cooled solution of 62.0 g of the anomeric mixture of **1** and **2** (as obtained above) in acetic anhydride (10 ml) was added 2 drops of concentrated H_2SO_4. After 1 hr at room temperature the solution was stirred into ice–water and the precipitate formed was recrystallized from ethanol to afford 1.0 g (42%) of trans isomer **4**: mp 143–145°; nmr ($CDCl_3$) τ 2.67 (s, 5, C_6H_5), 3.78 (m, 1, H-2), 4.66 (d, 1, $J_{6,7}$ = 10 Hz, H-7), 5.15 (broad m, 1, H-6), 7.84 (s, 3, OAc), 8.22 (m, 4, CH_2 at C-3 and C-5), 8.70 (m, 2, CH_2 at C-3); nmr (DMSO-d_6) τ 4.00 (m, 1, H-2) and 4.40 (d, 1, $J_{6,7}$ = 10 Hz).

Anal. Calcd for $C_{14}H_{17}NO_5$: C, 60.20; H, 6.14; N, 5.02. Found: C, 60.36; H, 6.37; N, 4.93.

The ethanolic mother liquors, remaining after the isolation of **4**, yielded on evaporation and five recrystallizations a product, melting at 235°, which, on the basis of the intensities of the acetoxy resonances in $CDCl_3$ (7.84 for **4** and 7.91 for **3**) contained approximately 80% of the cis isomer **3**.

2-Methoxy-6-(α-nitrobenzyl)tetrahydropyran (5 and 6).—To 1.0 g of an anomeric mixture of **1** and **2** (*cf.* above) in 10 ml of methanol was added 0.5 g of a strongly acidic ion exchange resin, and the solution was refluxed for 12 hr. Removal of the resin, evaporation to dryness, and filtration of the crystalline residue with a little cold methanol afforded 750 mg (68%) of a product, composed of **5** and **6** in a 1:4 mixture (nmr). Separation was achieved by elution of the mixture from a silica gel column (2.5 × 60 cm) with chloroform. Examination of the 10-ml samples collected, by tlc [R_f values 0.73 (**6**) and 0.50 (**5**) in chloroform], evaporation of the appropriate fractions, and recrystallization, in both cases, from isopropyl alcohol afforded 520 mg (70%) of the trans isomer **6** as felted needles, mp 105°, and 140 mg (19%) of the cis compound **5** as needles: mp 125–127°; nmr ($CDCl_3$) for **6**, τ 2.55 (m, 5, C_6H_5), 4.63 (d, 1, $J_{6,7}$ = 10 Hz, H-7), 5.25 (broad m, 2, H-2 and H-6), 6.59 (s, 3, OCH_3), 8.32 (m, 4, CH_2 at C-3 and C-5), 8.80 (m, 2, CH_2 at C-4). The cis isomer **5** had analogous nmr features except for the chemical shifts for H-7 (τ 4.40) and the methoxy group (6.47).

Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.08; H, 6.77; N, 5.58. Found: C, 62.20; H, 6.74; N, 5.51 (cis isomer). Found: C, 62.12; H, 6.82; N, 5.66 (trans isomer).

***trans*-2-Methoxy-6-(α-acetamidobenzyl)tetrahydropyran (7).**—To a suspension of Raney nickel T4 catalyst[23] (2 ml) in 50 ml of methanol was added 750 mg of the epimeric mixture of methoxy compounds **5** and **6**, as obtained above, followed by hydrogenation under pressure (100 atm H_2) at room temperature for 1 day. After removal of the catalyst the solution was concentrated to about 10 ml, and, upon addition of 2 ml of acetic anhydride, kept overnight at ambient temperature. Evaporation to dryness *in vacuo* (finally 0.2 mm) and trituration of the residue with a small amount of methanol induced crystallization, to afford, after recrystallization from ethanol–water, 530 mg (57%) of **7** as colorless crystals: mp 84–85°; nmr (DMSO-d_6) τ 1.80 (d, 1, $J_{7,NH}$ = 9 Hz, NH), 2.66 (m, 5, C_6H_5), 5.08 (q, 1, $J_{2,7}$ = 4 and $J_{7,NH}$ = 9 Hz, H-7), 5.36 (narrow m, 1, H-2), 6.16 (broad m, 1, H-6), 7.08 (s, 3, OCH_3), 8.07 (s, 3, NHAc), 8.5 (m, 6, ring CH_2).

Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.35; H, 7.96; N, 5.26.

Cyclization of Glutaraldehyde with 1-Nitropropane.—To a mixture of 120 g (0.3 mol) of 25% aqueous glutaraldehyde and 40 ml (0.425 mol) of 1-nitropropane was added, with cooling, 1 *N* NaOH (20 ml). The solution was kept at ambient temperature for 3 days and subsequently deionized with a strongly acidic ion exchange resin (Merck I, H^+ form). After removal of the resin and thorough washing with methanol (200 ml) the combined filtrate and washings were evaporated to about 100 ml and, after treatment with activated carbon, taken to dryness, followed by repeated reevaporations from ethanol. Trituration of the residue with chloroform caused crystallization to give on filtration 21.7 g of crude product. Recrystallization from chloroform–petroleum ether (bp 60–80°) (1:2) afforded 20.2 g (36%) of **8** as colorless crystals, mp 90–91°, nmr in ref 10. The mother liquor, remaining after isolation of crude **8**, was evaporated to dryness and the sirupy residue was dissolved in a little ethanol followed by gradual addition of petroleum ether. The crystals that had separated after standing for 2 days consisted of an approximate 1:1 mixture of **8** and **9** (tlc in 20:1 chloroform–methanol, R_f 0.45 (**8**) and 0.62 (**9**), and were subjected to another three recrystallizations from the same solvent mixture, the separation being followed by tlc. Thus, 1.6 g (3%) of **9** was obtained as colorless rhombs. Since partial epimerization of **9** into **8** occurs on melting, as evidenced by tlc, the observed melting point on fast heating of 102–109° does not represent the melting point of pure **9**: nmr ($CDCl_3$) τ 5.60 (m, 2, $W_{1/2}$ = 18 Hz, H-2 and H-6), 6.15 (d, 2, J = 8 Hz, C-2 and C-6 OH), 8.1 (m, 8, 4 CH_2), 9.11 (t, 3, J = 7 Hz, $EtCH_3$); addition of trifluoroacetic acid eliminates the OH doublet, and reduces the half-width of the τ 5.60 multiplet to 10 Hz.

Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found (**9**): C, 50.80; H, 7.91; N, 7.24.

2,6-Diacetoxy-1-nitro-1-ethylcyclohexane (10).—A solution of 500 mg of **9** in acetic anhydride (2 ml) containing a trace of concentrated H_2SO_4 was kept at room temperature for 1 hr, and subsequently stirred into ice–water. Recrystallization of the resulting precipitate from petroleum ether–ethyl acetate (10:1) afforded 310 mg (54%) of **10** as colorless spears: mp 88–89°; nmr ($CDCl_3$) τ 4.64 (q, 2, J = 6 and 3 Hz, H-2 and H-6), 7.95 (s, 6, OAc), ~8.1 (m, 8, CH_2), 9.02 (t, 3, $EtCH_3$).

Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.74; H, 7.01; N, 5.13. Found: C, 52.80; H, 7.04; N, 4.98.

1-Acetamido-2,6-diacetoxy-1-ethylcyclohexane (11).—To a prehydrogenated suspension of 500 mg of PtO_2 in 10 ml of glacial acetic acid was added a solution of 1.0 g of nitrodiol **9** in acetic acid (30 ml) and the hydrogenation was continued. After uptake of the theoretical amount of H_2 (380 ml, 2 days) the catalyst was filtered off and washed with acetic acid (25 ml) and the combined filtrate and washings were taken to dryness with repeated reevaporations from ethanol. The remaining sirup was acetylated in a mixture of acetic anhydride (10 ml) and pyridine (25 ml) by standing overnight at ambient temperature. Removal of the solvents *in vacuo* (0.1 mm) and trituration of the residue with ice–water (50 ml) afforded a first crop of crystals, concentration of the mother liquor similarly a second, to give 890 mg of crude **11**. Two recrystallizations from water–methanol (10:1) gave 310 mg (24%) of **11** as rhombs: mp 149–151°; nmr ($CDCl_3$) τ 4.31 (s, 1, NH), 4.79 (m, 2, $W_{1/2}$ = 10 Hz, H-2 and H-6), 7.91 (s, 6, OAc), 8.07 (s, 3, NHAc), ~8.15 (broad m, 8, CH_2), 9.21 (t, 3, J = 8 Hz, $EtCH_3$); DMSO-d_6 shifts the NH signal to τ 3.09 and the acetyl resonances to 7.99 (OAc) and 8.16 (NHAc), respectively.

Anal. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.13; N, 4.91. Found: C, 58.82; H, 8.16; N, 4.85.

Registry No.—**1** and **2**, 21891-46-3; **3** and **4**, 21891-47-4; **5** and **6**, 34288-57-8; **7**, 34288-58-9; **8**, 34289-82-2; **9**, 34289-83-3; **10**, 34289-84-4; **11**, 34289-85-5.

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Oxidation of 4-Alkyl-2,6-di-*tert*-butylphenols with β-Manganese Dioxide

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The preparation of 2,6-di-*tert*-butyl-*p*-benzoquinone (**1**) by the salcomine-catalyzed air oxidation of 2,6-di-*tert*-butylphenol (**2**) was recently reported.[1,2] The oxidation of **2** or 4-alkyl-2,6-di-*tert*-butylphenols (**3a**) with most oxidizing agents gives only a low yield of **1**.[3–5]

(1) H. M. van Dort and H. J. Geursen, *Recl. Trav. Chim. Pays-Bas*, **86**, 520 (1967).

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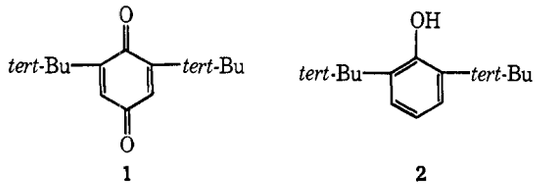

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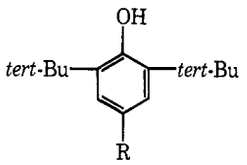
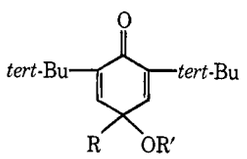


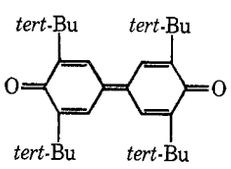
3a, R = alykl
b, R = CH_3
c, R = *tert*-Bu

Therefore, it is surprising that β-manganese dioxide (pyrolusite) oxidizes 2,6-di-*tert*-butyl-4-methylphenol (**3b**) in good yields either to **1** or to 4-alkoxy-2,6-di-*tert*-butyl-4-methyl-2,5-cyclohexadien-1-ones (**4a**), depending on the reaction conditions.



4a, R = CH_3; R′ = alykl
b, R = R′ = CH_3
c, R = CH_3; R′ = CH_3CH_2; $CH_3CH_2CH_2$
d, R = *tert*-Bu; R′ = CH_3

We obtained **1** in 74% yield by treating **3b** with finely divided β-manganese dioxide in a mixture (2/1 w/w) of 40% aqueous sulfuric acid and acetic acid at 60° for 5 hr. Oxidation of **2** under the same conditions gave only a 10% yield of **1**; the main product was 3,3′5,5′-tetra-*tert*-butyldiphenoquinone (**5**). To obtain a good yield of **1** from **3b**, the presence of both water and acetic acid (besides sulfuric acid) is essential. For example, in 40% aqueous sulfuric acid (without acetic acid), only a 15% yield of **1** was obtained after treatment of **3b** with β-manganese dioxide at 60° for 18 hr; in 40% sulfuric acid in acetic acid (water absent), only an 11% yield of **1** was obtained.



5

By oxidation of **3b** with β-manganese dioxide in 40% aqueous sulfuric acid containing methanol (1.5/1 w/w) at 55° for 4 hr, 2,6-di-*tert*-butyl-4-methoxy-4-methyl-2,5-cyclohexadien-1-one (**4b**) was obtained in 60% yield. As by-products, 11% of **1** and 12% of **5** were obtained. Replacement of methanol by ethanol or propanol gave the corresponding ethoxy and propoxy compounds **4c**. When the reaction was carried out in 40% methanolic sulfuric acid (no water present), a 25% yield of **1** was obtained in addition to **5**. No **4b** was detected in this case.

Oxidation of 2,6-di-*tert*-butylphenol (**2**), in which the para position is not blocked by a methyl group, in a 40% aqueous sulfuric acid–methanol mixture at 50° gave no cyclohexadienone. The main product was **5**, and a trace of **1** was found.

The oxidation of 2,4,6-tri-*tert*-butylphenol (**3c**) in a 40% aqueous sulfuric acid–acetic acid mixture gave **1** in 70% yield. In a 40% aqueous sulfuric acid–methanol mixture, a 40% yield of **4d** and a 40% yield of **1** were obtained.

Experimental Section

Oxidation of 2,6-Di-*tert*-butyl-4-methylphenol (3b) to 2,6-Di-*tert*-butyl-*p*-benzoquinone (1).—Twenty grams of **3b** was added to a mixture containing 150 g of 40% aqueous sulfuric acid and 75 g of glacial acetic acid. The mixture was heated to 60° with stirring, and 40 g of finely divided β-MnO_2 (pyrolusite) was added over a period of 2 hr at 60°. After the addition of MnO_2 was completed, stirring was continued for 3 hr at 60°. After the reaction mixture was cooled to room temperature, it was diluted with 600 ml of water and steam distilled. The distillate was extracted with ether, and the ether was allowed to evaporate to give 15 g (75% yield) of **1**.

Oxidation of 2,6-Di-*tert*-butyl-4-methylphenol (3b) to 2,6-Di-*tert*-butyl-4-methoxy-4-methyl-2,5-cyclohexadien-1-one (4b).—Twenty grams of **3b** was added to a mixture containing 150 g of 40% aqueous sulfuric acid and 100 g of methanol. The mixture was heated to 55° with stirring, and 40 g of finely divided β-MnO_2 was added over a period of 2 hr at 55°. After the reaction mixture was cooled to room temperature, it was diluted with 600 ml of water and steam distilled. The distillate was extracted with ether, and the ether was evaporated. Recrystallization of the residue from ethanol gave a 60% yield of **4b**, mp 92–94°.

Registry No.—**1**, 719-22-2; **3b**, 128-37-0; **4b**, 2411-18-9; β-manganese dioxide, 14854-26-3.

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A New Method for the Methylation of Amines

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The introduction of methyl groups into a primary or secondary amine by reductive alkylation with formaldehyde and formic acid derivatives (the Clarke–Eschweiler method[2]) has proved to be a useful method for the preparation of tertiary methylated amines. In some cases, however, complex mixtures have resulted from the multiplicity of side reactions which can occur.[3] Our need for a milder procedure in connection with another problem currently under investigation, coupled with our earlier interest in the chemistry of the cyanoborohydride (BH_3CN^-)[4] ion, led us to examine the feasibility of a formaldehyde–cyanoborohydride system for amine methylation. We describe here a mild and efficient method for the synthesis of tertiary methylated amines of high purity in good yield.

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