Found: N, 3.5.

*Conversion of the amine (VI) into (I).* To a well-stirred suspension of 9.5 g. of *6-tert-butyl-2-naphthylamine* in ice-cooled hydrochloric acid (150 ml. diluted with 100 ml. of water), a solution of sodium nitrite (3.5 g.) in water (35 ml.) was added dropwise. After the diazotization, nitrous acid in excess was destroyed by the addition of urea, and the solution was boiled for some minutes. After cooling, the precipitated naphthol (I) was purified through its sparingly soluble sodium salt. After repeated crystallizations from aqueous methanol, it melted at 117–119°, either alone or mixed with a sample obtained from  $\beta$ -naphthol; the *methyl ether* melted at 94–95°, and the *picrate* at 142–143° (mixed m.p. determinations).

*3'-tert-Butyl-1,2,5,6-dibenzacridine* (VII). One gram of paraformaldehyde was added in small portions to a boiling mixture of *6-tert-butyl-2-naphthol* (5 g.) and  $\alpha$ -naphthylamine (4.5 g.). When steam-evolution had ceased, the reaction product was brought to the boil for two minutes and then vacuum-distilled. The reddish resin thus obtained solidified on scratching in ethanol, and was recrystallized twice from benzene. A 40% yield of pale yellow needles melting at 208° was obtained, which gave with sulfuric acid a yellow solution with an intense yellow-green fluorescence. The products thus obtained with *6-tert-butyl-2-naphthol* from both sources were identical, and with the acridine obtained in a similar way from *6-tert-butyl-2-naphthylamine*,  $\alpha$ -naphthol, and paraformaldehyde, by reason of symmetry.

*Anal.* Calc'd for  $C_{26}H_{21}N$ : N, 4.1. Found: N, 4.2.

The corresponding *picrate* formed from nitrobenzene fine orange-yellow needles melting with decomposition at about 280°.

*Anal.* Calc'd for  $C_{31}H_{24}N_4O_7$ : N, 9.9. Found: N, 9.6.

*Ethers of 6-tert-butyl-1-chloro-2-naphthol.* These were prepared by refluxing naphthol (VIIIa) with a solution of sodium hydroxide in aqueous ethanol and the required alkyl (or arylalkyl) bromide for some hours. Purification of the resulting ethers was by vacuum-distillation and recrystallization from ethanol and ligroin.

#### SUMMARY

1. The constitution of the products resulting from the *tert*-butylation of  $\beta$ -naphthol has been investigated, and has been confirmed by synthesis.
2. Several new substitution-products of  $\beta$ -naphthol, some of practical biological interest, have been prepared.

PARIS V<sup>e</sup>, FRANCE  
RENORY-LIEGE, BELGIUM

#### REFERENCES

- (1) CAHEN, *Bull. soc. chim.*, [3] **19**, 1007 (1898).
- (2) KOENIGSBERGER, U. S. Patent 1,788,529.
- (3) LINNEN, U. S. Patent 1,892,990; NATIONAL ANILINE Co., U. S. Patent 2,090,938.

- (4) TSCHITSCHIBABIN, *Bull. soc. chim.*, [5] **2**, 515 (1935).
- (5) CONTRACTOR, PETERS, AND ROWE, *J. Chem. Soc.*, 1993 (1949).
- (6) See for instance PRICE, *Org. Reactions*, **3**, 58 (1946).
- (7) HAWORTH, LETSKY, AND MAVIN, *J. Chem. Soc.*, 1784 (1932); HAWORTH AND BOLAM *J. Chem. Soc.*, 2248 (1932); FIESER AND PETERS, *J. Am. Chem. Soc.*, **54**, 4347 (1932); RUZICKA AND KAUFMANN, *Helv. Chim. Acta*, **24**, 939 (1941).
- (8) BUU-HOÏ AND CAGNIANT, *Bull. soc. chim.*, [5] **8**, 887 (1941); BRIGGS, GILL, LIONS, AND TAYLOR, *J. Chem. Soc.*, 1098 (1949).
- (9) See reference (7), and BUU-HOÏ AND CAGNIANT, *Bull. soc. chim.*, [5] **12**, 307 (1945).
- (10) ULLMANN AND FETTVADJIAN, *Ber.*, **36**, 1029 (1903); BUU-HOÏ, *J. Chem. Soc.*, 792 (1946).
- (11) ALBERTI, *Ann.*, **450**, 309 (1926).
- (12) DZIEWÓŃSKI, SCHOENÓWNA, AND WALDMANN, *Ber.*, **58**, 1213 (1925).
- (13) LÉVY, *Compt. rend.*, **202**, 1679 (1936).
- (14) BUU-HOÏ, *Rec. trav. chim.*, **68**, 759 (1949).
- (15) See reference (14); all methyl ethers of known 6-substituted 2-naphthols are solid, too.
- (16) CLAUS AND ZIMMERMANN, *Ber.*, **14**, 1483 (1881).
- (17) ARMSTRONG AND DAVIS, *Chem. News*, **74**, 302 (1897).
- (18) SEXTON, *Chemical Constitution and Biological Activity*, Spon, London, 1949, p. 252.
- (19) CLEVE, *Ber.*, **21**, 895 (1888); ZINCKE, *Ber.*, **21**, 3384 (1888).
- (20) NIGHTINGALE, TAYLOR, AND SMELSER, *J. Am. Chem. Soc.*, **63**, 258 (1941).
- (21) See BUU-HOÏ, *Bull. soc. chim.*, [5] **11**, 578 (1944).