# *Synthesis of Trisubstituted Triptycenes and the Optical Resolution of 7-Carboxy-2, 5-diacetoxytriptycene**

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(Received October 23, 1961)

Triptycene is a novel type of cage compound which was synthesized by Bartlett and his coworkers[1] by the elaboration of the Diels-Alder type addition product of *p*-benzoquinone with anthracene. The three benzene rings in the molecule are tightly connected at their *o*-positions by the two sp$^3$-hybridized carbon atoms holding the aromatic rings in the fixed spatial positions. The rigid structure of the molecule has been demonstrated by the inert reactivity for various displacement reactions of the substituent group or atom attached to the central tetrahedral carbon atom[2].

Triptycene derivatives bearing different substituent groups in two of the three benzene rings should be capable of existing in the optically isomeric forms shown in Fig. 1.

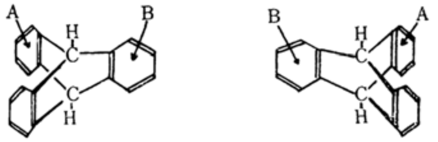
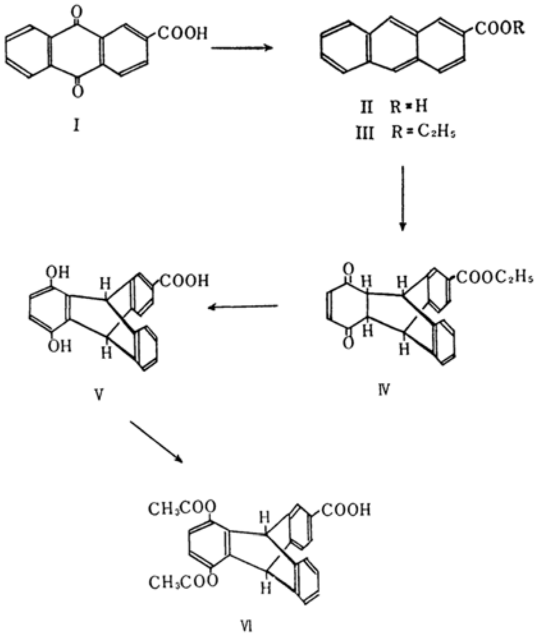


Fig. 1. Optical isomers of substituted triptycene.

Optical active triptycene derivatives may offer best means for studying the dependence of optical activity or rotatory dispersion on the nature of the substituent groups, since the rigid and fixed geometry of the molecule should exclude the influence of the complicated effects arising from the flexibility of the molecule. For the purpose of studying the above-mentioned relationships, the present authors have investigated the synthesis and optical resolution of trisubstituted triptycenes.

2-Methylanthraquinone was prepared according to the well-known procedure starting from toluene and phthalic anhydride[3]. The quinone was oxidized to 2-carboxyanthraquinone (I) by chromium trioxide in acetic acid[4]. This substance was submitted to the reduction by means of zinc dust in aqueous ammonia[5] to give 2-carboxyanthracene (II). The attempts to condense II with *p*-benzoquinone in various solvents such as ethanol, acetic acid and dioxane gave unsatisfactory results. II was converted into the corresponding ethyl ester III. The ester III was treated with an excess of *p*-benzoquinone in benzene to yield the adduct IV. The structure of IV was inferred from the comparison of the infrared spectrum of IV with that of the adduct of anthracene and *p*-benzoquinone[6]. The adduct was found to be sensitive to a strong alkali and the hydrolysis of IV with aqueous sodium hydroxide to the corresponding free acid resulted in the formation of a resinous material.



Treatment of IV in acetic acid with a small amount of hydrobromic acid yielded 8-carboxy-2, 5-dihydroxytriptycene (V). V was found to be difficult to purify owing to its unstable nature to oxygen. Therefore, the crude V was

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* Optically Active Triptycenes. I.

[1] P. D. Bartlett, M. J. Ryan and S. G. Cohen, *J. Am. Chem. Soc.*, **62**, 2649 (1942).

[2] P. D. Bartlett, S. G. Cohen, J. D. Cotman, Jr. and N. Kornblum, ibid., **72**, 1003 (1950); P. D. Bartlett and E. S. Lusis, ibid., **72**, 1005 (1950); P. D. Bartlett and F. G. Greene, ibid., **76**, 1088 (1954).

[3] L. F. Fieser, "Organic Syntheses", Coll. Vol. I (1948), pp. 517, 353.

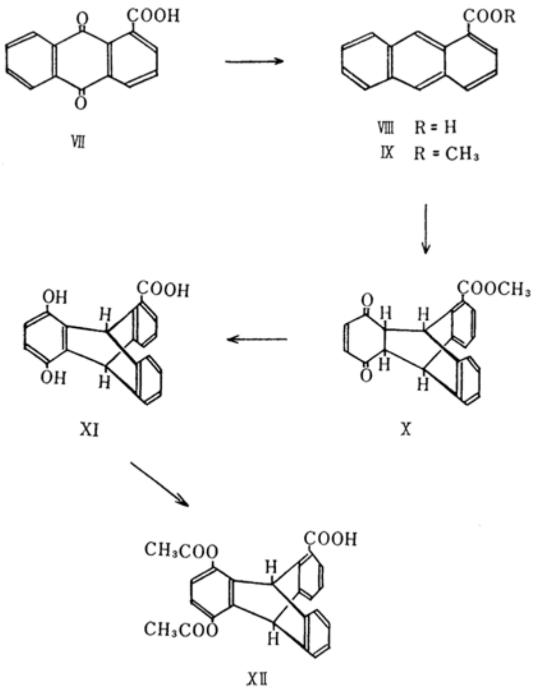
[4] C. Liebermann and G. Glock, *Ber.*, **17**, 888 (1884).

[5] E. Bornstein, ibid., **26**, 2609 (1883).

[6] Cf., P. D. Bartlett and F. D. Greene, *J. Am. Chem. Soc.*, **76**, 1088 (1954).

converted into the diacetyl derivative VI by treatment with acetic anhydride in the presence of anhydrous sodium acetate. The structure of VI was confirmed by the analytical data and the infrared spectroscopy.

Several unsuccessful attempts were made to resolve the *dl*-VI in its antipodes by using different kind of optical active amines such as quinine, brucine, ephedrine and cinchonine. It was found that the racemic acid VI gives no crystalline salts with these alkaloids. The failure in the optical resolution of VI urged the authors to the synthesis of the isomeric substituted triptycene. 1-Carboxyanthracene (VIII) was derived from 1, 9-benz-10-anthrone by chromic acid oxidation in dilute sulfuric acid[7] followed by the reduction of resulted 1-carboxyanthraquinone (VII) with zinc dust in aqueous ammonia[8]. The reaction of 1-carboxyanthracene (VIII) with *p*-benzoquinone under various conditions in different solvents resulted in the formation of a polymeric substance with high melting point or in the recovery of the starting materials. Treatment of VIII with absolute methanol in the presence of concentrated sulfuric acid yielded methyl ester IX in good yield. It is to be noted that the esterification of VIII with absolute ethanol under the same condition resulted in the recovery of the acid VIII. Two isomeric adducts $X_a$ (m. p. 190.5°C) and $X_b$ (m. p. 206°C) were obtained from the products of the condensation of *p*-benzoquinone with IX. The infrared spectra of these isomers were found to be almost identical over the entire region of wavelength, but a remarkable depression of the mixed melting point (175°C) was observed. It seems to be reasonable to attribute the formation of the two isomers to the *endo*- and the *exo*- addition of *p*-benzoquinone with regard to the benzene ring bearing methoxycarbonyl group yielding $X_a$ and $X_b$ as illustrated in Fig. 2.



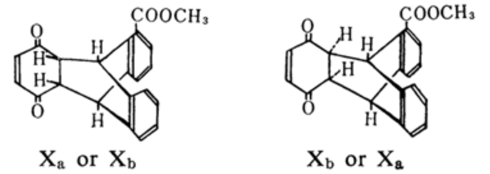


Fig. 2. Possible structures of the isomeric adducts, $X_a$ and $X_b$.

Both of the isomers gave 7-carboxy-2, 5-dihydroxytriptycene (XI) on treatment with a small amount of hydrobromic acid in acetic acid. XI was converted without further purification into the corresponding diacetyl derivative XII by the reaction with acetic anhydride and anhydrous sodium acetate.

7-Carboxy-2, 5-diacetoxytriptycene (XII) was dissolved in hot absolute ethanol and mixed with half the equivalent of brucine tetrahydrate. Well defined colorless needles were obtained on standing the mixture overnight at room temperature. The crystals were recrystallized five times from absolute ethanol to give an optically pure *d*-salt. The salt was decomposed with acetic acid to give pure *d*-acid, m. p. 269∼271°C, $[\alpha]^{13}_{5461} = +96.3°$ (*c* 0.7042, dioxane).

The filtrate was concentrated and treated with acetic acid to remove brucine. The crude *l*-acid thus obtained was converted into the quinine salt. Recrystallization of the salt from 95% ethanol gave the pure quinine salt. The optically pure *l*-acid, $[\alpha]^{24}_{5461} = -93.1°$ (*c* 1.0272, dioxane) was obtained by the decomposition of the pure quinine salt. The infrared spectra of the *d*- and *l*-acid are found to be identical over the entire region of wavelength as recorded in Fig. 3.

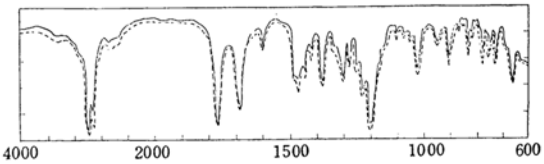


Fig. 3. The infrared spectra of *d*-XII (—) and *l*-XII (- - -) (Nujol mull).

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7) E. B. Barnett, J. W. Cook and H. H. Grainger, *Ber.*, **57**, 1775 (1924).

8) C. Graebe and S. Blumenfeld, ibid., **30**, 1115 (1897).

TABLE I. ADDITION OF *p*-BENZOQUINONE TO 2-ETHOXYCARBONYLANTHRACENE (III)

| Run | III g. | Quinone g. | Molar ratio III : quinone | Solvent (ml.) | Time hr. | Yield of IV | |
|---|---|---|---|---|---|---|---|
| | | | | | | g. | % |
| 1 | 2.1 | 1.4 | 1 : 1.6 | Xylene (35) | 5 | — | Resin |
| 2 | 2.0 | 1.1 | 1 : 1.2 | Benzene (20) | 10 | 0.3 | 10.5 |
| 3 | 4.0 | 2.5 | 1 : 2.5 | Toluene (15) | 15 | 0.4 | 7.0 |
| 4 | 1.8 | 1.1 | 1 : 1.3 | Ligroin (50) + Benzene (10) | 15 | 0.6 | 23.5 |
| 5 | 5.0 | 3.1 | 1 : 1.2 | Ligroin (300) | 12 | — | Recovery |
| 6 | 4.0 | 2.1 | 1 : 1.2 | Benzene (20) | 31 | — | Resin |
| 7 | 5.0 | 5.0 | 1 : 2.3 | Benzene (20) | 5 | 2.6 | 36.6 |
| 8 | 5.9 | 3.26 | 1 : 1.3 | Benzene (20) | 4 | 2.6 | 32 |

The ultraviolet spectrum and the rotatory dispersion of XII will be discussed together with its homologous series in the following paper.

## Experimental**

**2-Carboxyanthraquinone** (I).—Chromium trioxide (60 g.) was added gradually in small portions with constant mechanical stirring to the solution of 2-methylanthraquinone (20 g.) in acetic acid (500 ml.) at 70°C. After all chromium trioxide had been added, the mixture was stirred at 70~80°C for further 5 hr. The reaction mixture changed to dark brown and then the separation of a crystalline precipitate was observed. The reaction mixture was cooled to room temperature and poured into water (3 l.) yielding the crude I. The product was digested repeatedly with a hot diluted aqueous ammonia. Pure 2-carboxyanthraquinone (I), 19.9 g. (88%), m. p. 283~284°C (value in literature, m. p. 284~285°C⁴⁾) was obtained by neutralizing the ammoniacal solution with concentrated hydrochloric acid.

**2-Carboxyanthracene** (II).—The solution of II (19 g.) in a dilute aqueous ammonia (1 l.) was heated on a boiling water bath, zinc dust (50 g.) was added in small portions to the hot solution under vigorous mechanical stirring. A small amount of 28% aqueous ammonia was added occasionally to the reaction mixture. Development of a blood red color was observed on the addition of zinc dust and faded in accord with the progress of reduction. After 3 to 5 hr., the hot reaction mixture was filtered and the filtrate was acidified with concentrated hydrochloric acid to precipitate the crude II, m. p. 273°C. This was recrystallized from ethanol to yield pure II, 10 g. (60%), m. p. 277~278°C, (value in literature, 275~276°C⁵⁾).

**2-Ethoxycarbonylanthracene** (III).—The mixture of II (6 g.), 99% ethanol (500 ml.) and concentrated sulfuric acid (6 ml.) was refluxed for 5 hr. Light yellow crystals, 5.4 g., m. p. 139.5~140°C were obtained on standing the reaction mixture at room temperature. The concentration of the filtrate gave the second crop of III, 1.1 g., m. p. 138~139°C. Total yield, 6.5 g. (95%) (value in literature, m. p. 134°C⁹⁾).

**Formation of the Adduct** (IV).—The results of several experiments on the addition of *p*-benzoquinone to III are summarized in Table I. All the reactions were carried out at the temperature of the boiling point of the particular solvent. The formation of quinhydrone was generally observed throughout these experimental conditions. The experimental condition shown in Run 7 gave the best yield of the adduct. The reaction mixture was cooled to room temperature precipitating yellow crystal mixed with black crystals of quinhydrone. The crystals were filtered, washed with benzene, ethanol and hot water, successively. The crude crystals were digested with light petroleum under reflux to remove the unchaneged III. The yellow powder obtained (2.6 g. (36.5%), m. p. 187.5~188°C) was recrystallized from ethanol to give pure IV, m. p. 188~189°C.

Found: C, 76.71; H, 5.20. Calcd. for $C_{23}H_{18}O_4$: C, 77.08; H, 5.06%.

IR, 1619, 1661 (C=O); 1710 (C=O of ester); 1278 (-C-O-) and 1175 cm$^{-1}$ (-C-O-).

**Isomerization and Hydrolysis of IV to V.**—IV (3.3 g.) was dissolved in acetic acid (30 ml.) under reflux. Hydrobromic acid (47%, 15 ml.) was added dropwise to the solution and the mixture was refluxed for 5 hr. The reaction mixture was poured into ice-water (350 g.) to precipitate crude V. The precipitate was filtered and washed with water yielding crude V, 2.1 g. (68%), m. p. 210~214°C (decomp.).

**Acetylation of V.**—The crude V (2.1 g.) was heated on a boiling water bath for 4 hr. with acetic anhydride (40 ml.) in the presence of a small amount of anhydrous sodium acetate. Water (10 ml.) was

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** All melting points were not corrected.

9) C. Liebermann and A. Bischof, ibid., 13, 47 (1880).

added to the reaction mixture. After heating for several minutes the mixture was poured into water (400 ml.). The precipitate formed was recrystallized twice from acetic acid yielding pure 8-carboxy-2,5-diacetoxytriptycene (VI), 1.9 g. (49.5% from IV), m. p. 235∼237°C.

Found: C, 72.06; H, 4.43. Calcd. for $C_{25}H_{18}\cdot O_6$: C, 72.46; H, 4.38%.

IR, 3200∼2500 (-COOH); 1690 (C=O of aromatic acid); 1766 (C=O of phenolic acetate) and 1187 $cm^{-1}$ (-C-O- of phenolic acetate).

**1-Carboxyanthraquinone (VII).**—1, 9-Benz-10-anthrone was oxidized according to the Bernett's procedure with slight modification. M. p. 286∼289°C, yield, 68%.

**1-Carboxyanthracene (VIII).**—Reduction of VII (22 g.) with zinc dust (40 g.) and diluted aqueous ammonia (50 ml. of 28% aqueous ammonia + 600 ml. of water) with occasional addition of 28% aqueous ammonia (60 ml.) in small portions yielded VIII, 11.8 g. (60%), m. p. 235∼243°C. Recrystallization of the crude VIII from ethanol gave pure VIII, yellow rods, m. p. 242∼244°C (value in literature, m. p. 245°C[8]).

**1-Methoxycarbonylanthracene (IX).**—The mixture of the crude VIII (5.2 g., m. p. 235∼243°C), absolute methanol (150 ml.) and concentrated sulfuric acid (5 ml.) was refluxed for 3 hr. The mixture was kept for several hours at room temperature precipitating IX as yellow plates. The precipitate was filtered and the filtrate was concentrated under reduced pressure yielding second crop of IX. The total yield of the crude IX (m. p. 101∼103°C) was found to be 4.2 g. (77%). This was recrystallized from methanol to give pure IX, m. p. 103.5∼104°C.

Found: C, 81.40; H, 5.40. Calcd. for $C_{16}H_{12}\cdot O_2$: C, 81.34; H, 5.12%.

**Formation of the Adduct (X).**—IX (17.7 g., 0.075 mol.) and *p*-benzoquinone (8.9 g., 0.083 mol.) was added to anhydrous benzene (100 ml.). Immediate development of red color was observed. The mixture was refluxed for 3 hr. and cooled to room temperature. Yellow crystals deposited were separated, washed with a small amount of benzene and hot water successively, yielding the crude low melting isomer ($X_a$), 7.8 g. (32.1%), m. p. 181∼183°C. This was recrystallized from benzene to yield the pure material, m. p. 190.5°C.

Found: C, 76.38; H, 4.70. Calcd. for $C_{22}H_{16}O_4$: C, 76.73; H, 4.68%.

Rapid stream of steam was passed into the mother liquor to remove the unchanged quinone and the solvent. The dried residue was ground down into fine powder and then refluxed with methanol (80 ml.) to remove the unchanged IX. The yellow powder thus obtained (8.8 g. (36.2%), m. p. 182∼186°C, sintering at 175°C) was successively recrystallized from ethyl acetate, acetone and benzene giving the pure high melting isomer ($X_b$), m. p. 206∼206.5°C.

Found: C, 76.48; H, 4.41. Calcd. for $C_{22}H_{16}O_4$: C, 76.73; H, 4.68%.

$X_b$ showed a depression of the melting point on admixture with $X_a$ (mixed melting point, 174∼180°C).

IR, $X_a$: 1667 (C=O of dihydroquinone), 1717 (C=O of ester) and 1283, 1144 $cm^{-1}$ (-C-O- of ester). $X_b$: 1667 (C=O of dihydroquinone), 1717 (C=O of ester) and 1285, 1137 $cm^{-1}$ (-C-O- of ester).

**7-Carboxy-2,5-diacetoxytriptycene (XII.)**—Hydrobromic acid (6 ml., 20% aqueous solution) was added to the hot solution of $X_a$ (6.9 g.) in acetic acid (140 ml.). The mixture was heated on a boiling water bath for 5 hr. The solvent was removed under reduced pressure. The residue was washed with water and dried to give the crude XI, 5.9 g., m. p. 305∼310°C (decomp.) as a light brown crystalline mass. The mixture of the crude XI (5.9 g.), acetic anhydride (30 ml.) and a small amount of anhydrous sodium acetate was heated on a boiling water bath for 1 hr. Water (40 ml.) was added to the cooled reaction mixture. The crude XII, 7 g. (84.2%), m. p. 220∼231°C was obtained on standing the dilute mixture at room temperature for several hours. This substance was recrystallized 4 times from acetic acid to yield the pure XII, 5 g., m. p. 261∼263°C. $X_b$ (14.2 g.) was heated with 20% hydrobromic acid (40 ml.) in acetic acid (280 ml.) to yield the crude XI, 14.7 g. (85.9%), m. p. 245∼250°C. This substance was acetylated and recrystallized twice from acetic acid to give pure XII, 11.1 g. (65%), m. p. 261∼264°C. This substance showed no depression of the melting point on admixture with XII which was derived from $X_a$. The analytical sample of XII was obtained by sublimation under reduced pressure (220∼230°C/1 mmHg).

Found: C, 72.92; H, 4.16. Calcd. for $C_{25}H_{18}\cdot O_6$: C, 72.46; H, 4.38%.

IR, 3200∼2500 (-COOH), 1758 (C=O of acetate), 1685 (C=O of -COOH) and 1188 $cm^{-1}$ (-C-O- of acetate).

**Optical Resolution of *dl*-7-Carboxy-2, 5-diacetoxytriptycene (XII).**—*d-XII.*—The racemic XII (5.950 g., 0.0144 mol.) was dissolved in absolute ethanol (160 ml.). Brucine tetrahydrate (3.344 g., 0.00722 mol.) was added at once to the hot solution and the mixture was refluxed for 30 min. The mixture was allowed to stand overnight at room temperature to precipitate well-defined colorless needles. The mother liquor was separated by decantation and the crystals thus obtained was washed several times with a small amount of ethanol. The crystals obtained were dried under reduced pressure yielding the brucine salt, 5.7 g., $[\alpha]_D^{10} = -7.28°$ (*c* 0.906, acetone). The brucine salt was recrystallized 3 times from absolute ethanol yielding a salt with $[\alpha]_D^{10} = +6.2°$ (*c* 1.46, acetone). This salt was recrystallized from ethanol 2 times affording an optically pure salt with a constant specific rotation $[\alpha]_D^{10} = +7.5°$, (*c* 0.69, acetone).

Found: C, 71.83; H, 5.40; N, 3.39. Calcd. for $C_{48}H_{44}O_{10}N_2$: C, 71.28; H, 5.48; N, 3.46%.

Water (24 ml.) was added to the hot solution of the optically pure salt (2.354 g.) in acetic acid (24 ml.) and the white precipitate formed was filtered, washed with water and dried to yield *d*-XII, 1.088 g., m. p. 263∼266°C. This was recrystallized from acetic acid to give pure *d*-XII, m. p. 269∼271°C, $[\alpha]_{5461}^{13} = +96.3°$, $[\alpha]_{4358}^{13} = +174.8°$ (*c* 0.7042, dioxane).

Found: C, 72.99; H, 4.40. Calcd. for $C_{25}H_{18}O_6$: C, 72.46: H, 4.38%.

*l-XII.*—The above-mentioned mother liquor which was obtained by decantation of the brucine salt was concentrated under reduced pressure. Treatment of the residue with 25% acetic acid gave the optically impure *l*-XII, m. p. 261∼263°C, $[\alpha]^{10}_{5461}=-49.25°$ (*c* 0.873, acetone). Quinine (6.5 g., 0.023 mol.) was added to the hot solution of the crude *l*-XII (9.6 g., 0.023 mol.) in 95% ethanol (120 ml.) and the mixture was refluxed for 30 min. The solution was allowed to stand overnight in a refrigerator. The colorless crystals deposited were filtered, washed with 95% ethanol to yield the crude quinine salt (9.8 g.). This was recrystallized 4 times from 95% ethanol to give optically pure *l*-salt (3.2 g.). This salt showed no definite melting point. Development of yellow color was observed near 140°C and it decomposed gradually at 155∼160°C with frothing. The specific rotation of the pure salt was found to be $[\alpha]^{19.5}_{5791}=-109°$, $[\alpha]^{19.5}_{5461}=-139°$ (*c* 1.028, acetone).

Found: C, 71.59; H, 6.33; N, 3.66. Calcd. for $C_{45}H_{42}N_2O_8\cdot H_2O$: C, 71.40; H, 5.86; N, 3.70%.

The pure quinine salt obtained (3.1 g.) was heated on a water bath with 25% acetic acid (50 ml.) for 30 min. The mixture was kept at room temperature overnight, and the precipitate formed was filtered, washed with 25% acetic acid and water successively, to result in *l*-acid, (1.5 g.), m. p. 252∼263°C. The *l*-acid was recrystallized twice from acetic acid yielding the pure *l*-XII, m. p. 269∼271°C, $[\alpha]^{24}_{5461}=-93.1°$, $[\alpha]^{24}_{4358}=-168.2°$ (*c* 1.0272, dioxane).

Found: C, 71.76; H, 4.46. Calcd. for $C_{25}H_{18}O_6$: C, 72.46; H, 4.38%.

The infrared spectra of the *d*- and *l*-acid were found to be completely identical over the entire region of wavelength.

The authors are grateful to Mr. Masakazu Okumiya and Miss Kiku Koike for performing the elementary analyses. Part of the cost of this research was defrayed from the grant-in-aid of the Ministry of Education, to which the authors thanks are also due.

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