in some of the literature cited.

The side reactions in some of the other unsuccessful cases led to very complicated mixtures as indicated by the HPLC traces. In addition, several of the substrates can undergo attack at multiple sites, which can lead to dimers other than the ones searched for. Finally, the facile loss of carbon monoxide from radicals derived from formates is consistent with the absence of ethyl oxalate among the products from ethyl formate.[32]

Several attempts to carry out the coupling of diphenylmethane with di-*tert*-butyl hyponitrite at 25 °C with ultrasound were unsuccessful.

Our initial reactions in this project were accompanied by a few irregularities. A stoichiometric mixture of *tert*-butylformamide and di-*tert*-butyl hyponitrite, which did not dissolve completely, underwent a sudden exotherm after being placed in a bath at 60 °C, and most of the contents of the tube were ejected as a small, mushroom-shaped cloud. The reaction was more successful when hyponitrite was added in small portions to the prehteated amide following the decomposition by the evolution of nitrogen. On another occasion, a loud pop was emitted from a tube containing a 2:1 formamide and undissolved di-*tert*-butylformamide under nitrogen in a bath at 70 °C. Thereafter we used diluents (frequently the substrate) or slow addition to insure that the hot solutions were always homogeneous. We took the additional precaution of flushing the mixture with an inert gas since di-*tert*-butyl hyponitrite is rather volatile.[28]

Experimental Section

Di-*tert*-butyl hyponitrite[27] was recrystallized from a mixture of ethanol and methanol at −60 °C. The substrates were usually reagent grade and were purified by conventional techniques of the oxidative propensity (aldehydes, ethers) or age suggested the presence of impurities. Reactions with small volumes of high-boiling substrates were carried out in screw-threaded test tubes (Ace glass) with a serum cap pierced by a syringe needle for relief of pressure. The tube was flushed with argon or nitrogen before being placed in an oil bath maintained at constant temperature with a Thermo-watch. The reaction mixtures were stirred magnetically. A slow stream of inert gas was passed into the liquid phase when a portionwise addition of hyponitrite was required.

Reactions with excess, volatile substrates were refluxed in the conventional manner after flushing initially with inert gas. The dimers were generally isolated by removing volatiles at 20 torr followed by purification of the residue as described in Table I. Product identification was made with IR and NMR techniques. Chromatographic isolation was carried out with a Sigma 3B and a $^1/_4$ in. × 25 ft column with Carbowax 20M (column A), a HP5830A and a 2 mm × 6 ft column of 3% SP-2250 DADA on 100–120-mesh Supelcoport (column B), or with a hybrid LC system and a Sphirogel 8 mm × 30 cm size exclusion column.

Note Added in Proof: *tert*-Butyl hyponitrite (8.74 mmol) and *tert*-butylformamide (35.5 mmol) in CCl_4 (10 mL) at 50 °C for 16 h precipitated crystalline *tert*-butylamine hydrochloride (12.8 mmol, mp 296 °C dec, ionic Cl 32.12%; lit.[33] mp 270–290 °C subl).

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

Registry No. DMF, 68-12-2; $B_2N_2O_2$, 14976-54-6; B_2O_2, 110-05-4; Fe^{2+}, 15438-31-0; H_2O_2, 7722-84-1; $[PhC(O)O]_2$, 94-36-0; $Am_2N_2O_2$, 24251-13-6; Ac_2O_2, 110-22-5; NH_2CHO, 75-12-7; CH_3NHCHO, 123-39-7; CH_3CO_2H, 64-19-7; $(CH_3)_3CC(O)OCH_3$, 598-98-1; $CH_3C(O)CH_3$, 67-64-1; CH_3CH_2OCHO, 109-94-4; $(CH_3)_3CNHCHO$, 2425-74-3; $(CH_3)_2CHCN$, 78-82-0; Ph_2CH_2, 101-81-5; $CD_3C(O)CD_3$, 666-52-4; $(CH_3)_3COCH_3$, 1634-04-4; $(CH_3)_3COH$, 75-65-0; $PhCH_3$, 108-88-3; $PhCH(CH_3)_2$, 98-82-8; CH_3OPh, 100-66-3; PhCHO, 100-52-7; $PhCH_2C(O)CH_3$, 103-79-7; $PhCH_2CN$, 140-29-4; $[CH_3CH_2OC(O)]_2$, 95-92-1; $[(CH_3)_2NC(O)]_2$, 1608-14-6; $[(CH_3)_3CNHC(O)]_2$, 37486-48-9; $[H_2NC(O)]_2$, 471-46-5; $[CH_3NHC(O)]_2$, 615-35-0; $(HO_2CCH_2)_2$, 110-15-6; $[(CH_3)_3CC(O)OCH_2]_2$, 20267-20-3; $[CH_3C(O)CH_2]2$, 110-13-4; $[CD_3C(O)CD_2]_2$, 97135-07-4; $[(CH_3)_3COCH_2]_2$, 26547-47-7; $[HOC(CH_3)_2CH_2]_2$, 110-03-2; $[(CH_3)_2C(CN)]_2$, 3333-52-6; $(Ph_2CH)_2$, 632-50-8; $(PhCH_2)_2$, 612-00-0; $[Ph(CH_3)_2C]_2$, 1889-67-4; $(PhOCH_2)_2$, 104-66-5; *meso*-$[PhC(O)OCH(Ph)]_2$, 38036-63-4; (±)-$[PhC(O)OCH(Ph)]_2$, 86703-60-8; *meso*-$[CH_3(O)CH(Ph)]_2$, 69373-33-7; (±)-$[CH_3C(O)CH(Ph)]_2$, 69373-32-6; *meso*-$[PhCH(CN)]_2$, 15146-07-3; (±)-$[PhCH(CN)]_2$, 19657-49-9.

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Strained Benzene Derivatives by Copper-Catalyzed *tert*-Butylation

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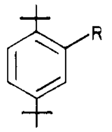
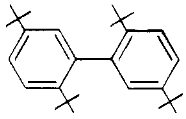
During our research on long-range deuterium isotope effects in ^{13}C NMR spectra[1] we became interested in an isotopomer of 1,2,4-tri-*tert*-butylbenzene (**1a**) bearing a perdeuterated *tert*-butyl group specifically at carbon atom 2, **1b**. The parent compound **1a** has been prepared by cobalt-mediated trimerization of *tert*-butylacetylene and photochemically induced isomerization of 1,3,5-tri-*tert*-butylbenzene.[2,3] Along these routes, however, the preparation of **1b**, free of regioisotopomers, is not possible. Any novel approach to the strained hydrocarbon **1a** thus has to accommodate this regiochemical problem, and for economic reasons, the introduction of the perdeuterated *tert*-butyl group in the last step is most attractive.



1a, R = $C(CH_3)_3$
1b, R = $C(CD_3)_3$
1c, R = Br
1d, R = H
1e, R = OH



2

We report here on a method of introducing a *tert*-butyl group adjacent to a preexisting one in a single step, starting from ortho brominated precursors.

2,5-Di-*tert*-butylbromobenzene (**1c**) obtained[4] from commercially available 1,4-di-*tert*-butylbenzene (**1d**) gave halogen/lithium exchange in tetrahydrofuran on addition of 2.5 equiv of *tert*-butyllithium in pentane at −78 °C. To this mixture of anions, cuprous iodide was added to create a solution containing mixed homocuprates. Subsequently the copper reagents were oxidized with molecular oxygen at −78 °C.[5,6]

GLC–MS analysis of the crude product revealed 1,2,4-tri-*tert*-butylbenzene (**1a**) to be present as the main product accompanied by 1,4-di-*tert*-butylbenzene (**1d**),

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[†] Dedicated to Professor K. Dimroth on the occasion of his 75th Birthday.

2,5-di-*tert*-butylphenol (**1e**), and a small amount of 2,2′,5,5′-tetra-*tert*-butylbiphenyl (**2**). Chromatography on silica gel gave a mixture of the hydrocarbons **1a**, **1d**, and **2** as the first fraction which was further separated by preparative gas chromatography to give **1a** in 18% isolated yield.

In view of the simplicity of the procedure this yield may be regarded as quite acceptable, giving **1** in essentially two steps from commercially available materials. Substituting *tert*-butyllithium by *tert*-butyl-d_9-lithium, prepared from *tert*-butyl-d_9 chloride,[7] the desired target molecule **1b** was obtained in 20% yield. As only 1.2 equiv of *tert*-butyllithium were used the oxidation of the copper reagents produced the biphenyl derivative **2** in 18% isolated yield.

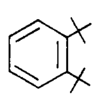
This oxidative coupling reaction of mixed homocuprates should be suitable for the preparation of the simpler hydrocarbon 1,2-di-*tert*-butylbenzene (**3**).[8] However, the analogous procedure gave this compound in only 10% yield together with appreciable amounts of the symmetrical biphenyl coupling product **4**.[9] Similarly, a *tert*-butyl group can be placed by this method between two methyl groups; for example, starting from bromomesitylene (**5a**) *tert*-butylmesitylene[10] (**5b**) is produced in 15% isolated yield. Our failure to introduce a *tert*-butyl group between two preexisting *tert*-butyl groups shows the limitations of this approach. Thus, 2,4,6-tri-*tert*-butylbromobenzene (**6a**) gave no higher alkylated products. Only hydrocarbon **6b**, phenol **6c**, and iodide **6d** were present according to GLC–MS analysis. Similarly, attempts to para-di-*tert*-butylate 1,4-dibromo-2,5-di-*tert*-butylbenzene (**7**)[11] as well as to ortho-di-*tert*-butylate *o*-dibromobenzene via its benzyne intermediate were unsuccessful.

Experimental Section

General Methods. NMR spectra were obtained on a Bruker WH-400 spectrometer in $CDCl_3$; chemical shifts are given in ppm downfield from TMS. GLC–MS analyses were performed on Varian 1700 gas chromatograph coupled to a Varian MAT 711 mass spectrometer, column 5% SE 52 on Chromosorb G, AW-DMCS, 2.5 m, $^1/_8$ in. Preparative gas chromatographic separations were run on a Aerograph A 90-P3 chromatograph, column 5% SE 30 on Chromosorb G, AW-DMCS, 60–80 mesh, 1.8 m, $^1/_4$ in., helium flow rate 120–130 mL/min. For column chromatography silica gel from Woelm, activity 1, was used. IR spectra were obtained on a Perkin Elmer 577 instrument.

Anhydrous tetrahydrofuran was obtained by the sodium benzophenone ketyl method. Aryl halides were prepared according to literature procedures as indicated. *tert*-Butyllithium was purchased from Aldrich.

1,2,4-Tri-*tert*-butylbenzene (1a). A two-necked flask equipped with a stirring bar was flame dried in a stream of nitrogen and closed with a rubber septum. The flask was charged with 30 mL of anhydrous tetrahydrofuran and 0.81 g (3 mmol) of the bromide **1c**. With stirring, this solution was cooled to −78 °C by means of a dry ice/acetone bath. *tert*-Butyllithium (5 mL, 7.5 mmol) in pentane was slowly added by syringe. After complete addition, the mixture was stirred for 10 min. The septum was removed and 0.76 g (4 mmol) of finely ground dry cuprous iodide were added. The flask was closed again and the reaction mixture was stirred for 15–20 min at −78 °C during which time the color of the solution became green-black. Meanwhile a balloon was filled with 500 mL of dry oxygen and subsequently exchanged for the nitrogen supply. (*See cautionary note at the end of this paragraph!*) Diffusion of the oxygen was accelerated by removal of the nitrogen atmosphere from the reaction vessel via syringe. The mixture was stirred vigorously under the oxygen atmosphere for 15 min at −78 °C and then allowed to warm to room temperature. The mixture was poured on 70 mL of saturated aqueous ammonium chloride solution and extracted with hexane. The organic layer was washed with water, dried over anhydrous sodium sulphate, and concentrated in vacuo. The resulting oil was purified by chromatography on 30 g of silica gel with pentane as eluent. The first fraction contained the desired hydrocarbons. After concentrating, this mixture was separated by preparative gas chromatography, column temperature 210 °C, to yield 0.13 g of **1a** (18%), mp 46 °C.



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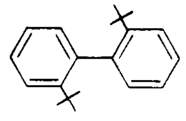

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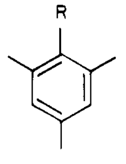
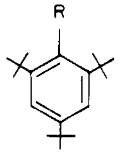
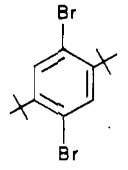


5a, R = Br
5b, R = C(CH$_3$)$_3$



6a, R = Br
6b, R = H
6c, R = OH
6d, R = J



7

Caution. If excess of *tert*-butyllithium is used, the reaction vessel can explode violently even at −78 °C during addition of the oxygen. This reaction should only be carried out behind a shield!

Spectral Data. **1a**: ^{1}H NMR δ 1.32 (s, 9 H), 1.55 (s, 9 H), 1.57 (s, 9 H), 7.13 (dd, 1 H, J(H5,H6) = 8.4 Hz, J(H5,H3) = 2.3 Hz) (H-5), 7.52 (d, 1 H, J(H6,H5) = 8.4 Hz) (H-6), 7.63 (d, 1 H, J(H3,H5) = 2.3 Hz) (H-3);

^{13}C NMR δ 31.3 ($C(CH_3)_3$, C-4), 34.3 ($C(CH_3)_3$, C4), 34.85 (C-$(CH_3)_3$,C-1 or C-2), 34.89 ($C(CH_3)_3$, C-1 or C-2), 37.2 ($C(CH_3)_3$, C-1), 38.0 ($C(CH_3)_3$, C-2), 122.2 (C-5), 126.8 (C-3), 129.1 (C-6), 145.6 (C-1), 147.4 (C-4), 148.1 (C-2).

2: mp 154 °C; MS, m/e calcd for $C_{28}H_{42}$ 378.3286, m/e found 378.3285; IR (KBr) 2960, 2900, 2860, 1480, 1460, 1395, 1380, 1360, 1270, 1250, 1140, 1040, 900, 825; ^{1}H NMR (C_3D_6O) δ 1.14 (s, 9 H), 1.28 (s, 9 H), 6.97 (d, 1 H, J = 2.4 Hz), 7.31 (dd, 1 H, J = 8.5 Hz, J = 2.4 Hz), 7.49 (d, 1 H, 8.5 Hz);

^{13}C NMR δ 31.3, 33.3, 34.0, 36.5, 123.4, 127.9, 130.0, 142.4, 143.6, 146.0.

5b: ^{1}H NMR δ 1.6 (s, 9 H), 2.3 (s, 3 H), 2.6 (s, 6 H), 6.9 (s, 2 H);

^{13}C NMR δ 20.1, 26.1, 33.3, 38.2, 132.3, 134.1, 136.7, 144.0.

Acknowledgment. This work was supported by the Fonds der Chemischen Industrie and by the Deutsche Forschungsgemeinschaft (Be 631/6-2).

Registry No. **1a**, 1459-11-6; **1b**, 97135-80-3; **1c**, 6683-74-5; **1d**, 1012-72-2; **1e**, 5875-45-6; **2**, 97135-79-0; **3**, 1012-76-6; **4**, 36919-89-8; **5a**, 576-83-0; **5b**, 1985-65-5; **6a**, 3975-77-7; **6b**, 1460-02-2; **6c**, 732-26-3; **6d**, 31039-82-4; *tert*-butylbenzene, 98-06-6.

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(6) *ATTENTION*: See cautionary note in the Experimental Section.

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