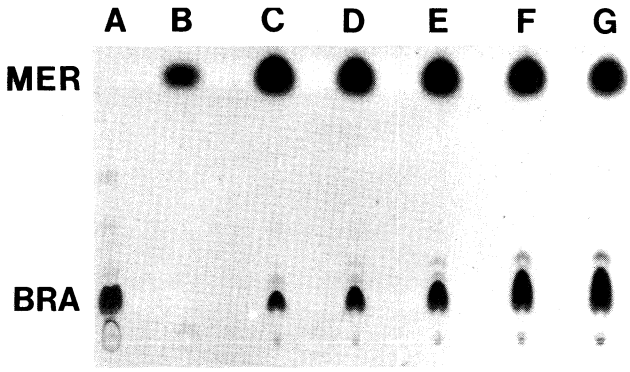

FIG. 3. Time course of the amidation of the methyl ricinoleate (MER) with *n*-butylamine. Lane A, N-*n*-butyl ricinoleamide (BRA) reference standard. Lane B, MER. Lanes C, D, E, F and G, 1.0 g MER and 0.42 mL *n*-butylamine incubated at 45°C for 1, 2, 3, 6 and 10 d, respectively. No solvent was present.

Amidation was attempted with MER, rather than with the castor oil, and *n*-butylamine (Fig. 3). Even after 10 d (lane G) the reaction was not complete. The reason why the esters of glycerol react so much more quickly than those of methanol remains unclear at this point.

Finally, an attempt was made to prepare amides from castor oil and methyl-*n*-butylamine. No product formation was observed. The best procedure for the amidation of hydroxylated fats with secondary amines remains that developed by Applewhite and co-workers (5,7).

In conclusion, *n*-butylamine reacts efficiently with castor oil to yield the amide of ricinoleate. Detailed mechanistic studies of this reaction have not yet been conducted but initial attempts to fit data to the integrated expression for a simple bimolecular reaction have failed. Also, it was predicted that the introduction of water would slow amide formation, through the introduction of competing hydrolysis, and also through dilution of *n*-butylamine, as this amine is infinitely soluble in water. This prediction was not supported by the data. The addition of dioxane dramatically reduced the extent of amidation. Castor oil is very soluble in dioxane, and thus this observation, in conjunction with the observation that MER reacts slowly, demonstrates that the amidation rate is critically dependent upon the concentration of acylglycerol.

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A Novel Technique for the Preparation of Secondary Fatty Amides II: The Preparation of Ricinoleamide from Castor Oil

The butyl amide of ricinoleic acid (N-*n*-butyl-12-hydroxy-(9*Z*)-octadecenamide) was prepared from a neat mixture of castor oil and *n*-butylamine (fatty ester/amine molar ratio, 1:1.3). No catalyst was required. The identity and purity of the amide was assessed by thin-layer chromatography and confirmed by elemental analysis and by infrared and C^{13} nuclear magnetic resonance spectroscopy. High product yields were achieved at 45 and 65°C in 48 and 20 h, respectively. The reaction was inhibited by the addition of trimethylpentane and dioxane, but not by water. An attempt was made to prepare the amide from methyl ricinoleate, rather than castor oil; even after 10 d only partial conversion was achieved. Attempts to prepare the amide from methyl-*n*-butylamine, rather than *n*-butylamine, were also unsuccessful. The ease with which secondary fatty amides can be produced from an oil that consists primarily of the glycerol esters of hydroxylated fatty acids indicates that the described procedure has industrial utility.

KEY WORDS: **Amidation, amide, *n*-butylamine, N-*n*-butyl-12-hydroxy-(9*Z*)-octadecenamide, castor oil, 1,4-dioxane, 12-hydroxy-9(*Z*)-octadecenoic acid, methyl-*n*-butylamine, O-methyl-12-hydroxy-(9*Z*)-octadecenate.**

Castor oil is derived from the bean of the castor plant, *Ricinus communis* (L.). Approximately 90% of the fatty esters in the oil are derived from ricinoleic acid (RA). The hydroxyl group of RA may be subjected to many reactions, including dehydration, alkoxylation, esterification, phosphonolation, sulfation and replacement by halogens (1–3). The resulting materials have many important industrial uses. In our previous report (4) we showed that the fatty esters found in several fats and oils can be converted to amides by a simple procedure that requires no base catalyst other than the amine itself. In the present study we demonstrate that N-*n*-butyl-ricinoleamide (BRA) can also be prepared in high yield by this procedure. The effects of organic solvent and water on the reaction rate were investigated. Also investigated were the use of methylricinoleate (MER), rather than castor oil, and the use of methyl-*n*-butylamine rather than *n*-butylamine.

EXPERIMENTAL PROCEDURES

Materials. *n*-Butylamine (99%), thin-layer chromatography (TLC) plates and solvents were purchased as described previously (4). Castor oil was a medicinal grade from Barre-National, Inc. (Baltimore, MD). RA (99%) and MER (99%) were purchased from Sigma Chemical Co. (St. Louis, MO). Ethyl chloroformate (97%), 2,2,4-trimethylpentane (99.9%), and methyl-*n*-butylamine (96%) were purchased from Aldrich Chemical Co., Inc. (Milwaukee, WI). The dye, 2′,7′-dichlorofluorescein, was from Eastman Kodak Co., Inc. (Rochester, NY). All reagents were used without further purification. Elemental analyses were performed in duplicate by Micro-Analysis (Wilmington, DE)

Synthesis of standard. BRA was chemically synthesized from a commercial preparation of RA by the carboxylic-carbonic anhydride technique with reverse addition of reagents as described by Applewhite and Binder (5). The compound showed only one spot on TLC and was utilized as a standard without further purification: infrared (IR): 3309, 2918, 2851, 1644, 1558, 1458 cm^{-1}; ^{13}C nuclear magnetic resonance (NMR) ($CDCl_3$) δ, **relative integration area:** 13.64, 1 (CH_3); 13.95, 1 (CH_3); 19.96, 1 (CH_2); 22.48, 1 (CH_2); 25.60, 1 (CH_2); 25.66, 1 (CH_2); 27.21, 1 (CH_2); 28.94, 1 (CH_2); 29.07, 2 (CH_2); 29.25, 1 (CH_2); 29.43, 1 (CH_2); 31.62, 1 (CH_2); 31.71, 1 (CH_2); 35.23, 1 (CH_2); 36.65, 2 (CH_2); 39.05, 1 (CH_2NHCO); 71.32, 1 (*C*HOH); 112.52, 1 (*C*H=CH); 132.98, 1 (CH=*C*H); 173.05, 1 (*C*ONH). Analysis calculated for $C_{22}H_{43}O_2N_1$: C, 74.71; H, 12.28; O, 9.05; N, 3.96. Found: C, 73.91; H, 12.24; O, 9.80; N, 3.78.

Synthesis and analysis of BRA from castor oil. Reactions were conducted in 125-mL glass Erlenmeyer flasks with glass stoppers. Each reaction flask contained 5 g (5.41 mmol) castor oil and 2.1 mL (21.2 mmol) butylamine. The flasks were agitated at 200 rpm at the temperature indicated in the text. At the indicated time, the reaction mixture was diluted with dioxane to bring the final volume to 600 mL. A 16-μL aliquot was spotted onto a silica gel G TLC plate (width, 20 cm; height, 17 cm; thickness, 250 microns). The plate had been prewashed by placing it in a tank of methanol for 5 min (6). It was developed with a two-stage, one-dimensional system: (i) benzene/ethyl ether/ethyl acetate (72:14:14, vol/vol/vol), development to the top of the plate; (ii) hexane/ethyl ether (60:40, vol/vol), development to the top of the plate. The TLC plate was dried between steps. After development, the plate was sprayed with a solution of sulfuric acid and water (60:40, vol/vol) and charred on a hot plate to visualize the products.

The BRA produced from castor oil was isolated from the product mixture for detailed analysis. A silica gel G column (diameter, 4.5 cm; height, 11.5 cm) was prepared. The column was washed with ethyl acetate until all color was removed, and the column was allowed to dry under a fume hood overnight. Before the crude reaction mixture was applied, the column was prewashed with the first eluting solvent mixture. BRA was separated from other products by elution with (i) benzene/ethyl ether/ethyl acetate/acetic acid (72:14:14:0.033, by vol); (ii) benzene/ethyl ether/ethyl acetate (72:14:14, vol/vol/vol) and (iii) ethyl acetate. The purest fractions (as determined by TLC) were pooled, applied and eluted from a second silica gel G column. Note that new, ethyl acetate-washed silica gel was used. The yield of recovered material [2.1 g, m.p.

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26.5–27°C, lit. 28–29°C, (7)] was 42.0%: Analysis calculated for $C_{22}H_{43}O_2N_1$: C, 74.71; H, 12.28; O, 9.05; N, 3.96. Found: C, 75.81; H, 11.37; O, 8.56; N, 3.99. The C^{13} NMR spectrum and IR spectrum were indistinguishable from that obtained from BRA synthesized by the carboxylic-carbonic anhydride route.

BRA yields and triacylglycerol analysis. The yield of BRA was estimated with a TLC scanner (Camag, Linomat IV, Model 27220 Muttenz, Switzerland). Sample and standards of known concentration were applied to the TLC plate. The plate was developed and charred as described above.

The two major triacylglycerols in castor oil were isolated by the same procedure as used for BRA. The fatty acyl groups were converted to their methyl esters by saponification with 2N KOH in methanol. The composition of the fatty esters was determined in a gas-liquid chromatograph (Perkin-Elmer, Model 3920 Norwalk, CT) containing a J&W Scientific (Folsom, CA) fused silica megabore column (DB-225-30-M) and equipped with a flame-ionization detector.

RESULTS AND DISCUSSION

The reaction described here for the production of BRA has the advantage of simplicity. The amine acts as reactant and solvent. The exact correspondence of both IR and NMR spectra of the standard BRA and the material synthesized from castor oil leaves no doubt that the product is correctly identified (see Experimental Procedures). In addition, the NMR spectrum shows a resonance at 173 ppm that is indicative of an amide carbonyl carbon. The IR spectrum shows an absorbance at 1644 cm^{-1} that is also characteristic of an amide.

Figure 1 shows a TLC analysis of a time course study of the reaction of *n*-butylamine with castor oil at 45°C. Castor oil was spotted in lane B. After development and charring, two spots were visible. Isolation and analysis of the corresponding materials showed that the upper spot is composed of triacylglycerols that contain two ricinoleates and one nonhydroxylated fatty acid residue, mostly oleate and linoleate. The lower spot is triricinolein. As the reaction proceeds, these two spots gradually disappear while several others appear. Three of the new spots continue to grow in size while the other new spots ultimately disappeared, as did the two original spots. At 48 h, the major spot in lane G has the same mobility as that of the BRA reference standard in lane A. The yield of BRA calculated from the TLC plate was 89.8 ± 0.6% (SE, n = 3) after 48 h. Another spot had the same mobility as the *n*-butyl-palmitamide (BPA) reference standard and is probably composed of a mixture of the amides of the nonhydroxylated fatty acids mentioned above. The third spot has the same mobility as that of RA but could be a mixture of this compound, residual monoglycerides and polymers of RA (estolides). Other spots that appeared in early stages of the reaction and then disappeared migrate with mobilities characteristic of mixtures of various diglycerides. Attempts to crystallize the crude material failed, but after it had been purified by column chromatography it readily solidified when solvent was removed. This material was pure BRA. The amidation was repeated at 65°C, and at this higher temperature the reaction was complete in only 20 h (data not shown).

Although the reaction proceeds to near completion in the absence of solvent, the ability of solvent addition to increase the reaction rate by reducing the viscosity of the reaction mixture was explored. Figure 2 shows the effect of adding dioxane to the reaction mixture. Contrary to expectations, as the amount of added dioxane increased, the amount of BRA formed in 48 h decreased. The addition of 2,2,4-trimethylpentane also decreased BRA production (data not shown). Inhibition by solvent might be the reason why this reaction has previously gone unreported in the literature.

The effect of water on the amidation reaction was also investigated. The addition of 3 mL water to the reaction did not slow the amidation rate (data not shown). At this water level, the reagents are saturated and, if the reaction mixture is allowed to stand unshaken, a water layer separates from the organic phase. The insensitivity of the reaction to the addition of water demonstrates that at equilibrium, amidation is strongly favored over hydrolysis. Insensitivity to water makes the reaction more amenable to industrial adaptation, as the reactants do not need to be dried carefully.

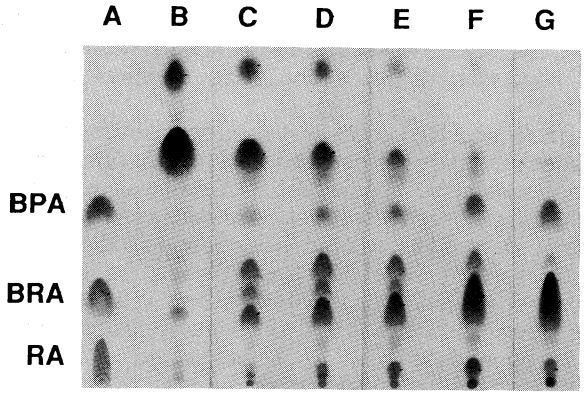

FIG. 1. Time course of the amidation of castor oil with *n*-butylamine. Lane A, reference standards: BPA, N-*n*-butyl palmitamide; BRA, N-*n*-butyl ricinoleamide; RA, ricinoleic acid. Lanes B, C, D, E, F and G, 5 g castor oil and 2.1 mL *n*-butylamine incubated at 45°C for 0, 2, 6, 12, 21 and 48 h, respectively. No solvent was present.

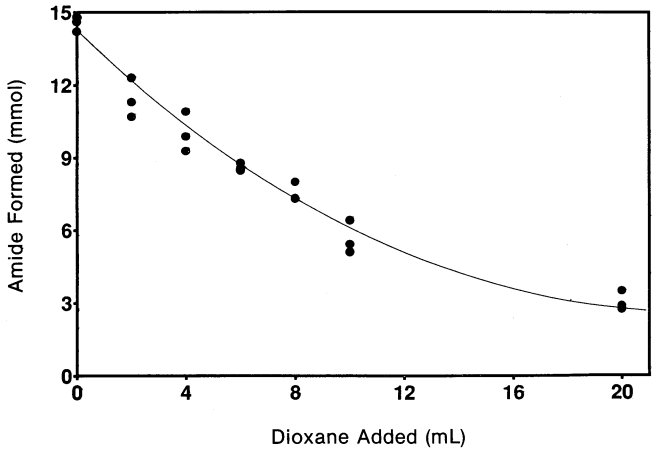

FIG. 2. Effect of dioxane on the amidation of castor oil with *n*-butylamine at 45°C for 48 h. The results from three experiments are shown. The line is solely a graphical aid.