[Contribution from the Department of Organic Chemistry, Radium Institute,
University of Paris]

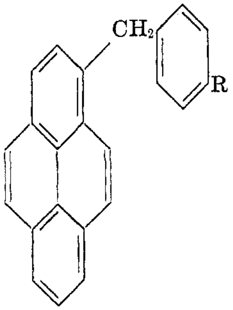
BENZYLATIONS AND ALLYLATIONS IN THE PRESENCE OF ZINC CHLORIDE

NG. PH. BUU-HOÏ, B. ECKERT, and P. DEMERSEMAN

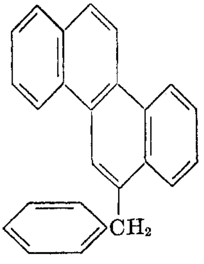
Received August 31, 1953

In the framework of a general study of Friedel-Crafts alkylations and arylalkylations (1), the behavior of benzyl chloride and similar halides has been examined. These compounds occupy a special place among alkyl and arylalkyl halides because of their outstanding reactivity, and it is known that various Friedel-Crafts benzylations can be effected in the presence of small amounts of such mild catalysts as zinc chloride (2). This behavior suggests that in such reactions involving weak catalysts, the free benzyl radical might play an important role, as in the case of the thermal decomposition of dibenzyl sulfide and disulfide (3), or in reactions of toluene and dibenzyl with sulfur (4). If this is so, then the benzyl group would preferentially enter the positions with greater free valency indices (5), other factors, particularly steric hindrance, being of less importance than in more typical Friedel-Crafts reactions with aluminum chloride. In fact, the benzylation of naphthalene (6) and β-naphthol (7) in the presence of zinc chloride is known to give 1-benzylnaphthalene and 1-benzyl-2-naphthol, in conformity with the results of the calculation of free valency indices, and at variance with other alkylations, which generally bring about substitution at the less hindered 6 position (8). More recently, Czerski found that benzylation of phenanthrene in the presence of zinc chloride yielded a mixture of 4- and 9-benzylphenanthrene (9), whereas Friedel-Crafts acetylation of the same hydrocarbon is known to give a mixture of 2- and 3-acetylphenanthrene (10). The first type of reaction is obviously more consistent with the molecular diagram of phenanthrene (11) than is the second one.

The condensation of benzyl chloride and similar halides has now been investigated from the same viewpoint. Pyrene was found to react vigorously with benzyl chloride in the presence of zinc chloride and in chloroform medium to

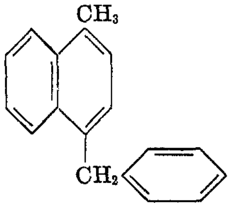


I R = H
II R = CH_3
III R = CH_2CH_3

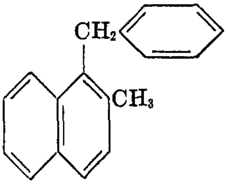


IV

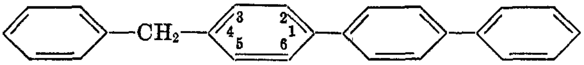
give a complex mixture of products from which 3-benzylpyrene (I) was readily isolated; the constitution of this hydrocarbon was established by identification with the Kishner-Wolff reduction product of 3-benzoylpyrene. Replacement of benzyl chloride by *p*-methyl- and *p*-ethyl-benzyl chloride similarly afforded 3-(*p*-methylbenzyl)pyrene (II) and 3-(*p*-ethylbenzyl)pyrene (III); these hydrocarbons were likewise identified with the reduction product of 3-(*p*-methylbenzoyl)pyrene and 3-(*p*-ethylbenzoyl)pyrene, respectively. These results are consistent with the theory (12) which assigns the highest free valency index to position 3. Benzylation of chrysene furnished 6-benzylchrysene, also in accordance with the theory (13). In the case of dicyclic hydrocarbons, 1-methylnaphthalene was found to give 4-benzyl-1-methylnaphthalene (V), a result which, along with the isolation of 1-benzyl-2-methylnaphthalene (VI) in a similar reaction on 2-methylnaphthalene (14), also gives full support to the theory (15). A less satisfactory agreement was recorded from the study of *p*-terphenyl, which gave mostly 4-benzyl-*p*-terphenyl (VII), identical with the Kishner-Wolff reduction product of 4-benzoyl-*p*-terphenyl, whereas the molecular diagram determined by the molecular orbital method assigns to position 4 only the third rank in respect to free valency indices, coming after positions 2 and 2′ (16). It should, however, be noted that with all the other substitution reactions with *p*-terphenyl hitherto studied, a similar discrepancy was observed (17).



V

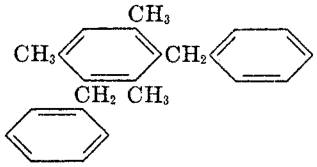


VI

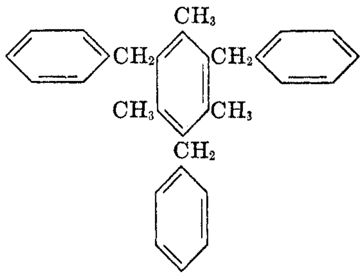


VII

A second feature of free radical reactions, which is shared by zinc chloride-catalyzed benzylations, is the high incidence of polysubstitution under relatively mild conditions. Thus, mesitylene was found to react smoothly with benzyl chloride in equimolecular amounts to give a mixture of monobenzyl-, dibenzyl- (VIII), and tribenzyl-mesitylene (IX). Dibenzylmesitylene has been the subject of conflicting statements in the literature; Louise (18) claimed to have prepared it from mesitylene, benzyl chloride, and aluminum chloride at 155°, and described it as a solid with m.p. 131° and b.p. 355°/12 mm. Mills and Easterfield (19), on the other hand, prepared dibenzylmesitylene by reduction of the corresponding diketone, and gave its m.p. as 89° and b.p. as 280°/20–30 mm. The present research confirms the latter description of dibenzylmesitylene, and shows that Louise's product was in fact tribenzylmesitylene.

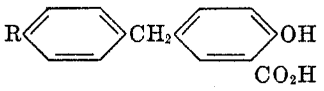


VIII

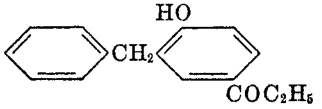


IX

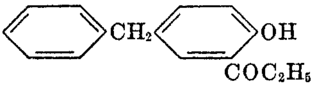
Another interesting feature of zinc chloride-catalyzed benzylations was that substitution could be effected with relatively unreactive molecules. Thus, methyl salicylate gave in good yield methyl 5-benzylsalicylate, whose constitution was determined by conversion to 5-benzylsalicylic acid (X), which was identical with the product of the Kolbe reaction on *p*-benzylphenol (20); replacement of benzyl chloride by 4-chlorobenzyl chloride similarly afforded 5-*p*-chlorobenzylsalicylic acid (XI). The benzylation product of *p*-hydroxypropiophenone proved to be 2-hydroxy-5-propionyldiphenylmethane (XII) since the possibility of any substitution on the methylene group adjacent to the ketone function was eliminated by a positive Pfitzinger reaction of its methyl ether with 5-bromoisatin. *o*-Hydroxypropiophenone gave under similar conditions 4-hydroxy-3-propionyldiphenylmethane (XIII), along with some *o*-benzyloxypropiophenone.



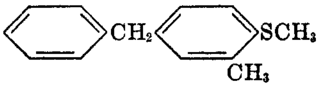
X R = H
XI R = Cl



XII

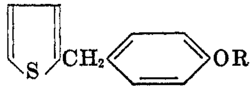


XIII



XIV

In regard to sulfur compounds, *o*-thiocresol methyl ether was smoothly benzylated to give 3-methyl-4-methylmercaptodiphenylmethane (XIV), identical with the Kishner-Wolff reduction product of 3-methyl-4-methylmercaptobenzophenone (21). On the other hand, an attempt to prepare 2-(4-hydroxybenzyl)thiophene (XV) from phenol, 2-thenyl chloride, and zinc chloride failed; this compound was readily obtained by pyridine hydrochloride dealkylation of its methyl ether (XVI).



XV R = H
XVI R = CH_3

XVII

From the theoretical viewpoint the allyl radical should be similar to the benzyl one, and it was therefore expected that zinc chloride-catalyzed allylations would follow a similar course as for benzylations. In fact, allyl chloride reacted vigorously with phenol in the presence of catalytic amounts of zinc chloride to give a mixture of *o*-allylphenol and chavicol (XVII).

EXPERIMENTAL

3-Benzylpyrene (I). (*a*). A mixture of 30 g. of pyrene, 15 g. of benzyl chloride, 5 g. of freshly fused, finely powdered zinc chloride, and 10 ml. of dry chloroform was refluxed until hydrogen chloride had ceased to evolve. The organic layer obtained on addition of water and more chloroform was washed with a dilute aqueous solution of acetic acid, and dried over sodium sulfate. The residue obtained after evaporation of solvent was vacuum-fractionated, and the oily portion, b.p. 280–323°/18 mm., was treated with a hot solution of picric acid in ethanol. An orange-red picrate separated on cooling, and was decomposed with aqueous ammonia to an oil, which slowly solidified to a crystalline mass. Recrystallization from cyclohexane, then from ethanol, yielded 3 g. of silky colorless needles, m.p. 91°.

Anal. Calc'd for $C_{23}H_{16}$: C, 94.8; H, 5.2.
Found: C, 94.7; H, 5.3.

The corresponding *picrate* crystallized from ethanol as orange-red prisms, m.p. 153–154°.

(*b*). A mixture of 2 g. of 3-benzoylpyrene (22), 2 g. of 100% hydrazine hydrate, 3 g. of potassium hydroxide, and 30 g. of diethylene glycol was heated with removal of water, then refluxed for 4 hours. After cooling, water was added, and the hydrocarbon formed was taken up in benzene, and purified by vacuum-distillation and crystallization from ethanol. *3-Benzylpyrene* thus obtained in 95% yield was identical with the foregoing hydrocarbon.

With tetrachlorophthalic anhydride, an *additional-compound* (23) was obtained, which crystallized from acetic acid as silky, golden-yellow needles, m.p. 188°.

3-(p-Methylbenzyl)pyrene (II). (*a*). A mixture of 30 g. of pyrene, 17 g. of *p*-methylbenzyl chloride, 5 g. of zinc chloride, and 10 ml. of chloroform was treated as in the case of benzyl chloride, giving 3 g. of pure *3-(p-methylbenzyl)pyrene*, which crystallized from ethanol as shiny colorless needles, m.p. 98°.

Anal. Calc'd for $C_{24}H_{18}$: C, 93.9; H, 6.1.
Found: C, 93.8; H, 6.0.

The corresponding *picrate* crystallized from ethanol as bright red needles, m.p. 175°.

(*b*). The same hydrocarbon was prepared in 95% yield from 1.5 g. of 3-(*p*-methylbenzoyl)-pyrene (24), 2 g. of hydrazine hydrate, 2 g. of potassium hydroxide, and 20 g. of diethylene glycol.

3-(p-Ethylbenzyl)pyrene (III) crystallized from ethanol as shiny colorless leaflets, m.p. 86°.

Anal. Calc'd for $C_{25}H_{20}$: C, 93.8; H, 6.2.
Found: C, 93.8; H, 6.3.

The *picrate* crystallized from ethanol as silky red needles, m.p. 142°; the *addition-compound* with tetrachlorophthalic anhydride crystallized from acetic acid as silky yellow needles, m.p. 186°.

The same hydrocarbon was obtained by the usual reduction of *3-(p-ethylbenzoyl)pyrene*, which was prepared in 90% yield from 22 g. of pyrene, 16 g. of *p*-ethylbenzoyl chloride, and 12 g. of aluminum chloride in tetrachlorethane at room temperature; this ketone crystallized from carbon tetrachloride as pale yellow needles, m.p. 115°.

Anal. Calc'd for $C_{25}H_{18}O$: C, 89.8; H, 5.4.
Found: C, 89.5; H, 5.5.

6-Benzylchrysene (IV). A mixture of 23 g. of chrysene, 20 g. of benzyl chloride, 5 g. of zinc chloride, and 10 ml. of chloroform was heated until evolution of hydrogen chloride had ceased, and the reaction product then was vacuum-fractionated. The portion b.p.

290–350°/16 mm. (5 g.) gave on repeated crystallization from cyclohexane colorless prisms, m.p. 198°, alone or mixed with a sample of the Kishner-Wolff reduction product of 6-benzoylchrysene (25).

Benzylation of 1-methylnaphthalene. A mixture of 71 g. of 1-methylnaphthalene, 64 g. of benzyl chloride, and 30 g. of zinc chloride was heated for 2 hours at 80–90° (the reaction started below 60°); after the usual treatment, 20 g. of *4-benzyl-1-methylnaphthalene* was obtained, as a colorless oil, b.p. 170–172°/0.4 mm., n_D^{23} 1.6445, giving a homogenous picrate; the same product was obtained by reduction of 4-benzoyl-1-methylnaphthalene.

Anal. Calc'd for $C_{18}H_{16}$: C, 93.1; H, 6.9.
Found: C, 93.0; H, 7.2.

The corresponding *picrate* crystallized from methanol as yellow prisms, m.p. 107°. The higher-boiling portions gave on repeated fractionation 20 g. of *dibenzyl-1-methylnaphthalene*, a viscous, pale yellow oil, b.p. 248–250°/0.4 mm., $n_D^{23.5}$ 1.6560.

Anal. Calc'd for $C_{25}H_{22}$: C, 93.2; H, 6.8.
Found: C, 93.0; H, 6.8.

Benzylation of 2-methylnaphthalene was performed as described above; it gave 35 g. of *1-benzyl-2-methylnaphthalene* (VI), b.p. 223–224°/15 mm., n_D^{26} 1.6436, and 20 g. of *dibenzyl-2-methylnaphthalene*, a viscous, pale yellow oil, b.p. 245–248°/0.4 mm.

Anal. Calc'd for $C_{25}H_{22}$: C, 93.2; H, 6.8.
Found: C, 93.1; H, 7.0.

3-Methyl-4-methylmercaptodiphenylmethane (XIV). (*a*). A mixture of 15 g. of 3-methyl-4-methylmercaptobenzophenone (21), 15 g. of hydrazine hydrate, 15 g. of potassium hydroxide, and 200 ml. of diethylene glycol was treated in the usual way. Yield, 10 g. of a pale yellow oil, b.p. 205–206°/15 mm., $n_D^{23.5}$ 1.6125.

Anal. Calc'd for $C_{15}H_{16}S$: C, 78.9; H, 7.0.
Found: C, 78.6; H, 6.9.

(*b*). The same product was obtained in 60% yield from 28 g. of *o*-thiocresol methyl ether, 12 g. of benzyl chloride, and 4 g. of zinc chloride.

4-Benzyl-p-terphenyl (VII). *4-Benzoyl-p-terphenyl* was prepared by a Friedel-Crafts reaction on 50 g. of *p*-terphenyl, 34 g. of benzoyl chloride, and 43 g. of aluminum chloride in carbon disulfide at room temperature. Yield, 28 g. of a ketone b.p. 295–297°/0.8 mm., crystallizing from acetic acid as colorless leaflets, m.p. 215°; its constitution was proved by a Schmidt degradation (26) to 4-amino-*p*-terphenyl, m.p. 198°.

Anal. Calc'd for $C_{25}H_{18}O$: C, 89.8; H, 5.4.
Found: C, 89.6; H, 5.6.

Reduction of 10 g. of this compound with 10 g. of hydrazine hydrate and 10 g. of potassium hydroxide in diethylene glycol gave in theoretical yield *4-benzyl-p-terphenyl*, b.p. 271–273°/0.5 mm., crystallizing from acetic acid as sublimable, colorless leaflets, m.p. 177°.

Anal. Calc'd for $C_{25}H_{20}$: C, 93.8; H, 6.3.
Found: C, 93.5; H, 6.3.

The same hydrocarbon was obtained on heating at 100–120° a mixture of 50 g. of *p*-terphenyl, 25 g. of benzyl chloride, and 30 g. of zinc chloride.

Benzylation of mesitylene. A mixture of 30 g. of mesitylene, 30 g. of benzyl chloride, and 10 g. of zinc chloride was heated at 100° in the usual way; yield, 15 g. of *benzylmesitylene*, b.p. 174°/16 mm., 7 g. of *dibenzylmesitylene*, b.p. 272–275°/16 mm., and 3 g. of *tribenzylmesitylene*, b.p. 348–350°/15 mm., crystallizing from ethanol as shiny colorless prisms, m.p. 132°.

Anal. Calc'd for $C_{30}H_{30}$: C, 92.3; H, 7.7.
Found: C, 92.2; H, 7.9.

The molecular weight determined by cryoscopy (Found: 386; Calc'd: 390) was also in favor of this formula.

Benzylation of methyl salicylate. A solution of 165 g. of methyl salicylate and 126 g. of benzyl chloride in 500 ml. of chloroform was treated in the usual way with 60 g. of zinc chloride. Yield, 80 g. of *methyl 5-benzylsalicylate*, b.p. 202–204°/12 mm., m.p. 78–79°; saponification gave *5-benzylsalicylic acid*, crystallizing from aqueous acetic acid as colorless needles, m.p. 134–135°; lit. (20) gives m.p. 135–136° for the acid, and 79–80° for its methyl ether.

5-p-Chlorobenzylsalicylic acid (XI). Reaction of 150 g. of *p*-chlorobenzyl chloride on 170 g. of methyl salicylate in the presence of 60 g. of zinc chloride in chloroform, yielded 105 g. of *methyl 5-p-chlorobenzylsalicylate*, b.p. 235–240°/14 mm., n_D^{23} 1.5950. Saponification afforded *5-p-chlorobenzylsalicylic acid*, crystallizing from aqueous acetic acid as silky colorless needles, m.p. 150°, sparingly soluble in water.

Anal. Calc'd for $C_{14}H_{11}ClO_3$: C, 64.0; H, 4.2.
Found: C, 63.7; H, 4.4.

2-Hydroxy-5-propionyldiphenylmethane (XII). A mixture of 170 g. of *p*-hydroxypropiophenone, 126 g. of benzyl chloride, and 70 g. of zinc chloride in 800 ml. of chloroform, was refluxed for 12 hours and treated in the usual way, except that the unreacted ketone which crystallized from the chloroform layer was filtered off before distillation. Yield, 50 g. of *2-hydroxy-5-propionyldiphenylmethane*, b.p. 216–220°/1 mm., crystallizing from methanol as colorless prisms, m.p. 157°.

Anal. Calc'd for $C_{16}H_{16}O_2$: C, 80.0; H, 6.7.
Found: C, 80.1; H, 6.9.

The *methyl ether*, prepared with dimethyl sulfate and potassium hydroxide, crystallized from ethanol as large colorless plates, m.p. 120°, b.p. 187–188°/0.5 mm.

Anal. Calc'd for $C_{17}H_{18}O_2$: C, 80.3; H, 7.1.
Found: C, 80.0; H, 7.3.

It gave on 24 hours' refluxing with 5-bromoisation (1 mole) and potassium hydroxide (3 moles) in ethanol an almost quantitative yield of *6-bromo-3-methyl-2-(4'-methoxyphenyl)-cinchoninic acid*, crystallizing from ethanol as long colorless needles, m.p. 253° (dec.).

Anal. Calc'd for $C_{25}H_{20}BrNO_3$: C, 64.9; H, 4.3.
Found: C, 65.0; H, 4.3.

3-Benzyl-4-ethoxypropiophenone, similarly prepared from ketone XII, crystallized from ethanol as colorless plates, m.p. 87°, and also gave a positive Pfitzinger reaction with 5-bromoisatin.

Anal. Calc'd for $C_{18}H_{20}O_2$: C, 80.6; H, 7.5.
Found: C, 80.6; H, 7.6.

Benzylation of o-hydroxypropiophenone. From 120 g. of this ketone, 75 g. of benzyl chloride, and 40 g. of zinc chloride in chloroform, 58 g. of *4-hydroxy-3-propionyldiphenylmethane* (XIII) (purified through its water-soluble sodium derivative) was obtained as a pale yellow oil, b.p. 148–150°/0.6 mm.,$_D^{24.5}$ 1.5601.

Anal. Calc'd for $C_{16}H_{16}O_2$: C, 80.0; H, 6.7.
Found: C, 80.2; H, 6.6.

2-p-Methoxybenzylthiophene (XV). 2-Anisoylthiophene (10 g.) was reduced by means of 95% hydrazine hydrate, potassium hydroxide, and diethylene glycol in the usual way (27), to yield 5 g. of a mobile, colorless oil, b.p. 188–190°/14 mm., n_D^{23} 1.6056.

Anal. Calc'd for $C_{12}H_{12}OS$: C, 70.6; H, 5.9.
Found: C, 70.6; H, 6.1.

2-(4-Hydroxybenzyl)thiophene (XVI). A mixture of 4.8 g. of the foregoing ether and 20 g. of redistilled pyridine hydrochloride, was refluxed for 10 minutes; after cooling, water was added, and the reaction product taken up in ether and purified by vacuum-distillation. Yield, 4 g. of a substance b.p. 195–200°, crystallizing from petroleum ether as shiny colorless prisms, m.p. 58°.

Anal. Calc'd for $C_{11}H_{10}OS$: C, 69.5; H, 5.3.
Found: C, 69.4; H, 5.5.

This substance is an isoster of the anthelmintic 4-benzylphenol (28).

Allylation of phenol. A mixture of 50 g. of phenol, 60 g. of allyl bromide, and 10 g. of zinc chloride was cautiously heated on the water-bath until a vigorous reaction set up;

the reaction was left to continue at room temperature for one hour, and the reaction mixture then was poured into water. The chloroform layer was repeatedly washed with a dilute aqueous solution of hydrogen sodium carbonate, and dried over sodium sulfate; after evaporation of solvent, the residue was vacuum-fractionated. Yield, 10 g. of *o-allylphenol*, b.p. 220°, and 6 g. of *chavicol*, b.p. 236–238°. Better yields of these condensation products were obtained with allyl chloride.

SUMMARY

1. Zinc chloride-catalyzed alkylations with halides of the benzyl chloride type have been investigated with a number of aromatic hydrocarbons, and phenolic ketones and acids.

2. The theoretical aspect of this reaction is discussed, and experimental findings are compared with predictions from the calculation of free valency indices.

Paris V^e, France

REFERENCES

(1) Buu-Hoï, Le Bihan, and Leroux, *J. Org. Chem.*, **18**, 4 (1953); Buu-Hoï, Le Bihan, Binon, and Maleyran, *J. Org. Chem.*, **17**, 1122 (1952); Buu-Hoï, Le Bihan, and Binon, *J. Org. Chem.*, **17**, 243 (1952); Buu-Hoï, Le Bihan, Binon, and Xuong, *J. Org. Chem.*, **16**, 988 (1951).
(2) See literature in Price, *Org. Reactions*, **3**, 2 (1946).
(3) Cutforth and Selwood, *J. Am. Chem. Soc.*, **70**, 278 (1948).
(4) Horton, *J. Org. Chem.*, **14**, 761 (1949).
(5) Daudel, Daudel, Buu-Hoï, and Martin, *Bull. soc. chim.*, **15**, 1202 (1948).
(6) Roux, *Ann. chim.*, [6]**12**, 289 (1887).
(7) Dziewoński and Dziecielewski, *Bull. intern. acad. polon. sci.*, [A], 275 (1927).
(8) See in particular Haworth, Letsky, and Mavin, *J. Chem. Soc.*, 1784 (1932); Fieser and Price, *J. Am. Chem. Soc.*, **58**, 1841 (1936); Price and Ciskowski, *J. Am. Chem. Soc.*, **60**, 2499 (1938); Buu-Hoï, Le Bihan, Binon, and Rayet, *J. Org. Chem.*, **15**, 1060 (1950); Buu-Hoï, Le Bihan, and Binon, *J. Org. Chem.*, **16**, 185 (1951).
(9) Czerski, *Roczniki Chem.*, **24**, 218 (1950).
(10) Mosettig and Van de Kamp, *J. Am. Chem. Soc.*, **52**, 3704 (1930).
(11) Nebbia, *Ann. chim. (Rome)*, **40**, 627 (1950).
(12) Buu-Hoï, Daudel, and Vroelant, *Bull. soc. chim.*, **16**, 211 (1949).
(13) Berthier, Pullman, and Pullman, *Bul. soc. chim.*, **15**, 1907 (1948).
(14) Dziewoński and Ritt, *Chem. Zentr.*, I, 57 (1928).
(15) Buu-Hoï and Daudel, *Rec. trav. chim.*, **65**, 731 (1946).
(16) Buu-Hoï, Coulson, Daudel, Daudel, Martin, Pullman, and Pullman, *Rev. sci.*, **85**, 1041 (1947).
(17) Olgiati, *Ber.*, **27**, 3393 (1894); France, Heibron, and Hey, *J. Chem. Soc.*, 1368 (1938); Buu-Hoï and Cagniant, *Compt. rend.*, **216**, 381 (1943).
(18) Louise, *Ann. chim.*, [6] **6**, 197 (1885).
(19) Mills and Easterfield, *J. Chem. Soc.*, **81**, 1323 (1904).
(20) Paternò and Fileti, *Gazz. chim. ital.*, **3**, 128 (1873).
(21) Buu-Hoï and Hoán, *J. Org. Chem.*, **17**, 350 (1952).
(22) Scholl and Seer, *Ann.*, **394**, 111 (1912).
(23) Buu-Hoï and Jacquignon, *Compt. rend.*, **234**, 1056 (1952).
(24) School, Meyer, and Donat, *Ber.*, **70**, 2180 (1937).
(25) Funke and Müller, *J. prakt. Chem.*, [2] **144**, 242 (1936).
(26) See Dice and Smith, *J. Org. Chem.*, **14**, 179 (1949).
(27) See Buu-Hoï, Hoán, and Xuong, *Rec. trav. chim.*, **71**, 285 (1952).
(28) Schulemann, *Deutsch. med. Wochschr.*, **46**, 1051 (1920).