1362, 1278, 1052, 1000, and 887 cm^{-1}); uv λ_{max} (cyclohexane) 232 mμ (log ε 4.17) [lit.[2] λ_{max} 233 (log ε 4.2)]; (C_2DCl_3) δ 1.27 [s, 6 H; $(CH_3)_2CO$], 1.7–2.6 (m, 3 H), 4.52 (broad d, 1 H, C=CCHCO, bridge H), *ca.* 4.81 (m, 2 H; C=CH_2), *ca.* 6.10 (m, 2 H; conj CH=CH). (2) *p*-Isopropenyltoluene (X): $n^{25}D$ 1.5325 (lit. $n^{25}D$ 1.5290,[11] $n^{20}D$ 1.5350[12]); uv λ_{max} (cyclohexane) 245 mμ (log ε 4.08) [lit.[13] λ_{max} 245 mμ (log ε 4.13)]; nmr ($CDCl_3$) δ 2.14 (d, 3 H, J = *ca.* 1 cps; CH_3C=C), 2.34 (s, 3 H; CH_3Ar), 5.10 and 5.34 (two m, 2 H; CCH_2), *ca.* 7.26 (m, 4 H; ArH); ir spectrum identical with that reproduced in the literature.[13] (3) Carvone (XI) was identified by glpc retention time and ir and nmr spectral comparisons with an authentic sample. (4) Carvacrol (XII) was identified by ir and nmr spectral comparisons with an authentic sample. In a second experiment, 5.0 g of VIII gave 1.22 g of the product mixture.

B. XIV.—In the same manner described for VIII, a mixture of 2.68 g of XIV and 0.06 g of β-naphthalenesulfonic acid in 20 ml of di-*n*-butyl phthalate was heated at 100-mm pressure under nitrogen. Work-up and distillation gave 0.58 g of yellow oil. Analysis by glpc indicated the oil to be primarily XI (65%) with lesser amounts of II (8.2%), X (8.5%), and XII (18.3%).

Registry No.—VIII, 20178-11-4; XIV, 20178-12-5.

(11) G. B. Bachman and H. M. Hellman, *J. Amer. Chem. Soc.*, **70**, 1772 (1948).
(12) V. N. Ipatieff, H. Pines, and R. C. Olberg, *ibid.*, **70**, 2123 (1948).
(13) M. J. Murray and W. S. Gallaway, *ibid.*, **70**, 3867 (1948).

A Novel Procedure for the Removal of *o*-Nitrophenoxyacetyl Amino-Protecting Groups[1]

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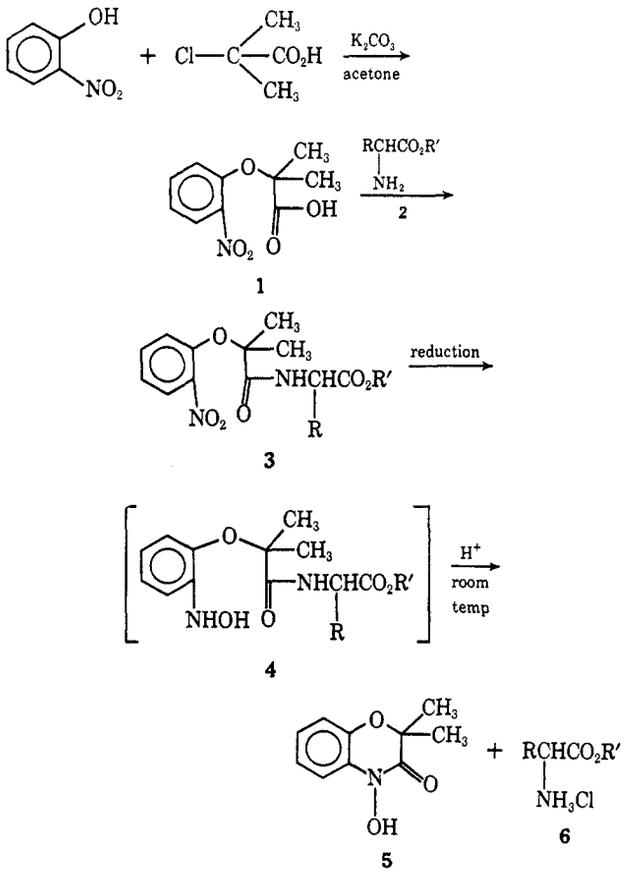
Several years ago, Holley and Holley[2] introduced the *o*-nitrophenoxyacetyl moiety as an amino-protecting group during the synthesis of peptides. They reported that this type of blocking group is removed by thermal cyclization of the corresponding *o*-aminophenoxyacetyl derivative which is obtained by catalytic reduction. Formation of the lactam of *o*-aminophenoxyacetic acid occurs with concomitant liberation of the amino group on the peptide.

We have found that the removal of the *o*-nitrophenoxyacetyl protecting group is facilitated by partial reduction of the nitro group to a hydroxylamino moiety. The deblocking is accomplished at room temperature, does not require a noble metal catalyst, and is unaffected by sulfur-containing amino acids. The procedure is illustrated in Scheme I.

The specific blocking group used in this work was derived from α-methyl-α-(*o*-nitrophenoxy)propionic acid (**1**).[3] It is easily coupled to an amino acid ester (**2**) *via* either the acid chloride or carbodiimide procedure. The amino-protected derivative (**3**) was named an MNP-amino acid ester. It has an infrared spectrum which contains a very characteristic peak at 1600 cm^{-1} (apparently an aromatic stretching band) among the other expected absorptions.

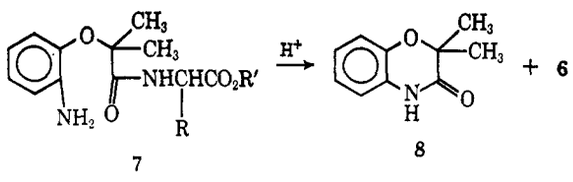
(1) Presented at the 20th Southeastern Regional Meeting of the American Chemical Society, Tallahassee, Fla., Dec 4, 1968.
(2) R. W. Holley and A. D. Holley, *J. Amer. Chem. Soc.*, **74**, 3069 (1952).
(3) D. A. Johnson, C. A. Panetta, and R. R. Smith, *J. Org. Chem.*, **31**, 2560 (1966).

SCHEME I



The reduction of the MNP-amino acid ester **3** to the *o*-hydroxylamino derivative (**4**) is accomplished using either aluminum amalgam or zinc and ammonium chloride in aqueous tetrahydrofuran. The former method was the less preferred one because it appeared, by tlc, to give a much larger amount of the *o*-aminophenoxyacetyl derivative (**7**) than did the latter. α-Methyl-α-(*o*-aminophenoxy)propionyl glycine ethyl ester (**7**, R = H, R′ = Et) was prepared by using a 10:1 molar ratio of aluminum amalgam to **3** (R = H, R′ = Et) and was characterized. According to tlc, **7** (R = H, R′ = Et) was found to deblock (Scheme II) much

SCHEME II



more slowly than did the ferric chloride positive[4] reduction product which is apparently the corresponding hydroxylamino derivative **4**, (R = H, R′ = Et). A proportionately smaller amount of aluminum amalgam afforded a larger yield of **4** (R = H, R′ = Et) from **3** (R = H, R′ = Et).

Compound **4** was not isolated, but a solution of it was acidified with alcoholic hydrogen chloride solution and stored at room temperature. The hydrochloride of the amino acid ester (**6**) crystallized and was separated

(4) R. L. Shriner, R. C. Tuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, John Wiley & Sons, Inc., New York, N. Y., 1964, p 135.

TABLE I

THE RESULTS OF ZINC AND AMMONIUM CHLORIDE DEBLOCKING EXPERIMENTS ON SEVERAL MNP-AMINO ACID ESTERS 3

MNP-amino acid ester 3			% yield of deblocked amino acid ester HCl	Mp (lit.[a] value), °C	[α] of product ([α] of starting material)
R	Optical isomer	R′			
H-(glycine)		Et	72.8	142.5–143.0 (144)	
$(CH_3)_2CHCH_2$-(leucine)	L	Et	41.6	120.5–126.0 (134)	
CH_3-(alanine)	L	Et	57.0		
CH_3-(alanine)	L	Me	44.6	101.0–104.0 (109)	
$C_6H_5CH_2$-(phenylalanine)	L	Me	46.7	158.0–159.0 (159)	+1.83° (*c* 0.5, MeOH) (+1.84°)
$(CH_3)_2CH$-(valine)	L	Me	78.1	164.0–167.0 (168)	+2.42° (*c* 0.5, MeOH) (+2.31°)

[a] See ref 7, pp 929–932.

from the reaction mixture by filtration. The by-product N-hydroxylactam (**5**) was isolated, in some cases, by evaporation of the filtrate.

Several MNP-amino acid esters were prepared and subsequently deblocked by the zinc and ammonium chloride procedure. The results of these experiments are summarized in Table I. Except in the case of glycine ethyl ester (**2**, R = H, R′ = Et) all of the MNP-protected derivatives **3** were made from the L-isomer of the corresponding amino acid ester hydrochloride. A check of the specific rotations of the methyl esters of valine and phenylalanine before and after blocking and deblocking experiments were completed showed essentially no change, indicating that racemization probably does not occur during these processes. The homogeneity of the amino acid ester hydrochloride products was established by tlc and the melting point and R_f of each product was compared with known values in order to prove identity.

Experimental Section[5]

The thin layer chromatograms of the amino acid ester hydrochlorides **6** were run on microscope slides coated with a 250-μ layer of Camag D-5 silica gel. Spotting was performed using 0.5–1.0 μl of a 1% solution and the solvent system was benzene–EtOH–NH_4OH (60:39:1). The thin layer chromatograms of the MNP-amino acid esters **3** and the reduction products **4**, **5**, **7**, and **8** were run on slides coated with neutral aluminum oxide G (E. Merck). The solvent system was benzene–EtOAc (70:30). The zones were detected as yellow areas on a purple background after spraying with a 0.5% aqueous $KMnO_4$ solution sometimes followed with heating. Cited R_f values are approximate figures.

General Procedure for the Preparation of MNP-Amino Acid Esters 3.—The general procedure is illustrated by the preparation of MNP-Gly-OEt[6] *via* the acid chloride method and by the preparation of MNP-Phe-OMe[6] *via* the carbodiimide process.

MNP-Gly-OEt (3, R = H, R′ = Et).—The acid chloride of **1** was prepared from 5.0 g (22.2 mmol) of **1**, 25 ml (0.344 mol) of $SOCl_2$, and 0.3 ml of DMF according to a published procedure.[3] A solution of the acid chloride in 20 ml of CH_2Cl_2 was added during a 10-min period to a cooled and stirred mixture of 3.10 g (22.2 mmol) of H-Gly-OEt·HCl,[6] 10 ml (7.25 g, 71.6 mmol) of triethylamine, and about 200 ml of CH_2Cl_2. The resultant mixture was stirred at room temperature for 16 hr and was then diluted with 100 ml of water. The phases were thoroughly mixed, after which the organic layer was washed with water at pH 1.5 and then with neutral water. The rich CH_2Cl_2 solution was dried ($MgSO_4$) and concentrated under reduced pressure to an amber oil which easily crystallized. One recrystallization from a warm mixture of benzene and petroleum ether (bp 30–60°) afforded 3.81 g (55.3%) of **3** (R = H, R′ = Et) from which an analytical sample was obtained after a second recrystallization: mp 102.5–104.0°; ir (CH_2Cl_2) 1730 (ester C=O), 1670 (amide I), 1520 (amide II), 1535 and 1360 (NO_2), and 1600 (aromatic stretching); nmr ($CDCl_3$) consistent with kind and number of protons present in **3** (R = H, R′ = Et); tlc showed the product to be homogeneous.

Anal. Calcd for $C_{14}H_{18}N_2O_6$: C, 54.19; H, 5.85; N, 9.03. Found: C, 53.91; H, 5.83; N, 9.10.

MNP-Phe-OMe (3, R = $C_6H_5CH_2$, R′ = Me).—To a solution of 2.16 g (10 mmol) of H-L-Phe-OMe·HCl,[6] 40 ml of acetonitrile, and 1.4 ml (1.01 g, 10.0 mmol) of triethylamine was added in succession, 2.25 g (10 mmol) of **1** and 4.24 g (10 mmol) of 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-*p*-toluenesulfonate (Aldrich Chemical Co.). A solution was the immediate result, but a solid separated slowly while the mixture was stirred at room temperature for 2 days. The solvent was removed under reduced pressure and the residue was distributed between 1.2 *N* aqueous HCl and ether (about 50 ml and 100 ml, respectively). The ether layer was washed consecutively with water, 1 *N* aqueous Na_2CO_3, and water and was dried ($MgSO_4$). Removal of the ether left a yellow oil **3** (R = $C_6H_5CH_2$, R′ = Me) which weighed 0.972 g (25.2%): ir (CH_2Cl_2) 1735 (ester C=O), 1665 (amide I), 1510 (amide II), 1537 and 1348 (NO_2), and 1600 (aromatic stretching); tlc showed the product to be essentially homogeneous.

General Procedure for the Deblocking of MNP-Amino Acid Esters 3.—The general procedure is illustrated by the removal of the MNP-protecting group from MNP-Gly-OEt.[6]

The Deblocking of MNP-Gly-OEt (3, R = H, R′ = Et).—A mixture of 0.31 g (1.0 mmol) of **3** (R = H, R′ = Et), 0.082 g (1.53 mmol) of NH_4Cl, 9 ml of THF, and 3 ml of water was vigorously stirred at room temperature while 0.654 g (10 mmol) of zinc dust was added in one portion. After 35 min a thin layer chromatogram was run on the reaction mixture. The zone for the starting material (MNP-Gly-OEt, $R_f \sim 0.9$) was completely missing, but two new and slower zones were visible. The spot at $R_f \sim 0.6$ was faint and small and was later shown to be **7** (R = H, R′ = Et). The spot at $R_f \sim 0.3$ was quite large and intense and was assumed to be **4** (R = H, R′ = Et). Vigorous agitation was continued for a total of 48 min, whereupon the mixture was filtered and the filtrate was distilled under reduced pressure until all of the THF was removed. The aqueous residue was extracted thrice with ether and the resultant ethereal solution was dried ($MgSO_4$) and diluted with 1.5 ml of EtOH. The rich solution was then acidified (to pH ~0) with alcoholic HCl solution. Crystals of **6** (R = H, R′ = Et) began to separate almost immediately. The mixture was stored at ambient temperature for 2½ hr (other amino acid ester hydrochlorides completely precipitated in up to 24 hr) and was then filtered in order to separate 0.1014 g (72.8%) of gray-white crystals: mp 142.5–143.0° (lit.[7] mp 144°); tlc showed the product to be homogeneous and to have an R_f value identical with that of authentic H-Gly-OEt·HCl.[6]

(5) Melting points are corrected. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

(6) Nomenclature according to E. Schröder and K. Lübke, "The Peptides," Vol. 1, Academic Press, New York, N. Y., 1965, p xiii.

(7) J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 2, John Wiley & Sons, Inc., New York, N. Y., 1961, p 932.

The ethereal filtrate from above gave a deep purple color when a sample of it in EtOH was treated with a few drops of 5% aqueous $FeCl_3$ solution. This test is indicative of the presence of a hydroxamic acid (such as **5**).[4] The solution was distilled at reduced pressure in order to remove the ether solvent, and the dark oily residue was crystallized from hot aqueous EtOH. The colored solid thus obtained, **5**, gave a positive test with $FeCl_3$ solution and was identical with an authentic sample of **5**[3] when these samples were compared by tlc. The yield of **5** was 84 mg (43.5%).

α-Methyl-α-(*o*-aminophenoxy)propionylglycine Ethyl Ester (7, R = H, R′ = Et).—A solution of 0.7868 g (2.54 mmol) of **3** (R = H, R′ = Et) in 25 ml of THF and 15 ml of water was treated with Al(Hg)[8] made from 0.685 g (0.0254 g-atom) of Al. The resultant mixture was stirred at room temperature and a tlc was run after 90 min. The only zone visible had an R_f of ~0.6, which was smaller than that of the starting material. After being stirred for 105 min, the reaction mixture was filtered and the filtrate was concentrated under reduced pressure in order to remove the THF. The aqueous residue contained a relatively large amount of crystals which gave a negative test with $FeCl_3$ in aqueous alcohol.[7] These were collected, washed with water, and dried. The yield of **7** (R = H, R′ = Et) was 0.5763 g (81%): mp 100.0–101.5°; ir (CH_2Cl_2) 3457 (NH), 1745 (ester C=O), 1681 (amide I), 1502 (amide II), and 1617 (aromatic stretching); nmr ($CDCl_3$) consistent with kind and number of protons present in **7** (R = H, R′ = Et). One recrystallization from benzene and petroleum ether (bp 30–60°) (1:5) afforded an antlytically pure sample: mp 101.0–101.5°.

Anal. Calcd for $C_{14}H_{20}N_2O_4$: C, 59.98; H, 7.19; N, 10.00. Found: C, 60.34, 60.54; H, 7.43, 7.28; N, 10.32, 10.13.

Compound **7** (R = H, R′ = Et) was converted into H-Gly-OEt·HCl by a procedure similar to that used on **4** (R = H, R′ = Et) above. The time required for cyclization and fragmentation to **8** and **6** (R = H, R′ = Et), however, was 18 hr, and the yield of the second product was 62%. Comparable figures *via* the hydroxylamino derivative **4** (R = H, R′ = Et) were 2½ hr and 72.8%.

Registry No.—**3** (R = H, R′ = Et), 20178-13-6; **3** (R = i-Bu, R′ = Et), 20178-14-7; **3** (R = CH_3, R′ = Et), 20178-15-8; **3** (R = CH_3, R′ = Me), 20178-16-9; **3** (R = $C_6H_5CH_2$, R′ = Me), 20178-17-0; **3** (R = i-Pr, R′ = Me), 20178-18-1; **7** (R = H, R′ = Et), 20178-19-2; zinc chloride, 7646-85-7; ammonium chloride, 12125-02-9.

Acknowledgment.—Support of this work in part by a Frederick Gardner Cottrell Grant in Aid of the Research Corporation, New York, N. Y., is gratefully acknowledged.

(8) I. Vogel, *J. Chem. Soc.*, 597 (1927).

Resin Acids. XVI. Some Transformations of Methyl 12α-Hydroxy-13β-abiet-8(9)-en-18-oate[1,2]

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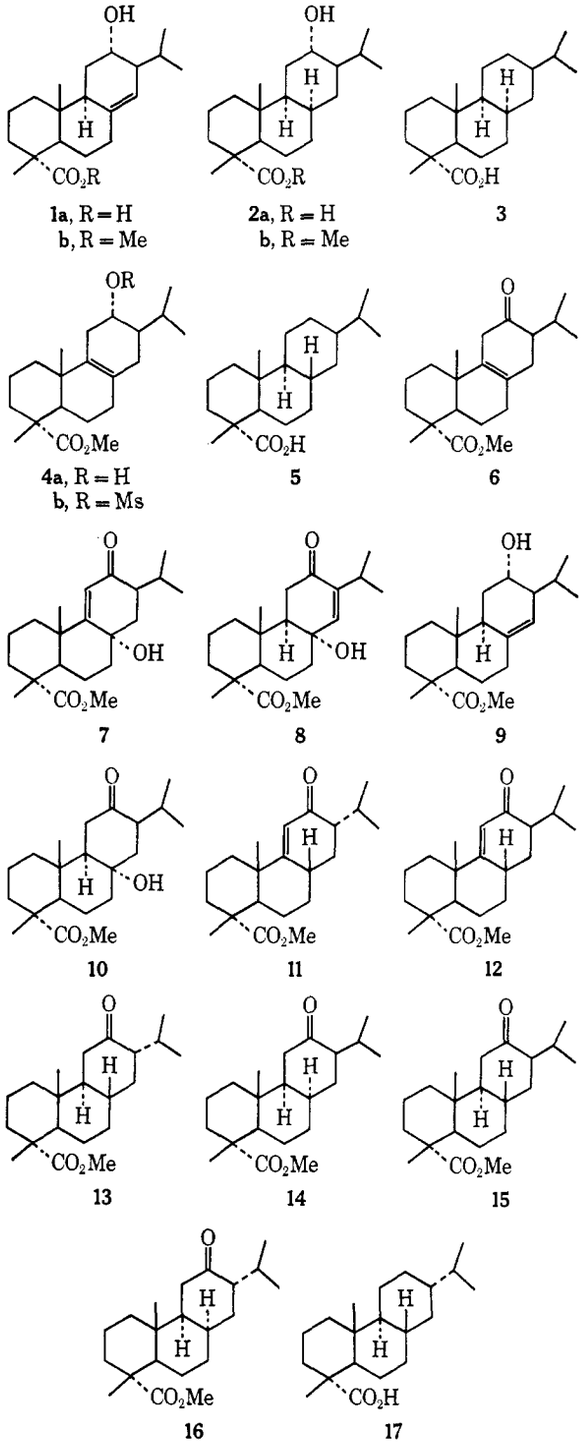
In an earlier[4] paper we reported the hydrogenation of **1a** to **2a** in acetic acid solution. The corresponding methyl ester **2b** was utilized[5] for our synthesis of authentic 8α,13β-abietan-18-oic acid (**3**),[6] and was generally prepared by hydrogenation of **1b**[8] in ethanol.



In an effort to improve the yield, the reduction was carried out in acetic acid, with the result that partial

(1) Previous paper, W. Herz and R. C. Blackstone, *J. Org. Chem.*, **34**, 1257 (1969).

(2) Supported in part by a grant from the National Science Foundation (GP-6362).

(3) National Science Foundation Fellow 1967–1968.

(4) W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller, and G. W. Hedrick, *J. Org. Chem.*, **30**, 3190 (1965).

(5) J. M. Huffman, T. Kamiya, L. H. Wright, J. J. Schmid, and W. Herz, *ibid.*, **31**, 4128 (1966).

(6) Numbering and nomenclature used in this paper are based on a recent proposal (third revision, October 1968) by J. W. Rowe, "The Common and Systematic Nomenclature of Cyclic Diterpenes," subscribed to by most workers in the area. The parent abietane skeleton possesses the *trans-anti-trans* configuration with a 13α-isopropyl group.[7] Inverted configurations are designated by the position number and the correct stereochemistry just before the skeletal name.

(7) E. Fujita, T. Fumita, and H. Katayama, *Chem. Commun.*, 968 (1967).

(8) W. G. Dauben and R. Coates, *J. Org. Chem.*, **28**, 1698 (1963).