ISOLATION AND STRUCTURE DETERMINATION OF LACCAIC ACID F FROM LAC-DYE PRODUCED FROM THAI STICKLAC

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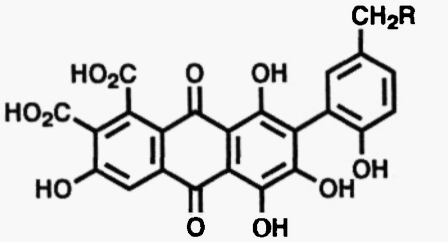
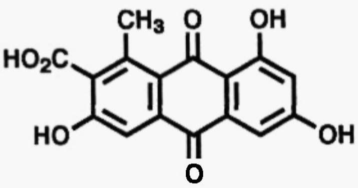
Abstract: A new red pigment, laccaic acid F **6**, was isolated from lac-dye produced from Thai sticklac and the structure was determined by its chemical conversions to anthra[2,3-*b*]benzofuran derivatives **8** *etc*.

Lac-dye is a red pigment isolated from sticklac produced by a tiny insect, *Laccifer lacca*, in India and Southeast Asia and has been used for over a thousand years. Chemical studies of lac-dye have been carried out for the past century and a half, and five colored components, laccaic acid A **1** (1), B **2** (1a, 2), C **3** (1a, 3), D **4** (4), and E **5** (3), have been isolated and their structures were determined. Since all of these chemical studies are related solely to the Indian sticklac, we started our chemical study on lac-dye from Thailand. Recently, we have found that the major components of lac-dye produced from Thai sticklac were also laccaic acid



1 Laccaic acid A $R=CH_2NHCOCH_3$
2 Laccaic acid B $R=CH_2OH$
3 Laccaic acid C $R=CHNH_2CO_2H$
5 Laccaic acid E $R=CH_2NH_2$
6 Laccaic acid F $R=CH_2OCOCH_3$



4 Laccaic acid D

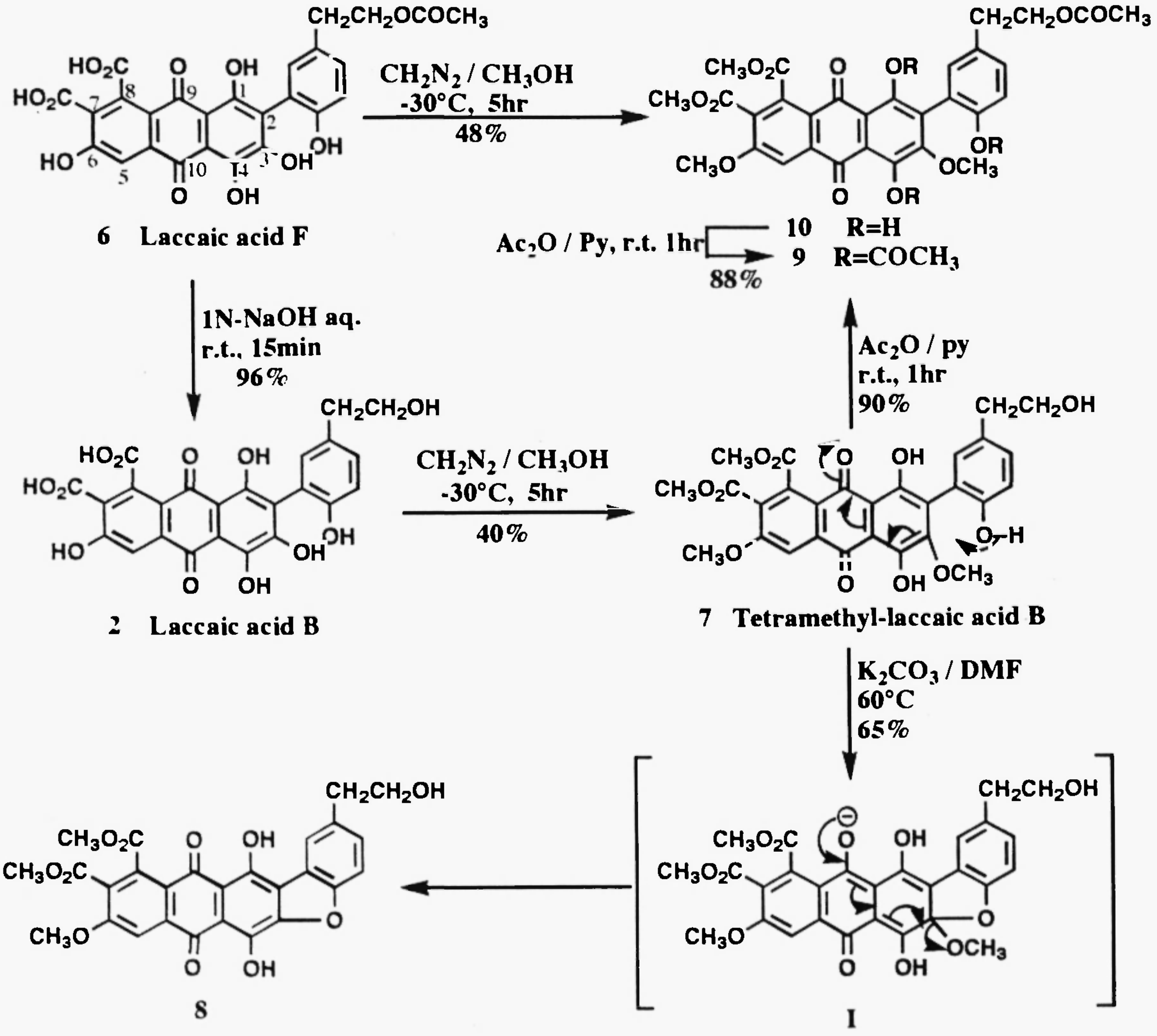
A, B, and C similar to those from Indian sticklac. In this paper, we describe a new red-colored component, laccaic acid F **6**, isolated from Thai lac-dye.

We separated Thai lac-dye (5, 6) by a combination of column chromatography on silica gel and ion exchange resin to obtain crude laccaic acid A **1**, B **2**, and C **3**. On the silica gel TLC plate of the crude laccaic acid B fraction (about 20% from Lac-dye), another non-polar red spot other than laccaic acid was also observed. The new colored component was isolated by a combination of silica gel column [1% $(CO_2H)_2$ / EtOAc], preparative TLC (1% $(CO_2H)_2$ / EtOAc) and HPLC (Namsil ODS-9, 50% MeOH / H_2O). The new component contained about 0.9% of crude laccaic acid B.

Since its spectral data and Rf-value on TLC plate indicated that this compound is a new member of laccaic acids, we named it laccaic acid F. UV and ^{1}H-NMR spectra of **6** were very similar to those of laccaic acid B **2** except for an additional methyl signal at δ 2.01 ppm and a methylene signal appeared at rather lower field [4.23 ppm (2H, t)] than that of **2**. From these data we concluded the structure of laccaic acid F **6** (7) to be a terminal *O*-acetate of laccaic acid B **2**. As might be expected, hydrolysis of laccaic acid F **6** in 1N NaOH solution at 25°C for 15min. afforded laccaic acid B **2** in 96% yield.

For our study of the chemical reactivity and structure-activity relationship, we developed a new methylating method using diazomethane at low temperature. Laccaic acid B **2** was selectively methylated with diazomethane in methanol at -30°C to give tetramethyl-laccaic acid B **7** (8) in 40% yield. The methylated positions of **7** were determined by its spectroscopic analysis (^{1}H, ^{13}C, ^{1}H-^{1}H cosy NMR, *etc.*) and sequential cyclization reaction. Tetramethyl-laccaic acid B **7** was easily cyclized, under loss of methanol, with K_2CO_3 in DMF at 60°C to afford anthra[2,3-*b*]benzofuran derivative **8** (9, 10) in 65% yield. Acetylation of **7** with Ac_2O / Py gave the correspoinding tetraacetate **9** (11) in 90% yield.

Selective methylation of laccaic acid F **6** with diazomethane at -30°C in a methanol-ether solution also afforded tetramethyl-laccaic acid F **10** (12) in 48% yield. Acetylation of **10** with Ac_2O / Py gave the corresponding triacetate (88%) which was identical with tetraacetyl-tetramethyl-laccaic acid B **9** derived from laccaic acid B **2**. Consequently, the structure of laccaic acid F was determined to be a terminal *O*-acetate of laccaic acid B **2** as shown in **6**. Laccaic acid F **6** is an extremely unstable component of laccaic acids and hydrolyzed to afford laccaic acid B **2** after 2h even in neutral water at 60°C. Further chemical study of laccaic acids is now in progress.



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(6) The purified Thai lac-dye (a mixture of laccaic acids) is commercially available from Gifu Shellac Co. Ltd., Higashiuzura, Gifu 500, Japan.

(7) **6**: ^{1}H-NMR (CD$_3$OD) δppm 2.01 (3H, s), 2.86 (2H, t, J=7.0), 4.23 (2H, t, J=7.0), 6.85 (1H, d, J= 8.3), 7.04 (1H, d, J=2.1), 7.11 (1H, dd, J=8.3 & 2.1), 7.79 (1H, s); UV (CH$_3$OH) λ_{max} nm (ε) 224 (49,400), 290 (52,900), 340 sh (20,400), 490 (16,700); IR (KBr) νcm^{-1} 3,370, 1,724, 1,573, 1,449, 1,412, 1289.

(8) **7**: ^{1}H-NMR (CDCl$_3$) δppm 2.81 (2H, t, J=6.8), 3.80 (2H, t, J=6.8), 3.84 (3H, s), 3.94 (3H, s), 3.95 3H, s), 4.10 (3H, s), 6.92 (1H, d, J=8.2), 7.02 (1H, d, J=2.7), 7.17 (1H, dd, J=8.2 & 2.7), 7.96 (1H, s); UV (CH$_3$OH) λ_{max} nm (ε) 223 (36,400), 278 (41,300), 340 sh (7,400), 497 (12,500), 535 (8,900); IR (KBr) νcm^{-1} 3,450, 2,946, 1,734, 1,573, 1,403, 1,261.

(9) D. Hu, Y. Shinoda & S. Nakatsuka, *Heterocyclic Commun.* in press

(10) **8**; ^{1}H-NMR (CDCl$_3$) δppm 3.06 (2H, t, J=7.2), 3.92 (2H, t, J=7.2), 3.96 (3H, s), 4.03 (3H, s), 4.11 (3H, s), 7.52 (1H, dd, J=8.2 & 2.1), 7.66 (1H, d, J=8.2), 7.99 (1H, s), 8.16 (1H, d, J=2.1); UV (CH$_3$OH) λ_{max} nm 223, 284.5, 340, 492.5, 524, 560.

(11) **9**: ^{1}H-NMR (CDCl$_3$) δppm 2.03 (3H, s), 2.09 (2H, s), 2.11 (3H, s), 2.51 (3H, s), 2.96 (2H, t, J=6.6), 3.53 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 4.04 (3H, s), 4.28 (2H, m), 7.19 (1H, br s), 7.23 (1H, d, J=8.2 & 7.33 (1H, br. d, J=8.2), 7.23 (1H, s); UV (CH$_3$OH) λ_{max} nm (ε) 208 (31,000), 280 (27,000), 340 (5,500); IR (KBr) νcm^{-1} 2,964, 1,780, 1,743, 1,688, 1,587, 1,353, 1,192.

(12) **10**: ^{1}H-NMR (CDCl$_3$) δppm 2.04 (3H, s), 2.92 (2H, t, J=7.0), 3.85 (3H, s), 3.94 (3H, s), 3.96 (3H, s), 4.09 (3H, s), 4.28 (2H, t, J=7.0), 7.01 (1H, d, J=8.2), 7.14 (1H, d, J=2.1), 7.23 (1H, dd, J=8.2 & 2.1), 7.94 (1H, s).

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