nmr ($CDCl_3$, 100 Mc) δ 8.93 (s, 1, C-6 proton) and 8.20–7.00 (m, 13, OH and aromatic).

Anal. Calcd for $C_{22}H_{14}N_2O$: C, 81.97; H, 4.38; N, 8.69. Found: C, 81.99; H, 4.64; N, 8.50.

2,5-Dimethylquinoxaline.—A mixture of 2,3-dinitro- and 2,5-dinitro-*p*-xylene (5.0 g, 0.026 mol) was hydrogenated in EtOAc over 10% Pd/C at 3 atm. The mixture was filtered, and the crude oil (0.018 mol containing 68% of the desired 2,3-diamino isomer), obtained by evaporation of the solvent, was heated for 2 hr at 60° with 4.65 g (0.018 mol) of the $NaHSO_3$ adduct of glyoxal (10% excess of the adduct was added after 1 hr). The solution was made strongly alkaline with aqueous KOH and extracted with Et_2O. The combined ether extracts were dried (Na_2SO_4), filtered, and evaporated to dryness *in vacuo*. The residue was deposited on a 2.5 × 25 cm silica gel column and elution with 1:1 CH_2Cl_2–CCl_4 ultimately afforded **2,5-dimethylquinoxaline** (0.30 g, 11%) as white needles: mp 71–72° (from 30–60° petroleum ether, Darco); uv max 245 mμ (ε 39,000) and 318 (5400); nmr ($CDCl_3$) δ 8.78 (s, 2, C-2,3 protons), 7.41 (s, 2, C-6,7 protons), and 2.70 (s, 6, CH_3).

Anal. Calcd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.70; H, 6.38; N, 17.92.

5,8-Dimethylquinoxaline 1-Oxide.—A mixture of 5,8-dimethylquinoxaline (1.0 g, 0.0063 mol) in 25 ml of $CHCl_3$ and 5 ml of 40% peracetic acid was refluxed for 16 hr. After cooling to room temperature, the solution was diluted with $CHCl_3$ and washed four times with H_2O. The $CHCl_3$ layer was dried (Na_2SO_4) and filtered, and the solvent was evaporated *in vacuo*. Deposition of the residue on a 2.5 × 25 cm silica gel column and elution with 1:1 CH_2Cl_2–CCl_4 ultimately gave 0.80 g of recovered starting material. Further elution with $CHCl_3$ yielded 0.15 g (12%) of **5,8-dimethylquinoxaline 1-oxide** as yellow needles: mp 109.5–110° (from 30–60° petroleum ether, Darco); uv max 252 mμ (ε 36,100), 292 (3850), 337 (4600), and 349 (5000); nmr ($CDCl_3$) δ 8.48–8.10 (AB pattern, 2, C-2,3 protons), 7.44–7.10 (AB pattern, 2, C-6,7 protons), 2.96 (s, 3, C-8 CH_3), and 2.60 (s, 3, C-5 CH_3).

Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 69.17; H, 5.94; N, 16.04.

Reduction of the *N*-**oxide** (0.10 g, 0.00052 mol) with 0.10 g (0.00058 mol) of sodium hydrosulfite in 20 ml of 80% EtOH gave **5,8-dimethylquinoxaline** (40%).

Registry No.—**4** *cis*, 26940-78-3; **4** *trans*, 26940-79-4; **5** *cis*, 26940-80-7; **5** *trans*, 26940-81-8; **6** *cis*, 26940-82-9; **6** *trans*, 26940-83-0; **7** *cis*, 26940-84-1; **7** *trans*, 26940-85-2; **8** *cis*, 26940-86-3; **8** *trans*, 26940-87-4; **9** *cis*, 26940-88-5; **9** *trans*, 26940-89-6; **10a** *cis*, 26940-90-9; **10a** *trans*, 26992-53-0; **10b** *cis*, 26940-91-0; **10b** *trans*, 26940-92-1; **13**, 26940-93-2; **14**, 26940-94-3; **15**, 26940-95-4; **16**, 26940-96-5; **17**, 26940-97-6; **18**, 26940-98-7; **19**, 26940-99-8; **20**, 26941-00-4; **21**, 26941-01-5; **22**, 26941-02-6; **24**, 26941-03-7; **26**, 26941-04-8; **27**, 26941-05-9; **28**, 26941-06-0; **31**, 26941-07-1; **32**, 26941-08-2; **33**, 26941-09-3; **34**, 26941-10-6; **35**, 26941-11-7; **38**, 26941-12-8; **39**, 26941-13-9; **40**, 26941-14-0; **41**, 26941-15-1; **42**, 26941-16-2; **43**, 26941-17-3; **44**, 26941-18-4; **45**, 26941-19-5; 2,5-dimethylquinoxaline, 26941-20-8; 5,8-dimethylquinoxaline, 26941-21-9.

Notes

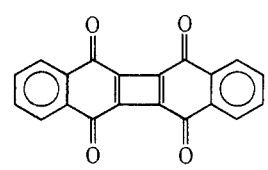
A Study of the Bromination of the Syn and Anti Photodimers of 1,4-Naphthoquinone. The Chemistry of the Brominated Derivatives

NICOLAAS P. DU PREEZ, DANIEL P. VENTER, PETRUS JANSE VAN VUUREN, GERT J. KRUGER, AND JOHANNES DEKKER*

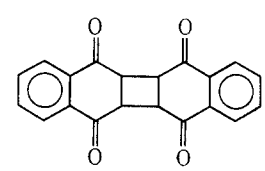
Department of Chemistry, Potchefstroom University for Christian Higher Education, Potchefstroom, South Africa

Received March 18, 1970

Various efforts to synthesize cyclobutadiene or derivatives thereof are cited in the literature.[1] These efforts were, however, unsuccessful, supporting calculations[2] which show zero aromatic nature for cyclobutadiene. In some cases[3,4] the presence of nonisolable cyclobutadiene derivatives has been claimed. The symmetrically substituted diphthaloylcyclobutadiene **1** should exhibit an enhanced stability compared to cyclobutadiene owing to the electronegative carbonyl groups adjacent to the four-membered ring. In order to attempt the synthesis of **1**, we first considered it necessary to investigate the bromination and chemistry of the syn (**2a**) and anti (**2b**) dimers[5,6] of 1,4-naphthoquinone.



1



2a, syn
b, anti

It has been shown that both **2a** and **2b** enolize in acidic media to establish an equilibrium between **2b** and **3**.[7] Both **3** and its fully enolized derivative **4**[8] exhibit typical olefinic reactions, *e.g.*, bromination[7] to **5** and **6**, respectively.

The bromination of **2** leads to various products, depending on the reaction conditions. If the reaction is carried out with 4 equiv of bromine in acetic acid

(1) M. P. Cava and M. J. Mitchell, "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967.

(2) M. J. S. Dewar and G. J. Gleicher, *J. Amer. Chem. Soc.*, **87**, 3255 (1965); L. Watts, J. D. Fitzpatrick, and R. Pettit, *ibid.*, **88**, 623 (1966); J. D. Roberts, A. Streitwieser, Jr., and C. M. Regan, *ibid.*, **74**, 4579 (1952).

(3) R. Criegee, W. Eberius, and H. Brune, *Chem. Ber.*, **101**, 94 (1968); G. Maier and U. Mende, *Tetrahedron Lett.*, **37**, 3155 (1969), and references therein; L. Watts, J. D. Fitzpatrick, and R. Pettit, *J. Amer. Chem. Soc.*, **87**, 3253 (1965); M. Neuenschwander and A. Niederhauser, *Chimia*, **22**, 491, (1968); G. Maier and U. Mende, *Angew. Chem.*, **81**, 932 (1969).

(4) R. Gompper and G. Seybold, *ibid.*, **80**, 804 (1968).

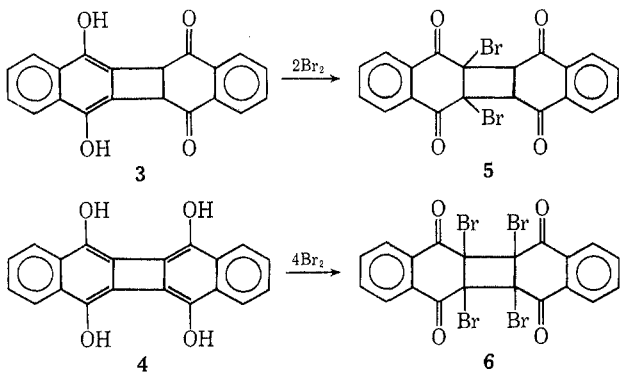
(5) A. Schönberg, M. Mustafa, M. Z. Barahat, N. Latif, R. Moubasher, and A. Mustafa, *J. Chem. Soc.*, 2126 (1948).

(6) J. Dekker, P. J. van Vuuren, and D. P. Venter, *J. Org. Chem.*, **33**, 464 (1968).

(7) D. P. Venter and J. Dekker, *ibid.*, **34**, 2224 (1969).

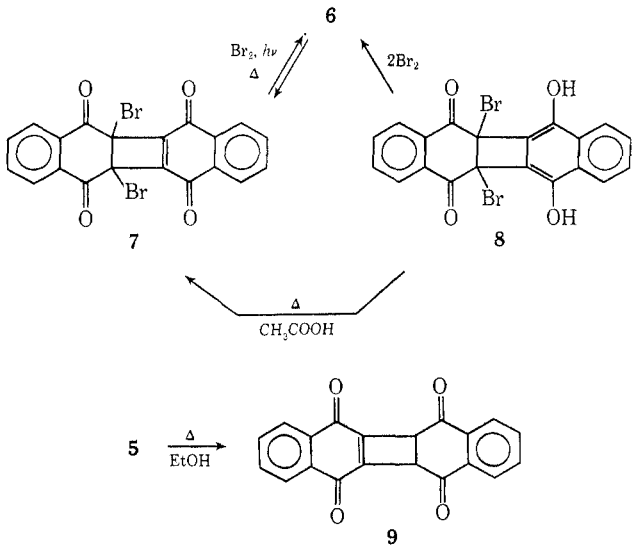
(8) J. M. Bruce, *J. Chem. Soc.*, 2782 (1962).

at 70°, the fairly insoluble **6** is obtained. The infrared spectrum of **6** closely resembles that of **2**,[6] showing a shift in carbonyl absorption to higher frequency (1692 cm^{-1}) with reference to that of **2a** (1678



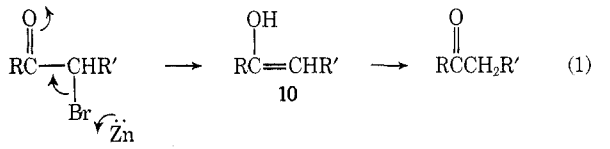
cm^{-1}). The mass spectrum and analysis are consistent with the structure. The structure and anti configuration of **6** recently have been proved[9] by means of X-ray crystallography.

The bromination of **2** with 4 equiv of bromine in boiling acetic acid produces a yellow crystalline dibromo derivative **7**, which exhibits α,β-unsaturated (1680 cm^{-1}) and α-brominated (1703 cm^{-1}) carbonyl absorption. It is logical to expect that the latter bromination should initially incorporate the formation of **6**, followed by a cis elimination of 1 mol of bromine. The labile character of two of the bromine atoms of **6** is demonstrated by its smooth conversion to **7** in boiling acetic acid. The reverse reaction, *i.e.*, the bromination of **7** to **6**, is accomplished by ultraviolet-induced bromination of a suspension of **7** in carbon tetrachloride. The phenomenon of cis elimination of 1 mol of bromine is also encountered in the case of **5**. A solution of **5** in boiling ethanol yields a yellow crystalline product, characterized as the quinone **9**. Treatment of **9** with 2 equiv of bromine in acetic acid leads to the formation of **7**, illustrating the correctness of structure **9**.



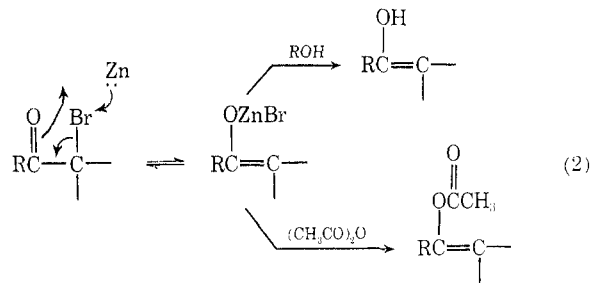
If the bromination of **2** is conducted in acetic acid at 90° with 2 equiv of bromine, an orange crystalline product **8**, which displays typical α-bromo ketonic (1685 cm^{-1}) and hydroxylic (3460 cm^{-1}) absorption in the infrared region, is obtained. Further bromination of **8** results in the formation of **6**. Further structural proof for **8** is obtained by thermal treatment (boiling acetic acid) of **8**, whereby **7** is produced.[10]

According to Corey,[11] the acidic debromination of α-bromo ketones with zinc proceeds according to eq 1.

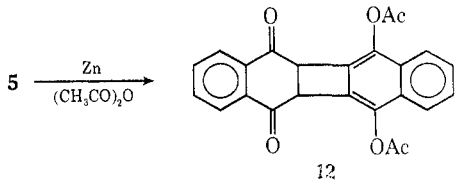


Zimmerman[12] showed that **10** does, in fact, exist as an intermediate.

Treatment of a suspension of **6** in acetic acid or ethanol with activated zinc powder at 20° accomplishes complete conversion to **4** within 20 min. Treatment of **6** with activated zinc powder in absolute acetic anhydride at 20° leads quantitatively to the formation of the tetraacetate[8] **11**. This reaction, which we prefer to call an acetylative dehalogenation, must proceed in much the same way as the acidic dehalogenation of α-bromo ketones, probably *via* the route of eq 2.



The proposed mechanism is favored by the fact that treatment of **4** with zinc powder in acetic anhydride at 20° for 2 hr produces **11** in less than 4% yield. Further supporting evidence for the proposed acetylative dehalogenation reaction is given by the fact that treatment of **5** with zinc powder in acetic anhydride at 20° yields the diacetate **12**[7] as sole product.



Treatment of **8** with zinc powder in ethanol or acetic acid leads quantitatively to **4**, while **11**[8] is obtained with zinc powder in acetic anhydride. The latter reaction indicates that the initially formed diacetate **13** suffers further acetylation owing to the presence of zinc acetate bromide. This statement is proved by the fact that, when treated with acetic

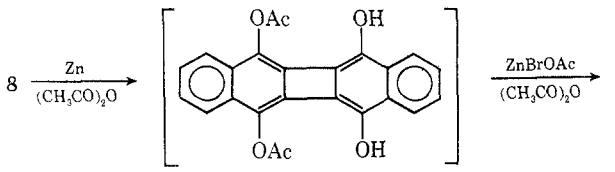
(9) G. J. Kruger and J. C. A. Boeyens, *J. Phys. Chem.*, **72**, 2120 (1968).

(10) A proposed mechanism for this dehydrogenation reaction will be published shortly.

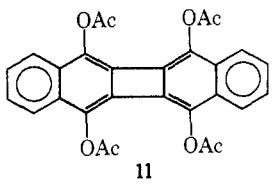
(11) E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, **78**, 6269 (1956).

(12) H. E. Zimmerman and A. Mais, *ibid.*, **81**, 3644 (1959).

anhydride and zinc bromide at 20°, **4** is converted rapidly and quantitatively to **11**.

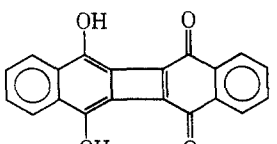


13



11

An attempt to obtain the "internal quinhydrone" **14** by treating **7** with zinc in acetic acid leads to the formation of **4**, showing that further reduction of **14** occurs. A noncrystalline, unidentified product is obtained when the reaction is carried out in ethanolic solution. The reaction of **7** with zinc powder in acetic anhydride at 20° yields **11**.



14

Dehalogenation of **6** with lithium amalgam should lead to the formation of **1**. A stirred suspension of **6** and lithium amalgam in sodium-dried ether yields a yellow solution, as can be expected for a bisquinonoid system, with an intense green fluorescence. The reaction is performed under a nitrogen atmosphere and in the absence of light. This compound is possibly **1**, which, however, is so light and air sensitive that its isolation or characterization is impossible.

Experimental Section

The following instruments were used for the recording of physical properties: a Perkin-Elmer Model 221 spectrophotometer, a MS 9 mass spectrometer, and a Gallenkamp (Design No. 889339) melting point apparatus. Melting points are uncorrected. Because of the low solubilities of the various compounds, no nmr spectra could be obtained. Microanalyses were done by the Council for Scientific and Industrial Research of South Africa.

5a,5b,11a,11b-Tetrabromo-5,6,11,12-tetraketo-5,5a,5b,6,11,-11b,12-octahydrodibenzo[*b*,*h*]biphenylene (**6**).[7]—Bromine (0.24 g) was added to a stirred solution of **2**[6] (0.1 g) in acetic acid (50 ml) at 90°. After 2 min the temperature was lowered to 70°; the reaction mixture was kept at this temperature for 1 hr and then cooled. Colorless needles of **6** (0.18 g, 91%) separated: mp 255–258° dec (lit.[7] mp 255–258°); ir (KBr) 1692 (C=O), 1591 (Ar), 1254 (C=O), 1005 cm^{-1} (cyclobutane ring); mass spectrum (70 eV) *m/e* (rel intensity) 628 (<5), 549 (34), 470 (38), 391 (93), 312 (52), 284 (22), 256 (15), 228 (34), 200 (100).

Anal. Calcd for $C_{20}H_8O_4Br_4$: C, 38.01; H, 1.28; Br, 50.59. Found: C, 38.00; H, 1.28; Br, 50.94.

1,2-Phthaloyl-2a,8a-dibromo-2a,3,8,8a-tetrahydro-3,8-diketonaphtho[*b*]cyclobutadiene (**7**). **1. From the Anti Dimer 2b.**[6]—Bromine (0.21 g) was added to a boiling solution of **2b** (0.1 g) in acetic acid (40 ml). The reaction mixture was refluxed for 30 min, concentrated to 10 ml, and cooled. Yellow needles of **7** (0.14 g, 95%) separated: mp 276–278° dec; ir (KBr) 1703 (α-bromo C=O), 1680 (α,β-unsaturated C=O), 1630 (C=C), 1590 (Ar), 1246 (C=O), 985 cm^{-1} (cyclobutene ring); mass spectrum (70 eV) *m/e* (rel intensity) 470 (21), 393 (100), 391 (98), 312 (40), 284 (13), 256 (7), 228 (28), 200 (74).

Anal. Calcd for $C_{20}H_8O_4Br_2$: C, 50.88; H, 1.71; Br, 33.85. Found: C, 50.71; H, 1.68; Br, 33.99.

2. From the Tetrabromide 6.[7]—A suspension of **6** (0.05 g) in acetic acid (50 ml) was refluxed for 30 min. The clear, yellow solution was concentrated to 10 ml and cooled. Yellow needles of **7** (0.03 g, 80%) separated.

5b,11a-Dibromo-5,12-dihydroxy-5b,6,11,11a-tetrahydro-6,11-diketodibenzo[*b*,*h*]biphenylene (**8**).—Bromine (0.1 g) was added to a stirred solution of **2**[6] (0.1 g) in acetic acid (15 ml) at 90°. After 5 min the solution was cooled. Light yellow needles of **8** (0.11 g, 74%) separated: mp 191–193° dec; ir (KBr) 3460 (OH), 1685 (C=O), 1632 (C=C), 1605 (Ar), 1590 (Ar), 1260 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 472 (<5), 393 (32), 314 (65), 313 (100), 286 (66), 258 (35), 229 (24), 200 (62).

Anal. Calcd for $C_{20}H_{10}O_4Br_2$: C, 50.67; H, 2.13; Br, 33.71. Found: C, 50.62; H, 2.11; Br, 33.96.

Bromination of 7.—Bromine (0.03 g) was added to a suspension of **7** (0.01 g) in carbon tetrachloride (5 ml). Ultraviolet irradiation of the reaction mixture for 30 min led to the formation of a clear solution, which was concentrated to 1 ml. Compound **6** (0.012 g, 90%) separated.[13]

Bromination of 8.—Bromine (0.08 g) was added to a stirred solution of **8** (0.1 g) in dichloromethane (100 ml). After 40 min the solution was concentrated to 10 ml. Colorless crystals of **6** (0.11 g, 83%) separated.

Thermal Treatment of 8.—A solution of **8** (0.1 g) in acetic acid (40 ml) was refluxed for 5 min. The solution was concentrated to 4 ml and cooled. Golden yellow needles of **7** (0.09 g, 90%) separated.

1,2-Phthaloyl-2a,3,8,8a-tetrahydro-3,8-diketonaphtho[*b*]cyclobutadiene (**9**). **1. From the Diol 3.**[7]—A solution of **3** (0.25 g) in benzene (100 ml) and acetone (30 ml) was treated with activated, powdered manganese dioxide (3 g) and anhydrous sodium sulfate (3 g), and the reaction mixture was shaken for 4 hr and filtered. The yellow solution was concentrated to 10 ml. Yellow needles of **9** (0.17 g, 66%) separated. Another 0.075 g was recovered from the mother liquor by precipitation with cyclohexane. Recrystallization from benzene yielded yellow needles of the quinone **9**: mp 233–237° dec; ir (KBr) 1691 (C=O), 1670 (α,β-unsaturated C=O), 1633 (C=C), 1590 (Ar), 1289 (C=O), 1230 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 314 (100), 286 (32), 258 (68), 230 (43), 202 (92).

Anal. Calcd for $C_{20}H_{10}O_4$: C, 76.43; H, 3.18. Found: C, 76.38; H, 3.20.

2. From the Dibromide 5.[7]—A solution of **5** (0.1 g) in ethanol (20 ml) was refluxed for 15 min and then cooled to 0°. Yellow needles of **9** (0.063 g, 95%) separated.[13]

Bromination of 9.—Bromine (0.1 g) was added to a stirred solution of **9** (0.1 g) in acetic acid (40 ml). The reaction mixture was refluxed for 30 min and concentrated to 6 ml. Yellow needles of **7** (0.12 g, 84%) separated.[13]

Acetylative Debromination of the Brominated Derivatives. 1. At 140°.—A suspension of **5**,[7] **6**,[7] **7**, or **8** (0.1 g) and activated zinc powder (0.5 g) in acetic anhydride (15 ml) was refluxed for 30 min. The reaction mixture was filtered and cooled. Colorless crystals of **11**[8] (0.08, 0.07, 0.095, and 0.09 g, respectively) were obtained, mp 358–360° dec (lit.[8] 358–360°).[13]

2. At 20°.—A suspension of **6**,[7] **7**, or **8** (0.1 g) and activated zinc powder (0.5 g) in acetic anhydride (5 ml) was stirred vigorously for 30 min. The insoluble crystalline product (**11**)[13] was separated from the zinc, filtered, and washed with acetic acid and water successively.

A suspension of **5**[7] (0.5 g) and activated zinc powder (3 g) in acetic anhydride (20 ml) was stirred vigorously for 15 min. The clear solution was filtered and decomposed with ethanol and water. The precipitated product was recrystallized from benzene, yielding **12** (0.25 g, 59%) as colorless needles: mp 192–194° dec; ir (KBr) 1768 (ester C=O), 1688 (C=O), 1643 (C=C), 1352 (ester C=O), 1279 (C=O), 1194 and 1177 cm^{-1} (ester C=O); mass spectrum (70 eV) *m/e* (rel intensity) 400 (24), 358 (74), 316 (100).

Anal. Calcd for $C_{24}H_{16}O_6$: C, 71.99; H, 4.03. Found: C, 71.94; H, 3.97.

Acetylation of the Tetraol 4.[8] **1. With Zinc Powder and Acetic Anhydride.**—A suspension of **4** (0.18 g) and activated

(13) The product was identified by ir spectroscopy and melting point.

zinc powder (0.3 g) in acetic anhydride (15 ml) was stirred vigorously for 3 hr at 20°. The insoluble product[13] (**4**, 0.17 g) was separated from the zinc, filtered, and washed with acetic acid and then water. The filtrate was concentrated to 5 ml. Colorless needles of **11** (0.01 g, <4%) separated.[13]

2. **With Zinc Bromide and Acetic Anhydride.**—A suspension of **4**[8] (0.1 g) and zinc bromide (0.5 g) in acetic anhydride (8 ml) was stirred vigorously for 20 min at 20°. The insoluble colorless needles of **11**[13] (0.15 g, 95%) were filtered and washed with acetic acid and water successively.

Acidic Debromination of the Brominated Derivatives.—A suspension of **6**,[7] **7**, or **8** (0.2 g) and activated zinc powder (0.5 g) in acetic acid[14] (15 ml) was stirred vigorously for 20 min. The suspended **4** was separated from the zinc. The insoluble **4**[13] (0.09, 0.11, and 0.1 g, respectively) was filtered and washed with diluted hydrochloric acid and water successively.

Registry No.—**2a**, 14734-20-4; **2b**, 14734-19-1; **7**, 27150-37-4; **8**, 27150-38-5; **9**, 27189-17-9; **12**, 19817-51-7.

Acknowledgment.—The authors are indebted to the Council for Scientific and Industrial Research of South Africa for financial support and for postgraduate grants to N. P. du P. and D. P. V. Grants by the Industrial Development Corporation of South Africa, Ltd., to N. P. du P and by "Afrikaanse Pers Beperk (1962)" to D. P. V. are gratefully acknowledged.

(14) If ethanol was used as solvent, **6** and **8** yielded **4**. In the case of **7**, however, an unidentified, noncrystalline product was obtained.

Sulfur-Containing Polypeptides. XIV. Removal of the *tert*-Butyloxycarbonyl Group with Boron Trifluoride Etherate[1,2]

RICHARD G. HISKEY,* LOWRIE M. BEACHAM, III, VICTOR G. MATL, J. NORTH SMITH, E. BRADY WILLIAMS, JR., A. M. THOMAS, AND ERIK T. WOLTERS

Venable Chemical Laboratory, The University of North Carolina, Chapel Hill, North Carolina 27514

Received July 13, 1970

In recent years the *tert*-butyloxycarbonyl (*t*-BOC) nitrogen protective group[3,4] has become widely used in peptide synthesis. The utility of the *t*-BOC group has been primarily due to the ease of introduction by the controlled pH technique,[5] the properties of *t*-BOC peptide derivatives, and the relatively mild conditions required for removal of the group. Although hydrogen chloride in various solvents[3,4] and neat trifluoroacetic acid[6] have been classically employed for cleavage of the *t*-BOC group, the availability of a reagent that would permit clean, rapid removal without the necessity of a strongly acidic solvent would be advantageous in many circumstances.[7]

These criteria can be met in many situations by use of boron trifluoride diethyl etherate in either glacial acetic acid or acetic acid–chloroform mixtures. While attempts to conduct the cleavage in chloroform alone have proved unsatisfactory, the addition of as little as 10% acetic acid gave good results. An important requirement is the exclusion of moisture from reagent and solvent.

In general, the *t*-BOC peptide is treated with a threefold excess of freshly distilled boron trifluoride diethyl etherate (0.4 ml/mmol). The reaction mixture is maintained at room temperature for 15–30 min and neutralized with either aqueous sodium acetate, 5% ammonium hydroxide, or potassium bicarbonate. The reaction is conveniently followed by tlc and generally goes to completion in 5 min although at 0° the reaction requires about 1 hr.

The *N*-carbobenzoxy group is not affected by these conditions; methyl, ethyl, benzyl, and trimethylbenzyl esters are likewise not affected, permitting possible use of this reagent with solid-phase resins. The stability of the *S*-trityl and *S*-benzhydryl thioethers of cysteine as well as the sulfur–sulfur bond of unsymmetrical cystine derivatives to these conditions has also been of considerable utility. Several protective groups are cleaved at rates comparable to cleavage of the *t*-BOC group; thus selective removal of the *t*-BOC group with boron trifluoride in the presence of benzhydryl or *tert*-butyl esters, *tert*-butyl ethers, of the *N*-triphenylmethyl group is uncertain and depends on the nature of the particular substrate.

Although this reagent has been superior for *t*-BOC removal with water-insoluble peptide derivatives, use with small water-soluble peptides must be approached with care due to the possible formation of boric acid salts. In such cases trifluoroacetic acid usually is the reagent of choice.

Experimental Section[8]

***N*-*tert*-Butyloxycarbonyl-*S*-diphenylmethyl-L-cysteine Dicyclohexylammonium Salt (I).**—A suspension of *S*-diphenylmethyl-L-cysteine[9] (57.4 g, 0.20 mol) in 400 ml of dioxane–water (1:1) was adjusted to pH 10.2 with 4.0 *N* NaOH. *tert*-Butyloxycarbonylazide (42.9 ml, 0.3 mol) was added and the reaction was stirred 9 hr at 25°, maintaining the pH at 10.2. The resulting clear yellow solution was extracted with ether and then acidified to pH 3 with 1 *N* H_2SO_4. The oily product was extracted into 500 ml of ether, washed with water and brine, dried over $MgSO_4$, and precipitated by addition of 40 g of dicyclohexylamine. The product was collected and dried over P_2O_5 to yield 101.3 g (90%): mp 158–159°; $[\alpha]^{22}D$ +6.38° (*c* 0.925, $CHCl_3$); homogeneous system D.

Anal. Calcd for $C_{38}H_{48}N_2O_4S$: C, 69.68; H, 8.51; N, 4.93; S, 5.64. Found: C, 69.64; H, 8.62; N, 4.82; S, 5.31.

***N*-*tert*-Butyloxycarbonyl-*S*-diphenylmethyl-L-cysteine *N*-Hydroxysuccinimide Ester (II).**—The salt, I (187 g, 0.33 mol), was neutralized with 2 *N* sulfuric acid. The resulting oil was dissolved in 300 ml of dimethoxyethane (DME) along with *N*-hydroxysuccinimide (37.5 g, 0.33 mol). The solution was cooled to −10° and treated with dicyclohexylcarbodiimide (DCC) (68.1

(1) The preceding paper of this series: R. G. Hiskey, G. W. Davis, M. E. Safdy, T. Inui, R. A. Upham, and W. C. Jones, Jr., *J. Org. Chem.*, **35**, 4148 (1970).

(2) Supported by Grants A-3416 and GM-07966 from the Institute of Arthritis and Metabolic Diseases and the Institute of General Medical Science, National Institutes of Health, U. S. Public Health Science.

(3) F. C. McKay and N. F. Anderson, *J. Amer. Chem. Soc.*, **79**, 4686 (1957).

(4) G. W. Anderson and A. C. McGregor, *ibid.*, **79**, 6180 (1957).

(5) E. Schnabel, *Justus Liebigs Ann. Chem.*, **702**, 188 (1967).

(6) H. Happeler and R. Schwyzer, *Helv. Chim. Acta*, **44**, 1136 (1961).

(7) J. Meienhofer, *J. Amer. Chem. Soc.*, **92**, 3771 (1970).

(8) Melting points are uncorrected. Elemental analyses were performed by Micro Tech Laboratories, Skokie, Ill. Optical rotations were performed on a Perkin-Elmer Model 141 polarimeter. Thin layer chromatograms were on 3-in. plates of silica gel GF. Solvent systems used were: chloroform–methanol (9:1), system A; chloroform–methanol–17% ammonia (3:3:1), system B; chloroform–methanol–34% ammonia (5.5:3.5:1), system C; chloroform–acetic acid (9:1), system D. Controlled pH reactions were carried out using a Radiometer titrimeter and magnetic valve. Solvents were dried over $CaSO_4$. Boron trifluoride etherate was Eastman Technical grade distilled from CaH_2.

(9) R. G. Hiskey and J. B. Adams, Jr., *J. Org. Chem.*, **30**, 1340 (1965).