in nonribosomal peptide biosynthesis[6], promizing practical value of alkylthiol esters in peptide synthesis[7].

In order to detect the possible occurrence of racemization during coupling of alkylthiol esters with amino functions, we investigated the supersensitive YOUNG test[8] involving the synthesis of Bz-Leu-Gly-OEt[9] from Bz-L-Leu-SEt and H-Gly-OEt. Little, if any, racemization was observed during the coupling. The reaction proceeds smoothly when pivalic acid or 2-hydroxypyridine is present as a bifunctional catalyst[10] resembling nonribosomal peptide biosynthesis. Preferred solvents are pyridine, dimethylformamide, and benzene. A typical procedure is as follows. A mixture of Bz-L-Leu-SEt[2] (0.279 g, 1 m*M*), H-Gly-OEt·HCl (0.167 g, 1.2 m*M*), pivalic acid (0.10 g, 1 m*M*), and triethylamine (0.17 g, 1.7 m*M*) in pyridine (2 ml) was stirred at 20° for 21 h. Benzene-ethyl acetate (1:1, 50 ml) was added to the reaction mixture, which was worked up with aqueous acid (5% HCl or 5% citric acid) and saturated aqueous $NaHCO_3$ and dried. The evaporated residue was purified by a silica gel column chromatography with *n*-hexane and ethyl acetate (9:1→1:1) to give Bz-Leu-Gly-OEt (0.249 g, 89%), mp 158–162°, $[\alpha]_D^{20}$–32.7° (c = 2.9, EtOH), corresponding to 96% L-isomer[11]. When no bifunctional catalyst was present under similar reaction conditions, Bz-Leu-Gly-OEt was obtained in poor yield with the recovery of most of the starting Bz-L-Leu-SEt. Furthermore none of Bz-Leu-Gly-OEt was produced when Bz-L-Leu-OMe was used in place of Bz-L-Leu-SEt, proving the functional specificity in the method.

A dual role of alkylthiol esters as protective and reactive functions[12] was examined on the IZUMIYA racemization test[13] which involves coupling of Boc-Gly-L-Ala-SEt with H-L-Leu-OBu^t. Z-L-Ala-OH was condensed with ethanethiol using DEPC[2] in the presence of triethylamine in dimethylformamide to give Z-L-Ala-SEt, mp 42–43°, $[\alpha]_D^{20}$–12.2° (c = 2.0, $CHCl_3$), in 94% yield. Deblocking with hydrogen bromide in acetic acid afforded H-L-Ala-SEt·HBr in 96% yield, which was coupled with Boc-Gly-OH by means of DPPA and triethylamine in dimethylformamide[4,5] to yield Boc-Gly-L-Ala-SEt, mp 76–79°, $[\alpha_D^{20}]$–64° (c=2.2, EtOH), in 82% yield. Condensation of the thiol ester with H-L-Leu-OBu^t (2 equiv) in the presence of pivalic acid in pyridine or dimethylformamide at 20° for 21 h as in the YOUNG test gave Boc-Gly-L-Ala-L-Leu-OBu^t in 90% yield, which was treated with trifluoroacetic acid to furnish H-Gly-L-Ala-L-Leu-OH. No peak of H-Gly-D-Ala-L-Leu-OH was detected by the amino acid analyzer[13], revealing that the coupling of the peptide alkylthiol ester with the amino acid ester in the presence of the bifunctional catalyst proceeds without any racemization.

Additional evidence of utility of alkylthiol esters was obtained by the preparation of Boc-L-Trp-L-Leu-L-Asp-L-Phe-NH_2 bearing the same gastric acid secretory activity as that of diagnostically useful tetragastrin Boc-L-Trp-L-Met-L-Asp-L-Phe-NH_2[14]. Boc-L-Asp(OBzl)-SEt, quantitatively obtained from Boc-L-Asp(OBzl)-OH and ethanethiol using either DEPC or DPPA method[2], was deblocked with 2.3 *N* HCl-ethyl acetate to give H-L-Asp(OBzl)-SEt·HCl. Stepwise addition of Boc-L-Leu-OH·H_2O and Boc-L-Trp-OH using DEPC[3,5] as a coupling reagent and 2.3 *N* HCl-ethyl acetate as a deprotecting reagent afforded Boc-L-Trp-L-Leu-L-Asp(OBzl)-SEt, mp 117–119°, $[\alpha]_D^{20}$–48.9° (c=0.97, EtOH), in 46% yield from Boc-L-Asp(OBzl)-SEt. Coupling of the tripeptide derivative with H-L-Phe-NH_2 in dimethylformamide in the presence of pivalic acid as a catalyst gave Boc-L-Trp-L-Leu-L-Asp(OBzl)-L-Phe-NH_2 in 47% yield. Hydrogenolysis over 5% Pd-C afforded Boc-L-Trp-L-Leu-L-Asp-L-Phe-NH_2[15], mp 215–219° (dec), $[\alpha]_D^{20}$–42° (c= 0.18, DMF). Inertness of the β-benzyl ester group of Asp toward the coupling reaction exhibits the functional specifity of the process.

The synthetic simulation of nonribosomal peptide biosynthesis thus highlights a dual role of alkylthiol esters as both protective and reactive functions in peptide synthesis, which may promise the added variation in laboratory strategy for the peptide synthesis.

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[11] Lit.[8] mp 156.5–157°, $[\alpha]_D^{20}$ – 34° (c = 3.1, EtOH).

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The Structure of Durantoside IV Tetraacetate

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Summary. Durantoside IV tetraacetate was isolated from *Duranta repens* Linn and identified by physical and chemical evidence.

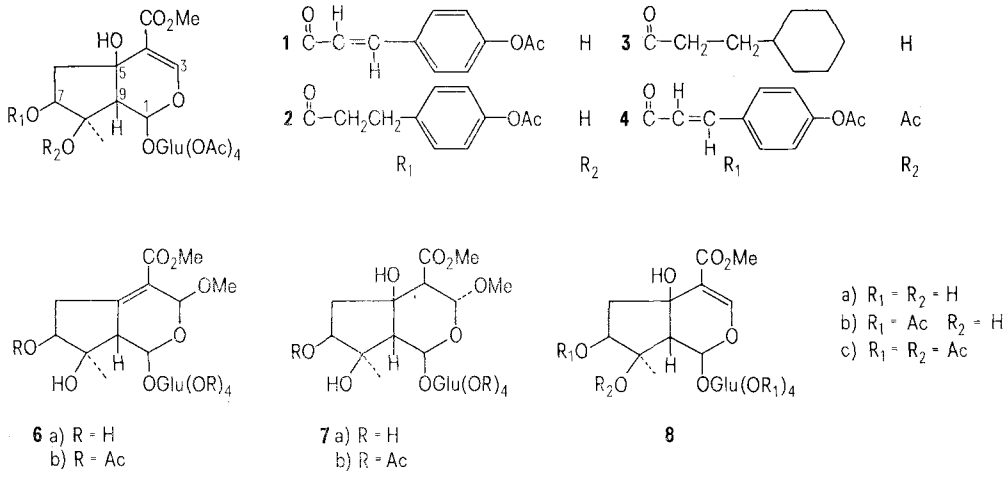
Material and methods. We have isolated several bitter principles from the ethanol extractive of the leaves of *Duranta repens* Linn, and one component, durantoside IV tetraacetate, was purified by acetylation.

Results and discussion. Durantoside IV tetraacetate 1 forms colorless needles, m.p. 215–217°, $(\alpha)_D$ –47.9° $C_{36}H_{42}O_{19}$, λ_{max} 220.5, 225 and 284 nm. The UV-spectrum (λ_{max} 225 nm) and the NMR-spectrum (τ_{CDCl_3} 2.71, s,

–OCOC=CH–O–) suggests the presence of an iridoid structure[2]. It contains 4 acetyl groups, a *p*-acetoxy-t-cinnamonyl group, a tertiary methyl group (τ_{CDCl_3} 8.79) attached on the carbon which carries the hydroxyl group, a methylene group, 3 methine protons, 2 hydroxyl groups, and carbomethoxy group as indicated by NMR- and IR-spectra.

Hydrogenation of **1** gave **2**, m.p. 162–163°, λ_{max} 223 nm. Further reduction with PtO_2 in EtOAc, **2** afforded **3** (m.p. 168–170°). Like other naturally occurring iridoids, **1** is converted by acid hydrolysis into glucose and black product. On acetylation with Ac_2O-pyridine at 75° for 5 h, **1** afforded **4** (m.p. 168–170°; ν_{max} 3550; τ_{CDCl_3} 8.56 (C_8–CH_3)). The remaining tertiary hydroxyl group in **4** was located at C_5 due to steric hindrance[3].

The tertiary methyl group is located at C_8 from biogenetic reasons[4]. Based on the NMR-signals at τ_{CDCl_3} 7.53 (2H, d, J=3.5 Hz) and 5.15 (1H, t, J=3.5 Hz) in **1** and 7.63 (2H, d, J=3 Hz) and 5.16 (1H, t, J=3 Hz) in **3** and the result of double resonance experiments, the partial structure $=C-CH_2-\underset{\underset{OCOR}{|}}{CH}-C=$ was confirmed unambiguously.



As **1** was allowed to react with NaOMe in MeOH under room temperature, following by neutralization with excess amberlite IR-120, 5 (*p*-hydroxy-methyl-t-cinnamate) and 3 glucosides, **6a**, **7a**, and **8a** were obtained. If the neutralization was adjusted to pH 6–7, only 3 hydrolytic products, **5**, **7a**, and **8a** were recovered. Compound **6a** showed a conjugated ester (λ_{max} 223.5 nm) and could be prepared quantitatively by treating **8a** in MeOH with amberlite IR-120 at 55°. The additional new signals in **6a** at τ_{D_2O} 6.47 (3H, s, $-OCH_3$) and 4.57 (1H, bs, $-O-\underset{\underset{OCH_3}{|}}{CH}-C=C-$) appeared instead of τ_{CDCl_3} 2.71 in **1**. The configuration of C_3H can be assigned in α-axial orientation by that C_3H coupled with C_6H_1, C_6H_2 and C_9H across 5 bands (homoallylic coupling). On acetylation of **6a**, **6b** was obtained. **7a** shows an isolated ester absorption and its NMR-spectrum exhibits a new 3 protons singlet at τ_{D_2O} 6.53 and 2 protons at τ_{D_2O} 6.59 and 5.02 (J=10 Hz, $-\underset{\underset{OCH_3}{|}}{OCH}-CH-COOMe$). The formation **7a** was caused by the addition of methanol to the conjugated double bond of **8a**. Further evidence was the formation of **7a** by the treatment of **8a** with NaOMe in MeOH for 3 days. The attack of a methoxide ion to **8a** from α-side is acceptable[5]. The physical data of **8a** (major product) were in good agreement with the structure. Pentaacetate **8b** (m.p. 204–6°, major) and hexaacetate **8c** (m.p. 196–8°) prepared from **8a** are identical with lamiide pentaacetate and hexaacetate[6], respectively. Therefore the structure of durantoside IV tetraacetate should be represented as formula **1**. Recently, lamiide and 3 new iridoids, durantoside I, II, and III, were isolated from same source[7] and identified by NMR and mass spectrometry. We have also isolated durantoside I tetraacetate (m.p. 227–8°), pentaacetate (m.p. 211– to 212°), and durantoside II tetraacetate (m.p. 231–233°) from the same extract.

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