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Reaction of Diazomethane with 2-Acetyl-5,5-diphenyl-2,4-pentadienoic Acid and Related Compounds

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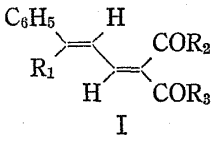
Reaction of 2-acetyl-5,5-diphenyl-2,4-pentadienoic acid (Ia) and its methyl ester (Ib) with diazomethane gave rise to 3-acetyl-3-methoxycarbonyl-4-(β-phenylstyryl)-1-pyrazoline (IIb), which by elimination of nitrogen afforded methyl 2-acetyl-6,6-diphenyl-3,5-hexadienoate (IIIb). Similar reaction of 3-(γ-phenylcinnamylidene)-2,4-pentanedione (Ic) and dimethyl γ-phenylcinnamylidenemalonate (Id) with diazomethane gave the adduct corresponding to 1-pyrazoline derivatives (IIc, IId), respectively. Heating of these compounds afforded denitrogenated products. Similarly, methyl 2-acetyl-5-phenyl-2,4-pentadienoate (Ie) and 3-cinnamylidene-2,4-pentanedione (If) reacted with diazomethane, followed by elimination of nitrogen, to afford methyl 2-acetyl-6-phenyl-3,5-hexadienoate (IIIe) and 3-(4-phenyl-1,3-butadienyl)-2,4-pentadione (IIIf), respectively.

The reaction of the pyrazoline (II) to give compound (III) involves the novel ring-cleavage of the cyclopropane intermediate, such as methyl 1-acetyl-2-(β-phenylstyryl)-cyclopropane-1-carboxylate (IX, where R_1=phenyl, R_2=methyl, R_3=methoxy).

We have reported previously that Carroll reaction of 1,1-diphenyl-2-propynyl acetoacetate gave rise to *cis* and *trans*-2-acetyl-5,5-diphenyl-2,4-pentadienoic acid (Ia and Ia'), methylation of which with methyl iodide afforded the corresponding methyl esters (Ib and Ib').[2] As a continuation of the study we attempted the synthesis of the ester (Ib) by the reaction of the acid (Ia) with diazomethane, and found that the reaction did not give the ester (Ib) but the pyrazoline derivative (IIb), decomposition of which yielded the hexadienoate derivative (IIIb). This reaction had to be considered in view of the reported reactions[3,4] of the thermal decomposition of the pyrazoline (X) to give the cyclopropane (VI) and the olefins (VII, VIII). However, the decomposition of the pyrazoline (IIb), in our case, proceeded in a rather different fashion from those reported in the literatures, which is the purpose of this paper. Furthermore we wish to report the similar reactions of some related compounds of the acid (Ia). Compounds used in this investigation are as follows: 2-acetyl-5,5-diphenyl-2,4-pentadienoic acid (Ia), and

Table I.



I

R	I								
	a	a'	b	b'	c	d	e[a)]	f[a)]	g[a)]
R_1	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	H	H	H
R_2	OH	CH_3	OCH_3	CH_3	CH_3	OCH_3	OCH_3	CH_3	OCH_3
R_3	CH_3	OH	CH_3	OCH_3	CH_3	OCH_3	CH_3	CH_3	OCH_3

a) *cis* and *trans* conformation of compounds (Ie,f,g) are not determined.

1) Location: *Aobayama, Sendai, 980, Japan.*
2) T. Kato and To. Chiba, *Chem. Pharm. Bull.* (Tokyo), **23**, 2263 (1975).
3) T. Auken and K. Rinehart, Jr., *J. Am. Chem. Soc.*, **84**, 3736 (1962).
4) W.M. Jones, *J. Am. Chem. Soc.*, **80**, 6687 (1958); *ibid.*, **81**, 5153 (1959); *ibid.*, **82**, 3136 (1960).

its methyl ester (Ib), 3-(γ-phenylcinnamylidene)-2,4-pentanedione (Ic),[2] dimethyl γ-phenylcinnamylidenemalonate (Id),[2] methyl 2-acetyl-5-phenyl-2,4-pentadienoate (Ie),[5] 3-cinnamylidene-2,4-pentanedione (If),[5] and dimethyl cinnamylidenemalonate (Ig).[6]

When the acid (Ia) was allowed to react with diazomethane at room temperature, a sole product corresponding to 1:1 adduct of Ia and diazomethane was obtained in 98% yield. This compound was assigned as 3-acetyl-3-methoxycarbonyl-4-(β-phenylstyryl)-1-pyrazoline (IIb) on the basis of elemental analysis and spectral data detailed in the experimental part.

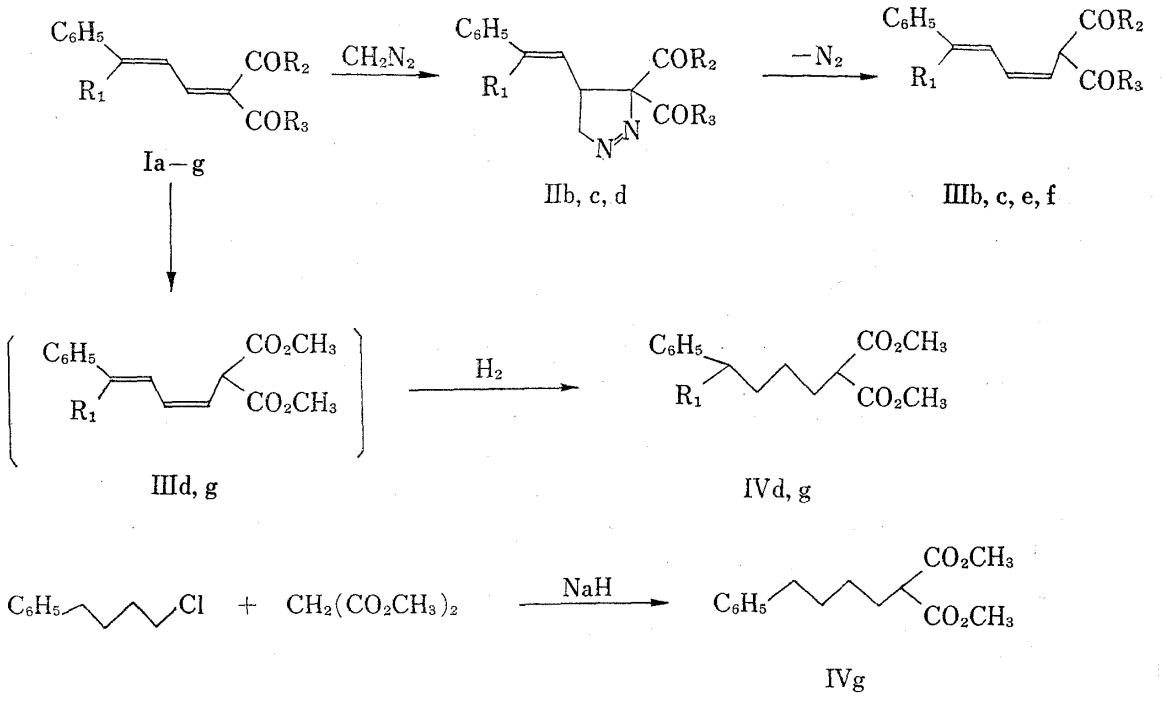
This reaction involves the methylation of the acid (Ia) to give the ester (Ib) in the first stage, followed by the 1,3-cycloaddition to give the 1-pyrazoline (IIb). Actually, the reaction of the ester (Ib) with diazomethane afforded readily the 1-pyrazoline (IIb) in almost quantitative yield.

Heating of compound (IIb) gave rise to the denitrogenized product, which was identified as methyl 2-acetyl-6,6-diphenyl-3,5-hexadienoate (IIIb) on the basis of elemental analysis and spectral data.

Similarly, 3-(γ-phenylcinnamylidene)-2,4-pentanedione (Ic) and dimethyl γ-phenylcinnamylidenemalonate (Id) reacted with diazomethane to give 3,3-diacetyl-4-(β-phenylstyryl)-1-pyrazoline (IIc) and 3,3-dimethoxycarbonyl-4-(β-phenylstyryl)-1-pyrazoline (IId), respectively.

Heating of compound (IIc) afforded 3-(4,4-diphenyl-1,3-butadienyl)-2,4-pentanedione (IIIc). Heating of compound (IId) followed by catalytic reduction gave rise to colorless liquid, which, on the basis of elemental analysis and the spectroscopic data, was assigned as dimethyl 4,4-diphenylbutylmalonate (IVd). In this reaction the denitrogenized intermediate corresponding to compound (III) could not be isolated.

Similar reactions of methyl 2-acetyl-5-phenyl-2,4-pentadienoate (Ie) and 3-cinnamylidene-2,4-pentanedione (If) with diazomethane did not give the adduct corresponding to the 1-pyrazoline (II) but afforded methyl 2-acetyl-6-phenyl-3,5-hexadienonoate (IIIe) and 3-(4-phenyl-1,3-butadienyl)-2,4-pentanedione (IIIf), respectively.



5) N.K. Son, F. Clease, H. Quiniou, and N. Lozach, *Bull. Soc. Chim. France*, **1966**, 3466.
6) P. Heinänen, *Ann. Acad. Sci. Fennicae*, **A59**, 3 (1943).

Lastly, dimethyl cinnamylidenemalonate (Ig) was allowed to react with diazomethane to give an oily product, which, upon catalytic reduction over palladium-charcol, was transformed into dimethyl 4-diphenylbutylmalonate (IVg) in 62% yield.

Compound (IVg) was identified by the comparison of its infrared (IR) spectrum with that of an authentic sample prepared by the reaction of dimethyl malonate with 4-phenylbutyl chloride.

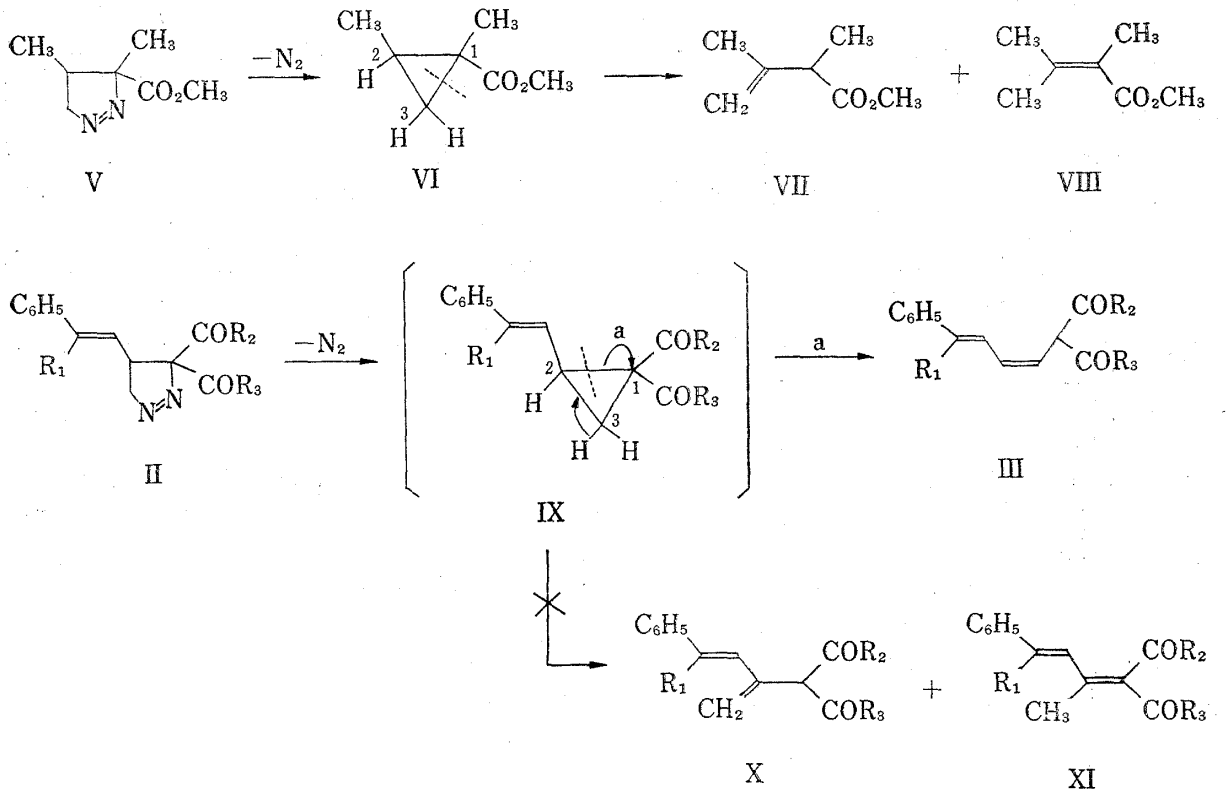


Chart 2

Auken[3] reported that the thermal decomposition of 3-methoxycarbonyl-*cis* (and *trans*)-3,4-dimethyl-1-pyrazoline (V) proceeded with loss of nitrogen to give 1-methoxycarbonyl-*cis* (and *trans*)-1,2-dimethylcyclopropane (V) in addition to unsaturated esters, methyl 2,3-dimethyl-3-butenoate (VII) and methyl 2,3-dimethyl-2-butenoate (VIII). Although several mechanisms have been proposed for the thermal decomposition of the 1-pyrazoline,[4] elimination of nitrogen from compound (V) followed by cyclization or prototropy is considered to give rise to the cyclopropane (VI) or the unsaturated esters (VII and VIII), respectively. The esters (VII and VIII) would also be formed from the cyclopropane (VI) by its ring cleavage between C_1 and C_3.

In our reaction, the unsaturated esters such as compound (X and XI), which are corresponding to compound (VII and VIII), could not be obtained. Though the details of the mechanism of the formation of compound (III) from the 1-pyrazoline (II) are not clear, a likely pathway is shown as follows; elimination of nitrogen gives rise to the cyclopropane (IX) as an intermediate, ring cleavage of which between C_1 and C_2 accompanied with prototropy affords the unsaturated ester (III).

Experimental

3-Acetyl-3-methoxycarbonyl-4-(β-phenylstyryl)-1-pyrazoline (IIb)——1) To a solution of Ia (0.6 g, 0.002 mole) in chloroform (20 ml), was added an ether solution of diazomethane prepared from N-methyl-N-nitroso-

p-toluenesulfonamide (*ca.* 1 g, *ca.* 0.004 mole) according to the literature.[7] The reaction mixture was allowed to stand at room temperature for 2 hr, and condensed at reduced pressure. The residue was purified by recrystallization from ether to give 0.65 g (95%) of colorless prisms, mp 117° (decomp.). *Anal.* Calcd. for $C_{21}H_{20}O_2N_2$ (IIb): C, 72.68; H, 6.04; N, 7.79. Found: C, 72.39; H, 5.79; N, 8.04. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (sh), 1720, 1550. NMR ($CDCl_3$): 2.49 (3H, s), 3.4—3.8 (1H, m), 4.55 (1H, d, J=6 Hz), 4.56 (1H, d, J=8 Hz), 5.52 (1H, d, J=11 Hz), 7.0—7.5 (10H, m).

2) To a solution of Ib (0.62 g, 0.002 mole) in chloroform (20 ml), was added a solution of diazomethane in ether prepared from N-methyl-N-nitroso-*p*-toluenesulfonamide (*ca.* 1 g). Similar treatment as above afforded 0.72 g (98%) of colorless prisms, mp 117° (decomp.), whose IR spectrum was identical with that of sample (IIb) obtained in the above run.

3,3-Diacetyl-4-(β-phenylstyryl)-1-pyrazoline (IIc)——Following the procedure given for compound IIb, Ic (0.58 g, 0.002 mole) was allowed to react with diazomethane, prepared from N-methyl-N-nitroso-*p*-toluenesulfonamide (*ca.* 1 g), at room temperature to give 0.59 g (90%) of the 1-pyrazoline (IIc), mp 109° (decomp.), colorless prisms (from ether). *Anal.* Calcd. for $C_{21}H_{20}O_2N_2$ (IIc): C, 72.68; H, 6.04; N, 7.79. Found: C, 72.39; H, 5.79; N, 8.04. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (sh), 1705, 1545. NMR ($CDCl_3$): 2.32 (6H, s), 3.4—3.9 (1H, m), 4.65 (2H, d, J=6 Hz), 5.45 (1H, d, J=11 Hz). 7.0—7.5 (10H, m).

3,3-Dimethoxycarbonyl-4-(β-phenylstyryl)-1-pyrazoline (IId)——Following the procedure given for IIb, Id (0.35 g, 0.001 mole) was allowed to react with diazomethane, prepared from N-methyl-N-nitroso-*p*-toluenesulfonamide (0.5 g), to give 0.33 g (90%) of IId, mp 106° (decomp.), colorless prisms. *Anal.* Calcd. for $C_{21}H_{20}O_2N_2$ (IId): C, 69.49; H, 5.63; N, 7.91. Found: C, 69.21; H, 5.53; N, 7.69. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1745 (sh), 1730, 1550. NMR ($CDCl_3$): 3.4—3.7 (1H, m), 3.75 (3H, s), 3.81 (3H, s), 4.63 (1H, d, J=6 Hz), 4.68 (1H, d, J=8 Hz), 5.55 (1H, d, J=11 Hz), 7.0—7.5 (10H, m).

Methyl 2-Acetyl-6,6-diphenyl-3,5-hexadienoate (IIIb)——1) A solution of IIb (0.1 g) in toluene (10 ml) was refluxed for 3 hr. After evaporating of the solvent under reduced pressure, the resulting residue was purified by recrystallization from methanol to give 0.07 g (75%) of IIIb, mp 106—107°, colorless prisms. *Anal.* Calcd. for $C_{21}H_{20}O_3$ (IIIb): C, 78.78; H, 6.44. Found: C, 78.72; H, 6.29. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750 (sh), 1735. NMR ($CDCl_3$): 2.10 (3H, s), 3.70 (3H, s), 6.2—7.0 (3H, m), 7.34 (10H, s), 13.18 (1H, s, disappeared by adding D_2O).

2) To a solution of Ib' (0.2 g, 0.0006 mole) in chloroform (10 ml), was added excess diazomethane in ether. After allowing to stand at room temperature for 3 hr, the reaction mixture was evaporated under reduced pressure. The residue (0.13 g) was crystallized by rubbing with a glass rod in petroleum ether and ether, mp 82—88° (decomp.). However, further purification by recrystallization failed. A solution of crude crystals in toluene (15 ml) was refluxed for 1 hr. Removal of the solvent by vacuum distillation gave a crystalline residue, which was recrystallized from ether–petroleum ether to give 0.07 g (32%) of colorless prisms, mp 106—107°, undepressed on admixture with a sample of IIIb obtained in the above run.

3-(4,4-Diphenyl-1,3-butadienyl)-2,4-pentanedione (IIIc)——A solution of IIc (0.1 g) in toluene (10 ml) was refluxed for 3 hr. After evaporation of the solvent, the resulting residue was purified by recrystallization from ethanol to give 0.07 g (78%) of colorless prisms, mp 122—124°. *Anal.* Calcd. for $C_{21}H_{20}O_2$ (IIIc): C, 82.58; H, 6.81. Found: C, 82.86; H, 6.62. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1590, NMR ($CDCl_3$): 2.10 (6H, s), 6.0—6.1 (2H, m), 6.68 (1H, t, J=10 Hz), 7.22 (10H, s), 16.61 (1H, s).

Methyl 2-Acetyl-6-phenyl-3,5-hexadienoate (IIIe)——To a solution of Ie (0.26 g, 0.001 mole) in chloroform (10 ml), was added an ether solution of diazomethane prepared from N-methyl-N-nitroso-*p*-toluenesulfonamide (0.5 g). After allowing to stand at room temperature for 5 hr, the reaction mixture was condensed under reduced pressure. The residue was dissolved in toluene (15 ml), and the solution was refluxed for 3 hr. After evaporation under reduced pressure, the resulting residue was purified by recrystallization from ether–petroleum ether to give 0.12 g (50%) of colorless prisms, mp 58—59°. *Anal.* Calcd. for $C_{15}H_{16}O_2$ (IIIe): C, 73.56; H, 6.87. Found: C, 73.75; H, 6.60. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1650 (sh), 1635. NMR ($CDCl_3$): 2.20 (3H, s), 3.81 (3H, s), 6.3—6.8 (4H, m), 7.2—7.5 (5H, m), 13.22 (1H, s).

3-(4-Phenyl-1,3-butadienyl)-2,4-pentanedione (IIIf)——Following the procedure given for IIIe, If (0.21 g, 0.001 mole) was allowed to react with diazomethane, prepared from N-methyl-N-nitroso-*p*-toluenesulfonamide (0.5 g), to give 0.12 g (51%) of colorless prisms (from ether-petroleum ether), mp 76—77°. *Anal.* Calcd. for $C_{15}H_{16}O_2$ (IIIf): C, 78.65; H, 7.26. Found: C, 78.92; H, 7.06. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1590. NMR ($CDCl_3$): 2.20 (6H, s), 6.1—6.9 (4H, m), 7.1—7.5 (5H, m), 16.69 (1H, s).

Dimethyl 4,4-Diphenylbutylmalonate (IXd)——A solution of IId (0.95 g) in toluene (20 ml) was refluxed for 2 hr. After condensation under reduced pressure, the oily residue was dissolved in ethanol (20 ml). The solution was shaken in hydrogen stream in the presence of 10% palladium-charcol (0.2 g). After absorption of hydrogen (*ca.* 120 ml, *ca.* 2-equivalent), the catalyst was removed by filtration. The filtrate was condensed, and the residual oil was purified by vacuum distillation to give 0.55 g (60%) of a colorless oil, bp 165° (2×10^{-4} mmHg). *Anal.* Calcd. for $C_{21}H_{24}O_4$ (IVd): C, 74.09; H, 7.11. Found: C, 73.82; H, 7.23. IR $\nu_{max}^{CHCl_3}$ cm^{-1}:

7) Th. J. de Boer and H.J. Backer, "Organic Synthesis," Coll. Vol. IV, ed. by N. Rabjohn, John Wiley and Sons, Inc., New York, N. Y. 1963, p. 250.

1740 (sh), 1720. NMR ($CDCl_3$): 0.9—2.3 (6H, m), 3.30 (1H, t, J=7 Hz), 3.64 (6H, s), 3.88 (1H, t, J=7 Hz), 7.20 (10H, s).

Dimethyl 4-Phenylbutylmalonate (IVg)——1) Following the procedure given for IIIc, Ig (1 g, 0.004 mole) was allowed to react with diazomethane, prepared from N-methyl-N-nitroso-*p*-toluenesulfonamide (*ca.* 2 g), followed by heating in toluene to give a colorless oil (crude IIIg) which was dissolved in ethanol (20 ml) and hydrogenated over 10% palladium-charcol (0.2 g). After removal of the catalyst by filtration, the filtrate was condensed. The residue was purified by distillation under reduced pressure to give 0.7 g (61%) of a colorless oil, bp 121° (5×10^{-4} mmHg). *Anal.* Calcd. for $C_{15}H_{20}O_4$ (IV): C, 68.16; H, 7.63. Found: C, 67.93; H, 7.50. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 (sh), 1720. NMR ($CDCl_3$): 1.0—2.2 (6H, m), 2.64 (2H, t, J=8 Hz), 3.37 (1H, t, J=8 Hz), 3.71 (6H, s), 7.20 (5H, s).

2) To a suspension of 50% sodium hydride (0.15 g) in dimethylformamide (10 ml), was added dropwise a solution of dimethyl malonate (0.4 g, 0.003 mole) in dimethylformamide (5 ml) with stirring. Stirring was continued for 10 min until in solution, to which was added dropwise a solution of 4-phenylbutyl chloride[8] (0.59 g, 0.003 mole) in dimethylformamide (6 ml). After refluxing for 3 hr, the reaction mixture was condensed *in vacuo*. The resulting residue was extracted with ether. The ether extract was purified by distillation to give 0.18 g (23%) of colorless oil, bp 121° (5×10^{-4} mmHg), whose IR spectrum was identical in every respect with that of a sample of IVg obtained in the above run.

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8) J.V. Braun, *Chem. Ber.*, 43, 2846 (1910).