Table I. Isomerization of Alkyn-1-ols with Sodium APA in DAP

starting alkyn-1-ol	time, h	product	yield,[a] %	mp,[b] °C
2-tetradecyn-1-ol	20	13-tetradecyn-1-ol	81	40–41 (34–36)[d]
5-hexadecyn-1-ol	2.5	15-hexadecyn-1-ol	63	52–54 (49–52)[e]
5-hexadecyn-1-ol	20	15-hexadecyn-1-ol	53	52–54 (49–52)[e]
2-nonadecyn-1-ol	20	18-nonadecyn-1-ol[c]	85	61–63
7-tetracosyn-1-ol	18	23-tetracosyn-1-ol[c]	47	77–78

[a] Yields reported are of crystalline material obtained after chromatography. Products are greater than 96% pure by GLC analysis. [b] Melting points are uncorrected. [c] Satisfactory analyses (C and H, ±0.3%) were obtained for all new products. [d] Reference 9. [e] Reference 3.

(KAPA). KAPA is prepared by the reaction of potassium hydride with 1,3-diaminopropane (DAP), the solvent of the reaction.

The foaming problem, which is particularly troublesome in larger scale work, along with the hazards of handling potassium hydride,[8] led us to search for an alternate method to prepare the isomerization reagent.

Working toward the same goal, Hommes and Brandsma[4] reported that an effective isomerization reagent could be obtained by the addition of DAP to freshly prepared potassium or sodium amide in liquid ammonia followed by evaporation of the ammonia. They stated that sodium hydride did not react with DAP.

We have developed a simpler, more convenient procedure to prepare the isomerization reagent. We have found that sodium hydride does, in fact, react with DAP at 70 °C with evolution of hydrogen, but no foaming, to give a clear brown solution which can be used to isomerize alkyn-1-ols.

Table I lists five isomerizations using our reagent (sodium APA). The starting materials we prepared in the standard manner[11] by reaction of the appropriate lithium (tetrahydropyranyloxy)acetylide with an alkyl bromide followed by deprotection with methanol and *p*-toluenesulfonic acid. The reactions were run with a fourfold excess of sodium APA (1 M in DAP) at 55 °C. Although reactions were usually complete within 2 h, they were normally allowed to proceed overnight.

With this procedure an "acetylenic zipper" reagent can routinely be prepared simply, quickly, and without foaming problems. Our modification should be particularly useful for large-scale experiments.

Experimental Section

All isomerizations were run under similar conditions. The reactions were carried out under a positive pressure of dry nitrogen in flame-dried glassware. The 1,3-diaminopropane (corrosive!) was distilled at reduced pressure from BaO and stored over 4A molecular sieves. The general procedure employed is described in detail for the case of the reaction of 2-nonadecyn-1-ol.

18-Nonadecyn-1-ol was synthesized as follows. To NaH (Ventron Corp., 57% in mineral oil, 720 mg, 17 mmol, washed free of oil three times with hexane) was added DAP (15 mL). The mixture was stirred in a constant-temperature oil bath at 70 °C. After 10 min gas evolution was noted and after 1 h a clear brown solution resulted. The reagent was cooled to ambient temperature, and a solution of 2-nonadecyn-1-ol (600 mg, 2.15 mmol) in DAP (8 mL) was added. The reddish brown mixture was stirred at 55 °C overnight and then cooled, water was added, and the organic product was extracted four times with ether. The combined ether phases were washed successively with water, dilute HCl, and NaCl solutions and then dried over Na_2SO_4. Filtration and evaporation of the solvent yielded 580 mg of crude product which was chromatographed over silicic acid (Bio-Rad, 200–400 mesh) to give 18-nonadecyn-1-ol: 510 mg; 85% yield; mp 61–63 °C (hexane); IR ($CHCl_3$) 3605, 3450 (OH), 3300, 2110 cm^{-1} ($C{\equiv}CH$); ^1H NMR (100 MHz, $CDCl_3$, internal Me_4Si) δ 1.2–1.7 (br m, 31 H, CH_2, OH), 1.88 (t, $J = 2.75$ Hz, 1 H, $C{\equiv}CH$), 2.18 (m, $w_{1/2} = 15$ Hz, 2 H, $CH_2C{\equiv}C$), 3.59 (t, $J = 6.0$ Hz, 2 H, OCH_2); ^{13}C NMR (25.16 MHz, $CDCl_3$) 84.86 (C-18), 68.07 (C-19), 63.10 (C-1), 32.90 (C-2), 28.84 (C-15), 28.58 (C-16), 25.82 (C-3), 18.46 (C-17) (from Me_4Si);[10] purity by GLC (FID, 1 m × 3 mm stainless-steel column packed with 80–100 mesh acid-washed silanized Chromosorb W coated with 1.5% Dexsil 300) 97%. The analysis was performed by Microanalysis Laboratories Ltd. Anal. Calcd for $C_{19}H_{36}O$: C, 81.36; H, 12.94. Found: C, 81.36; H, 12.75.

Acknowledgment. The author wishes to thank Dr. W. F. Steck (NRC) for gifts of 2-tetradecyn-1-ol and 5-hexadecyn-1-ol, Drs. A. P. Tulloch (NRC) and G. D. Abrams (University of Saskatchewan) for helpful discussions, and Mr. W. C. Haid and Mr. M. Mazurek for measuring the NMR spectra.

Registry No. 1,3-Diaminopropane, 109-76-2; sodium hydride, 7646-69-7; 2-tetradecyn-1-ol, 51309-22-9; 5-hexadecyn-1-ol, 72443-47-1; 2-nonadecyn-1-ol, 72443-48-2; 7-tetracosyn-1-ol, 72443-49-3; 13-tetradecyn-1-ol, 18202-12-5; 15-hexadecyn-1-ol, 62914-53-8; 18-nonadecyn-1-ol, 72443-50-6; 23-tetracosyn-1-ol, 72443-51-7.

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Metabolites of the Marine Sponge *Dercitus* sp.

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The tryptophan derivative aplysinopsin (**1**) has previously been reported from the sponges *Thorecta* (≡ *Aplysinopsis*?)[1] sp. and *Verongia spengelii*.[2] In the former report, Wells et al.[1] suggested the presence of a monobromo analogue which they were unable to isolate. In this note, we describe the isolation and identification of the related compounds 2′-de-*N*-methylaplysinopsin (**2**) and 6-bromo-2′-de-*N*-methylaplysinopsin (**3**).

The marine sponge *Dercitus* sp. was collected at Lighthouse Reef, Belize, and stored in methanol for 6 months. Soxhlet extraction of the sponge with methanol produced a brownish yellow extract which was fractionated on a Sephadex LH-20 column to yield aplysinopsin (**1**) (2.7% dry weight) as the major metabolite, 2′-de-*N*-methylaplysinopsin (**2**) (1.0% dry weight), and 6-bromo-2′-de-*N*-methylaplysinopsin (**3**) (1.0% dry weight).

The ^1H NMR spectrum of the monomethyl compound **2** was very similar to that of aplysinopsin (**1**) and showed signals at δ 3.06 (s, 3 H) attributed to the *N*-methyl, at δ 6.81 (s, 1 H) due to the olefinic proton attached to the glycocyamidine side chain, and at δ 7.11 (m, 2 H), 7.43 (d, 1 H, $J = 6$ Hz), 7.93 (d, 1 H, $J = 6$ Hz), and 8.52 (s, 1 H) due to the protons at C-5, C-6, C-4, C-7, and C-2, respec-

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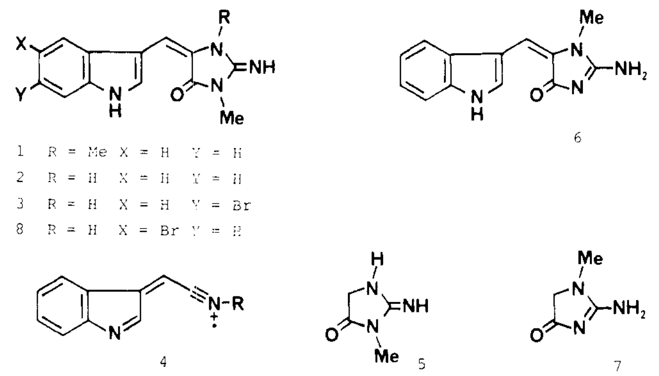
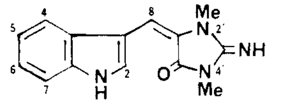
[2] Hollenbeak, K. H.; Schmitz, F. J. *Lloydia* **1977**, *10*, 480.

Chart I



1 R = Me X = H Y = H
2 R = H X = H Y = H
3 R = H X = H Y = Br
8 R = H X = Br Y = H

Table I. Comparison of the ^{1}H NMR Spectra (Me$_2$SO-d_6) of Aplysinopsin (1) and Derivatives 2, 3, 6, and 8[a]



	H-2	H-4	H-5	H-6	H-7	H-8	CH$_3$-2'	CH$_3$-4'
1	8.72	7.45	7.15	7.15	7.89	6.46	3.26	3.07
2	8.25	7.43	7.11	7.11	7.93	6.81		3.06
6	9.09	7.36	7.04	7.04	7.86	6.52	3.22	
3	8.09	7.13	7.88	Br	7.54	6.65		3.00
8	8.31[b]	8.09[b]	Br	7.27	7.43	7.02[b]		3.12
	8.36	8.13				7.09		

[a] Chemical shifts in parts per million. [b] 1:1 mixture of E and Z isomers.

tively, of a monosubstituted indole. Whereas the mass spectrum of aplysinopsin (1) gave a fragment ion at m/e 169, attributed to fragment 4 (R = Me), the mass spectrum of demethylaplysinopsin 2 contained a corresponding fragment ion at m/e 155 attributed to fragment 4 (R = H). This suggested that 2 lacked a methyl at the 2'-N position.

The structure of 2'-de-*N*-methylaplysinopsin (2) was confirmed by total synthesis. Condensation of indole-3-carboxaldehyde with 3-methyl-2-iminoimidazolidin-4-one (5)[3] gave compound 2 in 78% yield. The synthetic material was identical in all respects to the natural product. The alternative isomer 6 was formed by condensation of indole-3-carboxaldehyde with creatinine (7). The ^{1}H NMR spectrum of the isomer 6 showed an *N*-methyl resonance at δ 3.22, whereas the *N*-methyl resonance of the natural material 2 was at δ 3.06 (see Table I).

The ^{1}H NMR spectrum of 6-bromo-2'-de-*N*-methylaplysinopsin (3), mp 186–188 °C, contained signals at δ 3.00 (s, 3 H) due to the *N*-methyl group, at δ 6.65 (s, 1 H) due to the olefinic proton attached to the glycocyamidine side chain, and at δ 7.13 (d, 1 H, J = 6 Hz), 7.54 (s, 1 H), 7.88 (d, 1 H, J = 6 Hz), and 8.09 (s, 1 H) due to the protons at C-4, C-7, C-5, and C-2, respectively, of a disubstituted indole. Comparison of the ^{1}H NMR spectra of 5-bromoindole-3-carboxaldehyde and 6-bromoindole-3-carboxaldehyde with that of the naturally occurring compound 3 showed that the natural material was halogenated at the 6-position (see Table I).[4] The structure of 6-bromo-2'-de-*N*-methylaplysinopsin (3) was confirmed by total synthesis.

Condensation of 6-bromoindole-3-carboxaldehyde with 3-methyl-2-iminoimidazolidin-4-one (5) gave a 70% yield of compound 3, identical in all respects with the natural product. The alternative isomer formed by condensation of 5-bromoindole-3-carboxaldehyde with 3-methyl-2-iminoimidazolidin-4-one (5) gave a 50:50 mixture of the Z and E isomers of 5-bromo-2'-de-*N*-methylaplysinopsin (8) in 71% yield.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer. Ultraviolet spectra were recorded on a Perkin-Elmer 124 double-beam spectrophotometer. ^{1}H NMR spectra were recorded on a Varian HR-220 NMR spectrometer and ^{13}C NMR spectra on a Varian CFT-20 NMR spectrometer; all chemical shifts are reported with respect to Me$_4$Si (δ = 0). Low-resolution mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer. High-resolution mass spectra were supplied by the Chemistry Department, UCLA. Melting points were determined on a Fisher-Johns apparatus and are reported uncorrected. All solvents used were either spectral grade or distilled from glass prior to use.

Collection and Extraction. The sponge *Dercitus* sp. was collected by hand, using SCUBA (−20 m) at Lighthouse Reef, Belize, and was stored in methanol prior to extraction. The methanol solvent was decanted from the sponge which was then blended and Soxhlet extracted with methanol. The combined extracts were evaporated to yield a dark brown oil, yield 8.2 g (8.1% dry weight).

Chromatography. The crude extract (400 mg) was dissolved in methanol (5 mL) and fractionated on a Sephadex LH-20 column (50 × 3.5 cm), using methanol as the eluant. Early fractions afforded aplysinopsin (1) (133 mg, 2.7% dry weight) followed by 2'-de-*N*-methylaplysinopsin (2) (50 mg, 1% dry weight) and 6-bromo-2'-de-*N*-methylaplysinopsin (3) (52 mg, 1% dry weight).

A yellow solid that had precipitated from the methanol extract was later found to be aplysinopsin (1).

2'-De-*N*-methylaplysinopsin (2): mp 235 °C (with charring from 180 °C); IR (KBr) 3500–3000, 1680, 1610 cm^{-1}; UV (MeOH) 385 nm (ϵ 25 000); ^{1}H NMR (Me$_2$SO-d_6) (see Table I and text); mass spectrum, m/e (%) 240 (100), 156 (65), 155 (30), 149 (45); high-resolution mass spectrum, found 240.101 ($C_{13}H_{12}N_4O$ requires 240.101).

Synthesis of 2'-De-*N*-methylaplysinopsin (2). Indole-3-carboxaldehyde (25 mg, 0.17 mmol) and 3-methyl-2-iminoimidazolidin-4-one (5) (20 mg, 0.18 mmol) were mixed under an atmosphere of nitrogen and then gently heated over a Bunsen burner until reaction commenced. The reaction mixture was warmed for several minutes after effervescence had ceased. The crude material was dissolved in methanol, preadsorbed onto silica gel, and chromatographed over silica gel (3.5 × 40 cm), using acetone–ether (40:60) as the eluant to obtain the monomethyl compound 2 (32 mg, 78% theoretical), which was identical in all respects with the natural material.

6-Bromo-2'-de-*N*-methylaplysinopsin (3): mp 186–188 °C (with charring from 175 °C); IR (KBr) 3500–3000, 1690, 1610 cm^{-1}; UV (MeOH) 390 nm (ϵ 23 000); ^{1}H NMR (Me$_2$SO-d_6) (see Table I and text); mass spectrum, m/e (%) 320/318 (100), 236/234 (30), 235/233 (28), 155 (80), 154 (55), 149 (45); high-resolution mass spectrum, found 320.012/318.012 ($C_{12}H_{11}N_4OBr$ requires 320.009/318.011).

Condensation of Indole-3-carboxaldehyde with Creatinine (7). The indole-3-carboxaldehyde (1.5 g, 10.3 mmol) and creatinine (7) (1.2 g, 10.6 mmol) were reacted according to the procedure above to afford the monomethyl compound 6 (2.1 g, 84% of the theoretical yield), which was recrystallized from aqueous methanol to afford microprisms: mp 240–285 °C (dec); IR (Nujol) 3400–3000, 1680, 1620 cm^{-1}; UV (MeOH) 385 nm (30 000); ^{1}H NMR (Me$_2$SO-d_6) (see Table I); mass spectrum, m/e (%) 240 (95), 170 (25), 169 (25), 155 (100); high-resolution mass spectrum, found 240.098 ($C_{13}H_{12}N_4O$ requires 240.101).

5-Bromo-2'-de-*N*-methylaplysinopsin (8). 5-Bromoindole-3-carboxaldehyde (40 mg, 0.18 mmol) and 3-methyl-2-iminoimidazolidin-4-one (5) (20 mg, 0.18 mmol) were reacted according to the procedure above to afford compound 8 (40 mg, 71% of the theoretical yield), which was recrystallized from aqueous methanol to yield microprisms: mp 200–203 °C (dec); IR (KBr) 3500–3000,

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1690, 1610 cm^{-1}; UV (MeOH) 385 nm (ϵ 27 000); ^{1}H NMR ($Me_2SO\text{-}d_6$) (see Table I); mass spectrum, *m/e* (%) 320/318 (80), 192 (90), 191 (100), 163 (65), 155 (35), 149 (70); high-resolution mass spectrum, found 320.006/318.009 ($C_{13}H_{11}N_4OBr$ requires 320.009/318.011).

Acknowledgment. We thank Dr. K. Rützler for identifying the sponge. This research was supported by the Sea Grant Program, Department of Commerce (Grant 04-6-158-44110).

Registry No. 1, 63153-56-0; **2**, 72479-07-3; **3**, 72479-08-4; **5**, 34293-24-8; **6**, 72479-09-5; **7**, 60-27-5; **8** (*E* isomer), 72479-10-8; **8** (*Z* isomer), 72479-11-9; indole-3-carboxaldehyde, 487-89-8; 5-bromoindole-3-carboxaldehyde, 877-03-2.

Synthesis of Triacontanol via Metathesis–Hydroboration–Isomerization–Oxidation

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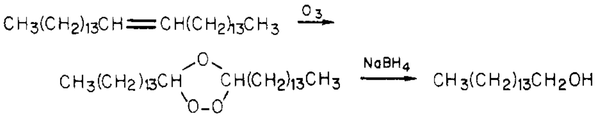
In 1977, triacontanol was reported to be a new naturally occurring plant-growth regulator.[1] This prompted us to investigate a general and practical procedure for the synthesis of fatty alcohols with extremely long chain lengths. We here report such an approach via (i) metathesis (Met) of olefins,[2] (ii) hydrometalation–isomerization (HI), and (iii) oxidation (Ox) (eq 1). Generally, the metathesis of

$$\begin{aligned}&CH_3(CH_2)_{13}CH{=}CH_2 \xrightarrow{\text{Met}}\\ &\quad CH_3(CH_2)_{13}CH{=}CH(CH_2)_{13}CH_3 \xrightarrow{\text{HI}}\\ &\quad CH_3(CH_2)_{27}CH_2CH_2M \xrightarrow{\text{Ox}} \underset{\text{1-triacontanol}}{CH_3(CH_2)_{28}CH_2OH} \qquad (1)\end{aligned}$$

terminal olefins is more difficult than that of internal olefins.[3] Although we initially employed Ichikawa and Fukuzumi's procedure[4] for 1-hexadecene, the result was unsatisfactory. Therefore, detailed investigations were performed on 1-heptene and soon revealed that the highest yield and selectivity were achieved by using the following reaction conditions: olefin (1.5 mmol), WCl_6 (0.072 mmol), $Cl_2C{=}CClH$ (1.5 mL), CH_3CN (0.048 mmol), Bu_4Sn (0.14 mmol), 80 °C, 5 h (Table I). This procedure was applied to 1-hexadecene, and 15-triacontene was isolated in 40–60% yields. The structure of the olefin was confirmed by ozonolysis (eq 2). The ozonolysis of the recovered



(2)

hexadecene gave 1-pentadecanol, indicating no isomerization occurred during the metathesis.

The conversion of internal olefins into terminal metal derivatives is realized by the following procedures: (i) hydroboration–isomerization,[5] (ii) hydroalumination–isomerization,[6] (iii) hydrozirconation–isomerization,[7] (iv) hydrosilylation–isomerization.[8] Previous literature indicates that these procedures are equally effective for olefins with short to medium chain lengths such as 3-hexene, 2-octene, and 5-decene. No data are available on olefins with extremely long chain lengths, apparently because they lack solubility in organic solvents.[9] We first examined the hydroalumination procedure, but only 15-triacontene was recovered.[10] Next we tried the hydrozirconation procedure and again only recovered the olefin. It should be noted that even the hydrometalation itself does not proceed in these two procedures. Finally, allowable yields of 1-triacontanol were obtained by the hydroboration procedure (Table II).

Table I. Systematic Investigation of the Metathesis of 1-Heptene[a]

reactn conditns		product yield, %[b]					selectivity, %[c]
reagent	amt, mmol	C_7	C_9	C_{10}	C_{11}	C_{12}	
WCl_6[d]	0.024	~90					0
	0.072	27	1	2	4	47	64
	0.12	22	3	4	8	23	29
CH_3CN[e]	0	7	12	11	8	4	4
	0.024	54	1	2	3	5	11
	0.048	27	1	2	4	47	64
	0.096	64				2	5
Bu_4Sn[f]	0	98				<1	~0
	0.024	94				5	83
	0.048	27	1	2	4	47	64
	0.096	35	1	1	3	43	66
	0.14	29			3	64	90
	0.24	*g*			1	11	*g*

[a] The same procedures as described in the Experimental Section were used. [b] Yield of olefins detected after the reaction, determined by GLC. C_7 = heptene, C_8 = octene, etc. Yield C_7 = [C_7 recovered (mmol)/C_7 used (mmol)] × 100. Yields for C_9–C_{12} = [C_9–C_{12} recovered (mmol)/C_7 used (mmol)] × 2 × 100. [c] [C_{12} recovered (mmol)/C_7 consumed (mmol)] × 2 × 100. [d] 1-Heptene (1.5 mmol), CH_3CN (0.048 mmol), Bu_4Sn (0.048 mmol), 80 °C, 5 h. [e] 1-Heptene (1.5 mmol), WCl_6 (0.072 mmol), Bu_4Sn (0.048 mmol), 80 °C, 5 h. [f] 1-Heptene (1.5 mmol), WCl_6 (0.072 mmol), CH_3CN (0.048 mmol), 80 °C, 5 h. [g] Not determined.

The yield of 1-triacontanol was improved by the addition of other 1-olefins at the monohydroboration stage (eq 3).

$$\begin{aligned}&CH_3(CH_2)_{13}CH{=}CH(CH_2)_{13}CH_3 + BH_3 \xrightarrow[\text{DG}]{}\\ &(C_{30}\text{-}BH_2) \xrightarrow{2RCH{=}CH_2} (C_{30}\text{-}BR'_2) \xrightarrow{160\ °C,\ 12\ h} \xrightarrow[\text{NaOH}]{H_2O_2}\\ &\quad \text{1-triacontanol} + sec\text{-}C_{30}H_{61}OH + C_{30}H_{60} \qquad (3)\\ &\quad 66\%,\ R^1 \qquad 13\%,\ R^1 \qquad 21\%,\ R^1\\ &\quad 63\%,\ R^2 \qquad 27\%,\ R^2 \qquad 7\%,\ R^2\end{aligned}$$

$$R^1 = n\text{-}C_{14}H_{29};\ R^2 = n\text{-}C_6H_{13}$$

This may be due to more facile hydroboration of the 1-

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[1] S. K. Ries and V. Wert, *Science*, **195**, 1339 (1977).

[2] 1-Hexadecene is obtained from natural sources, and the cost is reasonably cheap.

[3] The reaction is often accompanied by side reactions such as double bond migration and polymerization of alkenes: Y. Uchida, M. Hidai, and T. Tatsumi, *Bull. Chem. Soc. Jpn.*, **45**, 1158 (1972).

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(6) F. Sato, S. Sato, H. Kodama, and M. Sato, *J. Organomet. Chem.*, **142**, 71 (1977).

(7) T. F. Blackburn, J. A. Labinger, and J. Schwarz, *Tetrahedron Lett.*, 3041 (1975).

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(9) Solubility of 15-triacontene in ether, THF, diglyme, or triglyme, in which hydroboration and hydroalumination are carried out, is quite low, while that in hydrocarbon solvents is moderate.

(10) Our own examination revealed that this procedure was unsatisfactory even for 2-octene; 1-octanol was obtained in ~10% yield.

0022-3263/80/1945-0737$01.00/0