Table I

A. N^{α}-Formylamino Acid *tert*-Butyl Esters (For-AA-OBu^t)

Compd[a]	Formula[b]	Yield, %	R_f[c]	Bp, °C (mmHg)[d]	$[\alpha]^{25}_D$, deg, in EtOH
Gly (1)	$C_7H_{13}NO_3$	89	0.71	124–126 (0.5)	
Leu (2)	$C_{11}H_{21}NO_3$	87	0.79	143–144 (0.5)	−48.93 (*c* 2)
Pro (3)	$C_{10}H_{17}NO_3$	90	0.82	125.5–126.5 (0.6)	−109.79 (*c* 0.9)
Phe (4)	$C_{14}H_{19}NO_3$	88	0.83	171–172.5 (0.6)	15.97 (*c* 0.7)

B. 2-Isocyano Acid *tert*-Butyl Esters Derived from For-AA-OBu^t

Compd[a]	Parent amino acid	Formula[b]	Yield, %	R_f[c]	Bp, °C (mmHg)[d]	$[\alpha]^{25}_D$, deg, in EtOH
5	Gly	$C_7H_{11}NO_2$	94	0.90	91–93 (0.95)[e]	
6	Leu	$C_{11}H_{19}NO_2$	98	0.93	107 (0.45)[f]	−7.67 (*c* 1)

[a] NMR and IR spectral data agreed with the expected values. [b] Elemental analyses agreed with the calculated values within ±0.3%. [c] Solvent system for TLC (silica gel G) was $CHCl_3$–CH_3OH (96:4). [d] Boiling points were uncorrected. [e] Lit.[6] 87–89 °C (0.15 mm). [f] Compound 6 vaporized completely at this temperature.

mL). The mixture was then stirred for 4 h in an ice bath. Evaporation of the solvent was followed by addition of ether. The deposited dicyclohexylurea was removed by filtration and washed with ether. The combined filtrate was concentrated to an oil, which was purified by column chromatography on silica gel 60 (43 × 4.2 cm, 0.2–0.5 mm, E. Merck) using $CHCl_3$ followed by $CHCl_3$–CH_3OH (96:4) as eluents. Evaporation of the main peak fractions yielded 5.67 g of 1 as a colorless oil (89%). Several N^{α}-formylamino acid *tert*-butyl esters were prepared in this manner. The yields and physical constants of these compounds are summarized in Table IA.

A faster eluting side product was isolated by the above column chromatography and obtained as an oil (756 mg) which gradually crystallized. Recrystallization from ether–petroleum ether gave white needles. The compound was identified by NMR spectroscopy in $CDCl_3$ as 1,3-dicyclohexyl-1′,3′-diformylurea: mp 98.5–99.5 °C; R_f 0.94 (TLC, $CHCl_3$–CH_3OH, 96:4).

Anal. Calcd for $C_{15}H_{24}N_2O_3$ (280.4): C, 64.26; H, 8.63; N, 9.99. Found: C, 64.08; H, 8.68; N, 9.68.

***tert*-Butyl 2-Isocyanoacetate (5).** A solution of phosgene (990 mg, 10 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise to a vigorously stirred solution of 1 (1.59 g, 10 mmol) and triethylamine (3.4 mL, 24 mmol) in CH_2Cl_2 (5 mL) at 0 °C over a period of 30 min. The solution was stirred for an additional 30 min, filtered, and the filtrate concentrated in vacuo. Ether was added to the residue followed by filtration and concentration. The residue was purified by chromatography on a silica gel column (20 × 2.4 cm) with $CHCl_3$ as an eluent. The fractions containing 5 were combined and evaporated to yield a pale yellow oil (1.33 g, 94% yield). For physical constants see Table IB.

***tert*-Butyl 2-Isocyano-4-methylvalerate (6).** Prepared in 98% yield from 2 (215 mg, 1 mmol) as described above, but using *N*-methylmorpholine as a base and a reaction temperature of −30 °C.[3] The filtrate was concentrated in vacuo. Benzene was added to the residue followed by filtration and concentration. Chromatographic purification afforded 6 as a pale yellow oil, see Table IB.

Registry No.—1, 51354-15-5; 2, 61900-40-1; 3, 61930-75-4; 4, 61900-41-2; 5, 2769-72-4; 6, 61900-42-3; formic acid, 64-18-6; glycine *tert*-butyl ester, 6456-74-2; leucine *tert*-butyl ester, 21691-53-2; proline *tert*-butyl ester, 2812-46-6; phenylalanine *tert*-butyl ester, 16874-17-2; 1,3-dicyclohexyl-1′,3′-diformylurea, 61900-29-6.

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Alkylation of 2-Naphthol by Alcohols in the Presence of Base[1]

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1-Alkyl-2-naphthols and their derivatives are useful as antibacterial substances and antioxidants.[2] These compounds have been obtained by acylation of 2-naphthol and subsequent reduction of the carbonyl group,[3] as a by-product of the Williamson ether synthesis from alkyl halide and sodium naphthyl oxide,[4] by heating a mixture of 2-naphthol or 2,2′-dihydroxy-1,1′-dinaphthylmethane, an excess of sodium methoxide, and methanol,[5] by dehydrogenation of 1-methyl-2-oxo-2,3,4,6,7,8-hexahydronaphthalene or of 1-propyl-2-hydroxy-5,8-dihydronaphthalene,[6] and by reaction of 2-naphthol with formaldehyde and thiols ($C_nH_{2n+1}SH$) in ethanol in the presence of triethylamine.[7]

The authors have found a novel method to synthesize 1-alkyl-2-naphthols in good yield by a one-step reaction from alkali 2-naphthyl oxide and alcohol in the absence of catalyst.

Results and Discussion

Heating potassium 2-naphthyl oxide in primary alcohol gave 1-alkyl-2-naphthol. The yields and physical properties (boiling point and melting point) of the 1-alkyl-2-naphthols so obtained are listed in Table I. When potassium 2-naphthyl oxide was heated in pentyl alcohol at 200 °C for 5 h, 1-pentyl-2-naphthol was not obtained. Good yields were obtained, however, in 5 h at temperatures higher than 260 °C. In the present reaction, benzyl alcohol and primary aliphatic alcohols with more than three carbon atoms were effective.

Table I. Yields and Physical Properties of 1-Alkyl-2-naphthols

$$2\text{-}C_{10}H_7OM + ROH \xrightarrow[2.\ H^+]{1.\ \text{heat}\ (-H_2O)} C_{10}H_6ROH[1\text{-}2]$$

M	Alkyl group (R)	Conditions: Temp, °C	Conditions: Time, h	Yield, %	Bp, °C (mmHg)	Mp, °C	Registry no.
K	$CH_3(CH_2)_2$	270	5	44	116–121 (1.5)		17324-09-3
K	$CH_3(CH_2)_3$	270	5	77	120–124 (0.15)	80.8[a]	50882-63-8
K	$(CH_3)_2CHCH_2$	280	5	54	154–156 (3)		52096-47-6
K	$CH_3(CH_2)_4$	280	5	79	142–144 (0.6)	81.6	13255-83-9
Na	$CH_3(CH_2)_4$	280	5	75			
K	$(CH_3)_2CH(CH_2)_2$	280	5	85	135–138 (0.1)		61769-84-4
K	$CH_3(CH_2)_5$	260	12	76	135–136 (0.25)		57744-65-7
K	$CH_3(CH_2)_5$	280	5	84			
K	$CH_3(CH_2)_6$	280	5	90	159–160 (0.7)		61769-85-5
K	$CH_3(CH_2)_7$	280	5	74	143–144 (0.1)		61351-11-9
K	$CH_3(CH_2)_{11}$	280	6	55	205–210 (2)		57744-66-8
K	$C_6H_5CH_2$	280	5	50	163–167 (0.2)	109[b]	36441-31-3

[a] Lit. 79–81 °C (ref 4). [b] Lit. 111–112 °C (ref 4).

A product with a boiling point of 154–156 °C (3 mmHg) obtained from the reaction of potassium 2-naphthyl oxide and isobutyl alcohol was analyzed by gas chromatography–mass spectrometry (GC–MS). The product contained two components and the mass spectra were similar; one is 1-isobutyl-2-naphthol and the other is probably a nuclear isomer. There is steric hindrance between the hydrogen atom at the 8 position and a bulky isobutyl group when substitution occurs at the 1 position of 2-naphthol. The isomer is presumably formed for this reason.

The structures of these products were determined by means of mass spectrum, NMR, and IR. As an example, the confirmation of 1-butyl-2-naphthol will be described here.

The molecular formula ($C_{14}H_{16}O$) was obtained by high-resolution mass spectrometry. The NMR spectra suggest strongly that a normal butyl chain is attached to the 1 position of the naphthalene nucleus; that is, the butyl group did not isomerize. The IR absorptions at 806 and 742 cm^{-1} also support the presence of 1,2 disubstitution. The structures of other products were confirmed by similar methods. In addition, the NMR spectra (in acetone, 60 MHz) due to the aromatic protons of 1-butyl-, 1-isobutyl-, 1-pentyl-, and 1-hexyl-2-naphthol were compared with each other. These spectra were identical in detail.

In addition to 1-alkyl-2-naphthol, polyalkyl-2-naphthols and 2-substituted alcohols were formed in the present reaction; the former are produced by further alkylation of 1-alkyl-2-naphthol and the latter by the Guerbet reaction (eq 1).[8]

$$2RCH_2CH_2OH \xrightarrow[-H_2O]{\text{base}} RCH_2CH_2CHRCH_2OH \qquad (1)$$

The formation of dialkyl-2-naphthols was confirmed by the GC–MS method, but the positions of the two substituents are not yet determined. These results are not listed in Table I.

Experimental Section

The NMR spectra were obtained on a JEOL JNM-C-60 HL (60 MHz) or PS-100 (100 MHz) spectrometer, with Me_4Si used as the internal standard. The mass spectra were obtained on a Hitachi mass spectrometer (RMU-6L) and on a Shimadzu mass spectrometer (LKB-9000), using an electron-accelerating voltage of 70 eV. The IR spectra were measured with a Japan Spectroscopic spectrometer (IRA-2). Gas chromatography was performed with a Yanagimoto apparatus (G-1800).

Alkylation. Because of the similarity of the procedures, only one example will be described in detail.

In a 300-mL autoclave, with an electromagnetic stirrer, were placed 9.61 g (0.0528 mol) of potassium 2-naphthyl oxide and 48.0 g (0.648 mol) of butyl alcohol. After the air had been replaced by nitrogen, the autoclave was heated at 270 °C for 5 h. The pressure reached 32 kg/cm^2. The autoclave was cooled, and the reaction mixture was washed with 3% aqueous sodium hydroxide, in which most 1-alkyl-2-naphthols are practically insoluble, then dilute hydrochloric acid, and dried over anhydrous magnesium sulfate. Vacuum distillation of the mixture, with 15-cm Widmer column, gave 1-butyl-2-naphthol in a 77% yield. The boiling point and melting point are given in Table I.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.79; H, 8.07. NMR (CCl_4, 100 MHz) δ 8.0–6.9 (m, 6 H), 4.82 (s, 1 H), 3.00 (t, 2 H), 1.8–1.2 (m, 4 H), 0.96 (triplet but with some distortion, 3 H).

A singlet peak appearing at δ 7.16 of 2-naphthol in acetone (60 MHz) (a proton at the 1 position) was completely absent from the spectrum of 1-butyl-2-naphthol.

Registry No.—Potassium 2-naphthyloxide, 36294-21-0; sodium 2-naphthyloxide, 875-83-2; propanol, 71-23-8; butyl alcohol, 71-36-3; isobutyl alcohol, 78-83-1; pentanol, 71-41-0; isopentyl alcohol, 123-51-3; hexanol, 111-27-3; heptanol, 111-70-6; octanol, 111-87-5; dodecanol, 112-53-8; benzyl alcohol, 100-51-6.

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The Importance of Alkene and Alkyne Structure on Their Relative Rates of Bromination

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The effect of solvent upon the relative rates of bromination of alkenes and alkynes has been explained in two different