

However, a uniform procedure was used throughout the measurements reported, and repeated measurements were made with the unsubstituted compounds during the study to ensure internal consistency. The pK_a differences within each series are probably correct to within 0.01–0.02 unit.

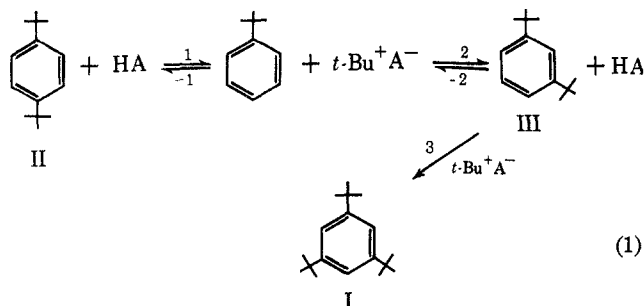
A Direct Synthesis of 1,3,5-Tri-*t*-butylbenzene

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Consideration of the mechanism of isomerization of *t*-butylbenzenes has led to the development of a direct, high-yield synthesis of 1,3,5-tri-*t*-butylbenzene (I). The normal method of synthesis of I involves *t*-butylation of 1,4-di-*t*-butylbenzene (II) in the presence of aluminum chloride.¹ Barclay has shown that alteration of the solvent composition and reaction temperature greatly enhances the preparative value of this reaction.² However, the use of II in the synthesis of I appears puzzling. Available data strongly indicate that *t*-butylbenzenes isomerize by dealkylation-alkylation processes.³ If this is correct, *t*-butylbenzene must be an intermediate in the synthesis of I (eq 1) and would appear to be an equally suitable and a much more convenient starting material.



It is possible that the conversion of II to I occurs *via* an intramolecular shift of a *t*-butyl group slightly prior to, or synchronous with, the attack of a third *t*-butyl cation. Such a situation might explain the need for II as a direct precursor to I.⁴ The investigation described here was designed to test the intramolecular character of the rearrangement of II and explore the utility of *t*-butylbenzene as a reactant in the synthesis of I.

Our studies confirm that the low-temperature alkylation of II with excess *t*-butyl chloride is an exceedingly rapid and efficient method of synthesis of I.² With careful temperature control, I can be isolated in 70–85% yield. Cyclialkylated products which have been isolated by the use of Bartlett's procedure are very

(1) P. D. Bartlett, M. Roha, and R. M. Stiles, *J. Am. Chem. Soc.*, **76**, 2349 (1954).

(2) L. R. C. Barclay and E. E. Betts, *Can. J. Chem.*, **33**, 672 (1955).

(3) (a) R. H. Allen, *J. Am. Chem. Soc.*, **82**, 4856 (1960); (b) M. J. Schlatter, *ibid.*, **76**, 4952 (1954); (c) M. J. Schlatter and R. D. Clark, *ibid.*, **75**, 361 (1953).

(4) The existence of intramolecular isomerizations of *t*-butyl groups remains the subject of speculation; see G. A. Olah, C. G. Carlson, and J. C. Lapiere, *J. Org. Chem.*, **29**, 2687 (1964); G. A. Olah, S. H. Flood, and M. E. Moffat, *J. Am. Chem. Soc.*, **86**, 1060 (1964).

minor components of the product mixture.⁵ Withdrawal and chromatographic analysis of aliquots of the reaction mixture reveal no detectable 1,3-di-*t*-butylbenzene at any stage of the reaction; II and I are the only major aromatic constituents.⁶

A study of the rearrangement and alkylation of 1,4-di-*t*-butylbenzene- β -*t* showed that the resulting 1,3,5-tri-*t*-butylbenzene contained less than 20% of the initial tritium activity. The constancy of the tritium activity of I as a function of reaction time (Table I) precludes significant loss of activity *via* dealkylation-alkylation of the product.

TABLE I
TRITIUM ACTIVITY OF 1,3,5-TRI-*t*-BUTYLBENZENE

Reaction time, min	1,3,5-Tri- <i>t</i> -butylbenzene, ^a %	Activity $\times 10^{-6}$ cpm mmole ^{-1b}
1	86	0.178
2	91	0.183
5	96	0.183
12	99	0.183
20	99	0.179

^a Denotes per cent of product in unpurified sample. Dimers of isobutylene were not included in product distribution computation (ref 5a). ^b Activity of the reactant was 0.915×10^6 cpm mmole⁻¹.

Alkylation of *t*-butylbenzene using conditions analogous to those employed in the alkylation of II proved to be somewhat hazardous. That is, addition of aluminum chloride to a cold (-7°) mixture of *t*-butylbenzene and *t*-butyl chloride normally resulted in an initial exothermic reaction evolving considerable quantities of isobutylene and hydrogen chloride.⁷ However, strong cooling of the reaction mixture to about -40° permitted smooth addition of aluminum chloride without loss of control. Following addition, slow warming of the reaction mixture to -10° and continued reaction at that temperature afforded I, isolable without distillation in 75–85% yield. The alkylation of *t*-butylbenzene- β -*t* was found to yield I with loss of about 75% of tritium activity.

These results are in harmony with the reaction scheme shown in eq 1. The loss of all but 20% of tritium activity upon rearrangement and alkylation of 1,4-di-*t*-butylbenzene- β -*t* clearly implies that predominant, if not complete, intermolecular transfer of *t*-butyl groups occurs during isomerization. The absence of significant quantities of 1,3-di-*t*-butylbenzene at any stage of the reaction may be indicative that the rate of step 2 is much slower than step 3 (eq 1).⁸ If this condition prevails, then suitably designed experiments measuring the loss of tritium activity upon rearrangement and alkylation of II can yield data concerning the relative rate of aluminum chloride catalyzed *t*-butylation of *t*-butylbenzene. Further investigation of this aspect is in progress. Of present importance, these results demonstrate that the once elusive hydrocarbon, 1,3,5-tri-*t*-butylbenzene, can be

(5) (a) P. C. Myhre and W. M. Schubert, *J. Org. Chem.*, **25**, 708 (1960); (b) L. R. C. Barclay and E. E. Betts, *J. Am. Chem. Soc.*, **77**, 5735 (1955).

(6) Prolonged reaction times, exceeding the time required to convert II to I, do lead to detectable amounts of various cyclialkylated products.⁶

(7) This gas evolution quickly subsides and that material remaining in the flask is converted to I in good yield.

(8) The results of S. Watari [*Bull. Chem. Soc. Japan*, **36**, 747 (1963)] are in accord with this conclusion.

rather easily prepared and isolated from readily accessible starting materials.

Experimental Section

Melting points were taken on a calibrated Fisher-Johns apparatus. Gas-liquid partition chromatographic analyses were performed using an Aerograph A-90P3 or A-700 equipped with an SE 30 column. Retention time data for one particular set of parameters are given in Table II. Tritium activity was measured using a Packard Tri-Carb spectrometer, Model 3324.⁹

TABLE II

CHARACTERISTIC RETENTION TIMES OF *t*-BUTYLBENZENES^a

Compound	Retention time, min
<i>t</i> -Butylbenzene	1.1
1,3-Di- <i>t</i> -butylbenzene	2.7
1,4-Di- <i>t</i> -butylbenzene	3.2
1,3,5-Tri- <i>t</i> -butylbenzene	5.2

^a A90-P3, SE 30, 6 ft × 0.25 in., 160°, 90 ml/min.

***t*-Butylbenzene- β -*t*.**—A solution of neophyl chloride¹⁰ (21.7 g, 0.128 mole) and 50 ml of anhydrous ether was added in portions to a flask containing 3.05 g (0.126 g-atom) of magnesium turnings. After a 1-hr period of reflux and addition of an iodine crystal the reaction became self-sustaining and proceeded with almost complete consumption of magnesium. The resulting chilled solution of neophylmagnesium chloride was added dropwise to an ice-cold, magnetically stirred flask containing a mixture of 40 ml of anhydrous ether, 7 g of hydrogen chloride, and 1.0 g of tritium-labeled water (250 mcuries/ml) and allowed to stand with stirring for 24 hr. Hydrolysis was completed by addition of ordinary water. After phase separation, washing, and drying, the ethereal layer was concentrated by careful distillation to yield 17.9 g of yellow oil. Fractional distillation afforded 9.05 g, bp 65–67° (21 mm). Two 5-ml portions of unlabeled *t*-butylbenzene were added to the still pot and distilled in order to strip the remaining labeled material from the column. These fractions were combined yielding 18.6 g of *t*-butylbenzene- β -*t* with a specific activity of 1.00×10^6 cpm mmole⁻¹.

1,4-Di-*t*-butylbenzene- β -*t*.—A 100-ml flask equipped for magnetic stirring was charged with 25 ml (0.23 mole) of *t*-butyl chloride and 0.25 g of anhydrous ferric chloride. After the contents cooled to 0°, *t*-butylbenzene- β -*t* (10 ml, 0.064 mole) was added dropwise, and the resulting mixture was stirred for 1 hr at 0° and for 24 hr at room temperature. The dark red reaction mixture was hydrolyzed and extracted with 30 ml of cyclohexane. After washing of the cyclohexane layer with water and 2% sodium carbonate and drying over sodium sulfate, the solvent was removed by rotary evaporation yielding 12.5 g of crude crystalline product. Glpc indicated 96% purity, the remaining material being 1,3-di-*t*-butylbenzene (4%) and 1,3,5-tri-*t*-butylbenzene (2%). Two recrystallizations from absolute ethanol gave 8.4 g of product, mp 77–78° (lit.¹¹ mp 78°), specific activity 0.915×10^6 cpm mmole⁻¹.

1,3,5-Tri-*t*-butylbenzene- β -*t* from 1,4-Di-*t*-butylbenzene- β -*t*.—A 250-ml, round-bottom flask equipped with a Teflon paddle stirrer was charged with 1,4-di-*t*-butylbenzene- β -*t* (6.2 g, 32.6 mmoles) and *t*-butyl chloride (50 ml, 0.46 mole). The resulting solution was cooled to –10° with resultant precipitation of much hydrocarbon. Aluminum chloride (2.2 g, 16.5 mmoles) was added, and, with the temperature maintained between –10 and –5°, aliquots (ca. 10 ml) were rapidly withdrawn at specified times and quenched in ice and water. After hydrolysis of these, the organic layer was separated (pentane solvent), washed several times with water, and dried over sodium sulfate. Rotary evaporation of the solvent left partially crystalline residues which were subjected to glpc analysis. Following analysis, 1,3,5-tri-*t*-butylbenzene was isolated by repeated (four or more times) crystallization from methanol. After thorough drying, the tritium activity

of weighed portions of each of the aliquots was determined. These data are summarized in Table I.

1,3,5-Tri-*t*-butylbenzene from *t*-Butylbenzene.—A 1-l., three-necked flask equipped with an efficient paddle stirrer, a low-temperature thermometer, and a solids-addition device was charged with *t*-butylbenzene (77.5 ml, 0.50 mole) and *t*-butyl chloride (500 ml, 4.6 moles). The solution was cooled to –40° with a Dry Ice-acetone bath, and anhydrous aluminum chloride (33 g, 0.25 mole) was added to the stirred solution in portions over a 10-min interval. Upon completion of addition the temperature was allowed to rise to between –15 and –10° and maintained with an ice-salt bath for a period of 2 hr. The bright yellow reaction mixture was then carefully poured into a 4-l. separatory funnel containing about 2 kg of crushed ice and water and the resulting mixture was agitated vigorously for about 10 min to complete hydrolysis. Following the separation of layers, the organic phase was washed well with water (three 300-ml portions) and dried over sodium sulfate. Distillation gave about 250 ml of unchanged *t*-butyl chloride, bp 50–52°. The remaining volatile material was removed by rotary evaporation, finally at 1 mm, to yield 120 g of partially crystalline product. The melted crystalline mass was transferred to a beaker thoroughly chilled in an ice-salt bath, suction filtered, and washed with two 75-ml portions of cold methanol (previously used to rinse vessels). A product (90 g, mp 65–70°) showing greater than 95% purity by glpc was obtained. Recrystallization from 150 ml of methanol gave 80 g, mp 72–74° (lit.¹ mp, 72.5–73°). Concentration and further recrystallization of the mother liquor gave an additional 10 g of product, mp 71–73°.

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Reaction of Alkali Metal Diphenylmethides with Halo Acid Derivatives. Alkylation vs. Elimination

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Previously it was shown² that lithium enolates in ether react with lithium salts of halo acids to give carboxyalkylated ketones. In contrast, the potassium derivative of either anion failed to give alkylated products, and the sodium derivatives gave poor yields. It has now been found that sodium and potassium diphenylmethide in liquid ammonia react with salts of halo acids to give good yields of the alkylated acids. Thus, potassium diphenylmethide reacts with 3-bromopropionic acid to give 4,4-diphenylbutyric acid in 85% yield. One molecular equivalent of the base is consumed in neutralization of the carboxylic acid function. Sodium chloroacetate can similarly be used, without the consumption of the diphenylmethide in the neutralization step, to give 3,3-diphenylpropionic acid in 80% yield; however, attempts to prepare the sodium salt of 3-bromopropionic acid gave only polymeric material.

In contrast to the 3-bromopropionate anion, ethyl 3-bromopropionate underwent exclusively dehydrohalogenation to ethyl acrylate when treated with potas-

(9) We are grateful to Dr. Joseph Gally, Pomona College, for generous allotments of instrument time.

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(2) W. H. Puterbaugh and R. L. Readshaw, *J. Am. Chem. Soc.*, **82**, 3635 (1960).