The Selective *N*-Monoalkylation of Amides with Alkyl Halides in the Presence of Alumina and KOH

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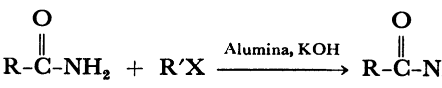
The effects of alumina impregnated with KOH (KOH/Al_2O_3) and a mixture of alumina and powdered KOH (KOH+Al_2O_3) have been examined using the alkylation of benzamide under various conditions. In each case, alkylation occurs exclusively in the pores of the alumina, the extent depending upon the alumina-pore size. For both yield and selectivity for *N*-monoalkylation, KOH+Al_2O_3 is superior to KOH/Al_2O_3. Dioxane is the best of the solvents employed. It is proposed that, in dioxane, an enolate-like species, $\mathrm{Ph}\overset{\mathrm{O^-K^+}}{\mathrm{C}}{=}\mathrm{NR'}$, exists as stable ion-pair aggregates, which are the true reactants in the pore. This method, using KOH/Al_2O_3 or KOH+Al_2O_3, has been applied to *N*-alkylation of the other amides, giving the *N*-monoalkylated products in substantial yields with extremely high selectivities. *2*-Phenylacetamide is regioselectively *N*-monoalkylated in high yields. This regioselectivity is explained in terms of steric hindrance.

It has recently been reported that amides are *N*-monoalkylated in substantial yields under phase-transfer catalytic conditions.[1] In the case of propanamide, which also has a weakly acidic N–H bond, however, the yields are considerably lower than those of benzamide (**1**). When highly-reactive benzyl chloride is employed as an alkylating agent, substantial quantities of *N,N*-dibenzylated products are obtained. More recently, Watanable *et al.* have reported the *N*-alkylation of amides with alcohols using ruthenium compounds as catalysts.[2] In this process, however, the yields and the selectivities for *N*-monoalkylation were low, with only a few exceptions.

In recent years, many studies have been reported on selective organic synthesis using inorganic solids.[3] Recently, the present author has himself reported the selective monoalkylation of phenylacetonitrile (PAN) using alumina impregnated with KOH or NaOH (KOH/Al_2O_3 or NaOH/Al_2O_3).[4a] It was shown that the reaction of the carbanion with alkyl halide occurs in the pores of the alumina and that the selectivity can be explained in terms of steric hindrance.

It has now been found that amides are selectively *N*-monoalkylated with alkyl halides in the presence of alumina and KOH.



$$\underset{(\mathbf{1}-\mathbf{4})}{\mathrm{R}-\overset{\overset{\displaystyle O}{\|}}{C}-\mathrm{NH_2}} + \underset{(\mathbf{5})}{\mathrm{R'X}} \xrightarrow{\text{Alumina, KOH}} \mathrm{R}-\overset{\overset{\displaystyle O}{\|}}{C}-\mathrm{NHR'}$$

(**1**), R=Ph (**a**), $R'=C_2H_5$
(**2**), $R=CH_3$ (**b**), $R'=n\text{-}C_3H_7$
(**3**), $R=n\text{-}C_3H_7$ (**c**), $R'=n\text{-}C_4H_9$
(**4**), $R=PhCH_2$ (**d**), $R'=CH_2{=}CHCH_2$
(**e**), $R'=PhCH_2$

Results and Discussion

The *N*-alkylation of **1** with alkyl halides (**5**) was carried out under various conditions using KOH/Al_2O_3 or a mixture of alumina and powdered KOH.

N-Alkylation of 1 Using KOH/Al_2O_3. In order to ascertain the effects of solvents, the *N*-alkylation of **1** with ethyl bromide was carried out using M-90-N alumina (Merck, Type 90, activity I, neutral, 70—230 mesh) impregnated with KOH (KOH/M-90-N) in several solvents. Table 1 shows the results. In the case of PAN, the order of the selectivities for monoalkylation has been found to be benzene>dioxane>THF>acetonitrile.[4a] In the case of **1**, however, the order of the selectivities for *N*-monoalkylation was dioxane≫benzene>THF>1,2-dimethoxyethane (DME)≈

Table 1. *N*-Ethylation of **1** using KOH/Al_2O_3 in several solvents[a)]

Solvent	Time / h	Yield[b)] / %	Selectivity Mono/%	; Di/%
Benzene	8	36	91	9
	2[c)]	45	84	16
Dioxane	8	49	98.5	1.5
THF	8	49	80	20
DME	8	48	58	42
Acetonitrile	2	52	58	42
DMSO[d)]	6	41	62	38

a) Unless otherwise noted, the reactions were carried out with **1** (10 mmol), ethyl bromide (12 mmol), KOH (50 mmol)/Al_2O_3 (M-90-N, 10 g), and hexadecane (0.3 g) as the internal standard in a solvent (20 ml) at 60 °C. b) Mono+Di; determined by GLC. c) The reaction was carried out with **1** (10 mmol), ethyl bromide (12 mmol), finely powdered KOH (50 mmol), hexadecane (0.3 g) as the internal standard, and $n\text{-}Bu_4N^+Br^-$ (2 mmol) at 60 °C. d) No catalyst was used.

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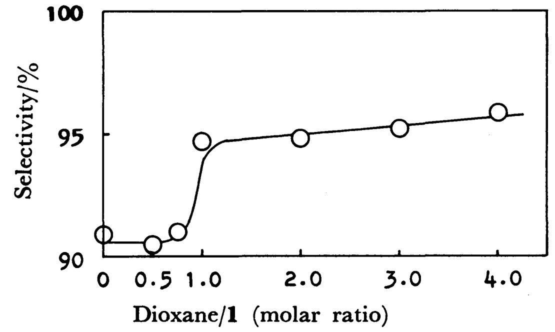


Fig. 1. The influence of the relative amount of dioxane to **1** on the selectivity for *N*-monoalkylation. The reactions were carried out with **1** (10 mmol), ethyl bromide (12 mmol), KOH (50 mmol)/M-90-N (10 g), and dioxane (0, 5, 7.5, 10, 20, 30, 40 mmol) in benzene (20 mL) at 60 °C for 8 h.

acetonitrile. An almost exclusive *N*-monoalkylation was achieved in dioxane.

In order to ascertain the specific solvent effect of dioxane, the influence of the amount of dioxane relative to that of **1** on the selectivity for *N*-monoalkylation was examined using alkylation with KOH/M-90-N and ethyl bromide in benzene (Fig. 1). At the dioxane/**1** molar ratio of *ca.* 1.0, a clear change in the selectivity was observed.

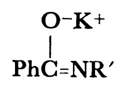
In order to establish the effect of the support pore size, the *N*-ethylation of **1** was carried out using several supports in benzene or in dioxane. Table 2 shows the results. The supports used were M-90-N, M-60-B alumina (Merck, Type 60, activity I, basic, 70—230 mesh), W-200-N alumina (Woelm, Type 200, neutral, activity super I), and Molecular Sieve 13X (MS-13X). The average pore diameters of M-90-N, M-60-B, and MS-13X are 90, 60, and 10 Å, respectively. The average pore diameter of W-200-N appears to be *ca.* 60 Å, based upon its specific surface area, which is *ca.* 200 m^2/g.[5] In the case of MS-13X, almost all of the **1** used was recovered. This resembles the alkylation of PAN.[4a] The pore diameter of MS-13X is too small for the reaction. The selectivities found in dioxane were much larger than those found in benzene in all cases examined.

TABLE 2. *N*-ETHYLATION OF **1** USING SEVERAL SUPPORTS IN BENZENE OR DIOXANE[a]

Solvent	Support	Yield[b] %	Selectivity Mono/% ;	Di/%
Benzene	M-90-N	36	91	9
	M-60-B	42	99	1
	W-200-N	36	96	4
	MS-13X (powder)[c]	≪1	—	—
	MS-13X (60—80 mesh)[c]	≪1	—	—
Dioxane	M-90-N	49	98.5	1.5
	M-60-B	55	≫99	0.2
	W-200-N	51	>99	0.5
	MS-13X (powder)[c]	≪1	—	—
	MS-13X (60—80 mesh)[c]	≪1	—	—

a) Unless otherwise noted, the reactions were carried out with **1** (10 mmol), ethyl bromide (12 mmol), KOH (50 mmol)/support (10 g), and hexadecane (0.3 g) as the internal standard in a solvent (20 ml) at 60 °C for 8 h. b) Mono+Di; determined by GLC. c) KOH (50 mmol)/MS-13X (15 g) and a solvent (30 ml) were used.

Apparent differences were observed in the selectivity for *N*-monoalkylation, depending upon the kind of alumina (Table 2). The yield of *N,N*-dialkylation obviously increased with the increase in the average pore diameter. This fact, and the fact that almost no **1** is observed in the organic phase during the reaction, indicate that the *N*-alkylation occurs predominantly in the pore. Jackman *et al.* have recently shown that lithium enolates exist as tetramers or dimers in ether solvents[6] and that ion-pair aggregates are the true reactants in the methylation of lithiobutyrophenone in weakly polar aprotic solvents.[7] Similarly, an enolate-like species (**6**) is also considered to exist as ion pairs or ion-pair aggregates and only in dioxane as stable ion-pair aggregates in the pore:



$$PhC(O^-K^+)=NR'$$

6 R′=H, Et

The clear change at the dioxane/**1** molar ratio of *ca.* 1.0 (Fig. 1) provides strong evidence for the strong interaction between dioxane and **6** of the 1:1 molar ratio, which is very compatible with the molar ratio of the solvent to solute in the structures of the tetramer and the dimer shown by Jackman *et al.*[6] This fact and the above results strongly suggest that ion-pair aggregates of **6**, a tetramer and/or a dimer, are the ture reactants in dioxane, resulting in a large steric hindrance, even in the pore of alumina, which has a relatively large pore diameter. When R′ is hydrogen in **6**, the steric hindrance to the reaction of **6** with **5** is very small.

N-Alkylation of 1 Using Nonimpregnated Alumina and Powdered KOH. Alumina and KOH were ground in a mortar. Hereafter, $KOH+Al_2O_3$ will represent the mixture of alumina and KOH prepared by this method. The *N*-ethylation of **1** using $KOH+Al_2O_3$ was carried out in several solvents. Table 3 shows the results. $KOH+Al_2O_3$ gave better

Table 3. N-Ethylation of **1** using $KOH+Al_2O_3$ in several solvents[a)]

Solvent	Time	Yield[b)]	Selectivity	
	h	%	Mono/% ;	Di/%
Benzene	8	36	99	1
Dioxane	8	63	$\gg 99$	≈ 0.2
	8	62[c)]	$\gg 99$	≈ 0.1
THF	8	55	86	14
DME	6	59	75	25
Acetonitrile	2	47	80	20

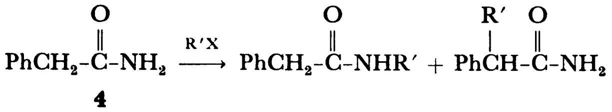
a) All the reactions were carried out with **1** (10 mmol), ethyl bromide (12 mmol), KOH (50 mmol) + Al_2O_3 (M-90-N, 10 g), and hexadecane (0.3 g) in a solvent (20 ml) at 60 °C. b) Mono+Di; determined by GLC. c) Al_2O_3 (M-60-B, 10 g).

yields than KOH/Al_2O_3 in a solvent except benzene and acetonitrile, and better selectivities than KOH/Al_2O_3 for N-monoalkylation in all solvents. These findings are quite in contrast to the results of the alkylation of PAN, in which KOH/Al_2O_3[4a)] is superior to $KOH+Al_2O_3$[4b)] in both yield and selectivity for monoalkylation. This fact indicates that the N-alkylation of **1** occurs in the pores of alumina even when $KOH+Al_2O_3$ is employed. The difference in selectivity between KOH/Al_2O_3 and $KOH+Al_2O_3$ can be interpreted as follows. For KOH/Al_2O_3, KOH is present in the pores. Therefore, KOH/Al_2O_3 must deprotonate the N-alkylated product formed in the pores more rapidly than $KOH+Al_2O_3$, thus lowering the selectivity. The difference in the yield can be interpreted as follows. Since alumina was ground together with KOH in the case of $KOH+Al_2O_3$, the particle size of the alumina in $KOH+Al_2O_3$ must be smaller than the particle size in KOH/Al_2O_3. Therefore, the increase in the yield may be thought to be due to the increase in the surface area of alumina. However, as is shown in Table 4, only slight changes in yield and selectivity for N-monoalkylation were observed when twice as much KOH and alumina were used as in the standard. Furthermore, for both KOH/Al_2O_3 and $KOH+Al_2O_3$, almost no **1** was observed in the organic phase during the reaction. These facts indicate that **1** is uniformly adsorbed on both active and inactive sites. To examine the influence of pulverization of alumina, alkylation of **1** with ethyl bromide was carried out using virgin alumina or alumina ground separately from KOH. In the cases of both M-90-N and M-60-B, the results were quite similar to those obtained by using alumina ground together with KOH. These results indicate that, since KOH/Al_2O_3 contains KOH in its pores, KOH/Al_2O_3 more strongly adsorbs **1** in its pores.

Table 4 summarizes the results of the N-alkylation of **1** with various alkylhalides using $KOH+Al_2O_3$ in dioxane. Alkyl bromide was better than alkyl iodide in both yield and selectivity for N-monoalkylation. This finding contrasts with the results of the alkylation of PAN using KOH/Al_2O_3,[4a)] where alkyl iodide was better than alkyl bromide. This indicates that the N-alkylation of **1** is more sterically retarded than the alkylation of PAN. This fact supports the idea that the ion-pair aggregates of **6** are the true reactants in dioxane. Alkyl iodide gave N,N-dialkylated products in higher yields than did alkyl bromide. N,N-Dialkylation should occur predominantly in the bulk organic phase and/or on the surface of KOH. The influence of the molecular size of the alkylating agents on the yield was more significant when M-60-B was employed than when M-90-N was used. This result seems surprising since the pore sizes of both M-90-M and M-60-B are much larger than the molecular sizes of **1** and **5**. However, this result can well be understood if the ion-pair aggregates of **6** are the true reactants. This result indicates that the yield and the selectivity for N-monoalkylation are intrinsically dependent upon the pore size.

For both KOH/Al_2O_3 and $KOH+Al_2O_3$, the reaction was very clean; GLC showed that the only products were N-mono- and N,N-dialkylated **1**. Almost all of the **1** was adsorbed on the alumina. Consequently, N-monoalkylated products were isolated in a highly pure state by filtering the solid material and removing the solvent. The unreacted **1** adsorbed on alumina was recovered in an 85—90% yield by adding a small amount of water to the alumina and by then extracting with benzene. Because of this recovery, the yields of N-monoalkylation were 89—92% (Table 4).

This method, using KOH/Al_2O_3 or $KOH+Al_2O_3$, was also utilized in the N-alkylation of other amides. Table 5 summarizes the results. In general, the N-monoalkylated products were obtained in good yields with extremely high selectivities. However, the use of highly reactive allyl bromide or benzyl bromide as an alkylating agent lowered the selectivity for N-monoalkylation. For selectivity in N-monoalkylation, $KOH+Al_2O_3$ and M-60-B were better than KOH/Al_2O_3 and M-90-N, respectively. Butanamide (**3**), bearing a bulkier alkyl group, gave more preferentially N-monoalkylated products than acetamide (**2**). For 2-phenylacetamide (**4**), the C–H bond at the α-position is also acidic, so the C-alkylation at the α-position is thought to accompany the N-alkylation.



$$PhCH_2\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}NH_2 \xrightarrow{R'X} PhCH_2\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}NHR' + Ph\overset{\overset{\displaystyle R'}{|}}{C}H\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}NH_2$$

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In fact, the components of the products were more complicated than in the cases of the other amides. GLC showed the presence of several components

TABLE 4. *N*-ALKYLATION OF **1** USING KOH+Al_2O_3 IN DIOXANE[a)]

5	Al_2O_3 (g)	KOH mmol	Yield[b)] %	Selectivity Mono/%	; Di/%
C_2H_5Br	M-90-N (10)	50	63 (92)[c)]	$\gg$99	$\approx$0.2
	M-60-B (10)	50	62	$\gg$99	$\approx$0.1
	M-90-N (20)	100	61	$>$99	$\approx$0.6
C_2H_5I	M-90-N (10)	50	62	98.7	1.3
n-C_3H_7Br	M-90-N (10)	50	58 (90)[c)]	$\gg$99	$\approx$0.2
	M-60-B (10)	50	32	$\approx$100	$\approx$0
	M-90-N (20)	100	59	$>$99	$\approx$0.8
n-C_3H_7I	M-90-N (10)	50	33	98	2
n-C_4H_9Br	M-90-N (10)	50	54 (89)[c)]	$\gg$99	$<$0.1
	M-60-B (10)	50	24	$\approx$100	$\approx$0
	M-90-N (20)	100	50	$>$99	$\approx$0.4
n-C_4H_9I	M-90-N (10)	50	32	98	2

a) All the reactions were carried out with **1** (10 mmol), **5** (12 mmol), and hexadecane (0.3 g) in dioxane (20 ml) at 60 °C for 8 h. b) Mono+Di; determined by GLC. c) Isolated yields based on the **1** consumed.

TABLE 5. *N*-ALKYLATION OF AMIDES USING KOH/Al_2O_3 OR KOH+Al_2O_3[a)]

Amide	Alkyl bromide	Method[b)]	Temp °C	Alumina	Yield[c)] %	Selectivity for *N*-monoalkylation/%
Acetamide	C_2H_5Br	A	60	M-60-B	(61)	88.5
(**2**)		B	60	M-60-B	74[d)]	97.1
	n-C_4H_9Br	A	60	M-60-B	57[d)]	97.8
		B	60	M-90-N	80[d)]	97.0
Butanamide	C_2H_5Br	A	60	M-60-B	80	98.9
(**3**)		B	60	M-60-B	(79)	99.2
		B	60	M-90-N	83	98.7
	n-C_4H_9Br	B	60	M-90-N	80	99.6
	$CH_2=CHCH_2Br$	B	40	M-60-B	(74)	97.0
		B	40	M-90-N	71 (81)	96.8
	$PhCH_2Br$	B	30	M-60-B	79	97.1
		B	30	M-90-N	76 (87)	95.8
2-Phenylacetamide	C_2H_5Br	A	60	M-60-B	71 (75)	97.5
(**4**)		B	60	M-60-B	(71)	97.6
	n-C_4H_9Br	A	60	M-90-N	60 (66)	99.5
		B	60	M-90-N	(57)	98.0
	$CH_2=CHCH_2Br$	A	40	M-60-B	57 (69)	82.0
		B	40	M-60-B	(66)	89.0
	$PhCH_2Br$	A	30	M-90-N	65 (69)	80.8
		B	30	M-90-N	69	86.0
Benzamide	$CH_2=CHCH_2Br$	B	40	M-90-N	(67)	93.2
(**1**)		B	40	M-60-B	56 (68)	95.5
	$PhCH_2Br$	B	30	M-90-N	71 (77)	96.5

a) All the reactions were carried out with amide (10 mmol), alkyl bromide (12 mmol), and dioxane (20 ml) for 8 h. b) A: KOH/Al_2O_3, B: KOH+Al_2O_3. c) Isolated yield. Unless otherwise noted, the purities were >97%. The values in parentheses are the yields determined by GLC. d) Purities were >96%.

other than *N*-monoalkylated products. In particular, when highly reactive allyl bromide or benzyl bromide was employed, GLC showed the presence of substantial quantities of several products, including the *N*-monoalkylated one.

For comparison, a solid-liquid phase-transfer alkylation of **4** was carried out using powdered KOH and tetrabutylammonium bromide (n-$Bu_4N^+Br^-$). Table 6 shows the results. These results indicate that the acidity of the C–H bond is similar to that of the N–H bond.[8)] The regioselectivity for the alkylation of **4** using KOH+Al_2O_3 or KOH/Al_2O_3 must be explained

TABLE 6. ALKYLATION OF **4** USING SOLID-LIQUID PHASE-TRANSFER METHOD[a)]

Alkyl bromide	Temp °C	Time h	Yield[b)] %	Selectivity for *N*-monoalkylation/%
C_2H_5Br	60	2.5	35	85
$CH_2{=}CHCH_2Br$	40	1.5	18	47
$PhCH_2Br$	30	1.5	21	49

a) All the reactions were carried out with **4** (10 mmol), powdered KOH (50 mmol), alkyl bromide (12 mmol), and *n*-$Bu_4N^+Br^-$ (5 mmol) in benzene (20 ml). An almost complete conversion of **4** was observed. b) Isolated yields.

in terms of the steric hindrance as follows. Since the reaction occurs in the pore, the steric hindrance preventing the *C*-alkylation at the internal position is much larger than that preventing the *N*-alkylation at the terminal position, so the *N*-alkylation occurs predominantly.

In conclusion, amides are selectively *N*-monoalkylated by using KOH+Al_2O_3 or KOH/Al_2O_3. Even 2-phenylacetamide (**4**) is regioselectively *N*-monoalkylated in good yields. In dioxane, the enolate-like species **6** exists as stable ion-pair aggregates, which are the true reactants in the pores.

Experimental

Materials. Unless otherwise noted, reagents were obtained commercially. Benzamide (**1**), acetamide (**2**), butanamide (**3**), 2-phenylacetamide (**4**) (reagent grade, Tokyo Kasei Kogyo Co.), alumina (Merck 90 neutral, 70—230 mesh, activity I, Catalog No. 1077; Merck 60 basic, 70—230 mesh, activity I, Catalog No. 1067; Woelm 200 neutral, activity super I), Molecular Sieve 13X (for gas chromatography, 60—80 mesh), and 85% KOH were used as obtained. Alkyl halide (**5**), benzene, dioxane, THF, DME, and acetonitrile were dried with Molecular Sieve 4A. KOH/Al_2O_3 was prepared by the method previously reported.[4a)] KOH+Al_2O_3 was prepared by the method similar to that reported by Regen where reagent and alumina were ground together in a mortar.[9)] The authentic samples of *N*-ethyl- (**1a**), *N*-propyl- (**1b**), *N*-butyl- (**1c**), *N,N*-diethyl-, *N,N*-dipropyl-, and *N,N*-dibutylbenzamide were prepared by the literature method.[1)]

Typical Procedure Using KOH/Al_2O_3. N-Alkylation of Benzamide (1): A mixture of KOH/Al_2O_3 obtained from 85% KOH (3.3 g, 50 mmol) and alumina (10 g), **1** (10 mmol), **5** (12 mmol), hexadecane (0.3 g) as an internal standard, and a solvent (20 ml) was vigorously stirred at 60 °C for 8 h. After the mixture had been cooled to room temperature, water (5 ml) was added to it with vigorous stirring. The yields of *N*-mono- and *N,N*-dialkylation were determined by GLC analysis of the organic phase. When acetonitrile was employed as a solvent, hexadecane (0.3 g) as an internal standard in benzene (10 ml) was added after the reaction had finished.

N-*Allyl-2-phenylacetamide (4d)*: A mixture of 85% KOH (3.3 g, 50 mmol)/M-60-B (10 g), **4** (1.35 g, 10 mmol), allyl bromide (1.45 g, 12 mmol), and dioxane (20 ml) was vigorously stirred at 40 °C for 8 h. GLC showed that the selectivity was 82%. The solid material was filtered off and washed with benzene (30 ml×2). Removing the solvent under reduced pressure gave 1.5 g of the crude product. Recrystallization from benzene-hexane gave 1.0 g (57% yield, 98% purity) of **4d**, mp 59—61 °C. Further recrystallization gave pure **4d** having mp 60—61 °C; IR (KBr) 3230, 1625, 1555 cm^{-1}. Found: C, 75.05; H, 7.62; N, 8.10%. Calcd for $C_{11}H_{13}NO$: C, 75.43; H, 7.43; N, 8.00%.

N-*Ethyl-2-phenylacetamide (4a)*: A mixture of 85% KOH (3.3 g, 50 mmol)/M-60-B (10 g), **4** (1.35 g, 10 mmol), ethyl bromide (1.3 g, 12 mmol), and dioxane (20 ml) was vigorously stirred at 60 °C for 8 h. GLC showed that the selectivity was 97.5%. The same treatment as **4d** gave 1.25 g (77% yield, 97% purity) of **4a**, mp 60—68 °C. Recrystallization from ether-hexane gave 1.15 g (71% yield) of pure **4a**, mp 69—70 °C (lit,[10)] mp 69.5 °C); IR (KBr) 3290, 1635, 1555 cm^{-1}.

N-*Butyl-2-phenylacetamide (4c)*: A mixture of 85% KOH (3.3 g, 50 mmol)/M-60-B (10 g), **4** (1.35 g, 10 mmol), butyl bromide (1.7 g, 12 mmol), and dioxane (20 ml) was vigorously stirred at 60 °C for 8 h. The same treatment as **4a** gave 1.25 g, (66% yield, 99% purity) of **4b**, mp 53—55 °C. Recrystallization from ether-hexane gave 1.15 g (60% yield) of **4b**, mp 55—56 °C (lit,[11)] mp 55—56 °C); Ir (KBr) 3250, 1630, 1560 cm^{-1}.

Typical Procedure Using KOH+Al_2O_3. N-*Alkylation of 1*: Alumina (10 g) and 85% KOH (3.3 g, 50 mmol)were ground together in a mortar. To this solid material was added a mixture of **1** (10 mmol), **5** (12 mmol), hexadecane (0.3 g) as an internal standard, and a solvent (20 ml). The mixture was vigorously stirred at 60 °C for 8 h. The reaction mixture was treated and GLC analyzed by the same method as described in the case of KOH/Al_2O_3.

N-*Allylbutanamide (3d)*: A mixture of 85% KOH (3.3 g, 50 mmol)+M-90-N (10 g), **3** (0.87 g, 10 mmol), allyl bromide (1.45 g, 12 mmol), and dioxane (20 ml) was vigorously stirred at 40 °C for 8 h. The solid material was filtered off and washed with benzene (30 ml×2). After removal of the solvent, distillation gave 0.9 g (71% yield, 97% purity) of **3d**, bp 80—87 °C/1 mmHg (1 mmHg=133.322Pa). Purification by column chromatography (W-200-N, benzene and benzene-THF) gave pure **3d** having bp 88—89 °C/1 mmHg; IR (neat) 3280, 1640, 1545 cm^{-1}. Found: C, 65.68; H, 10.31; N, 10.87%. Calcd for $C_7H_{13}NO$: C, 66.14; H, 10.24; N, 11.02%.

N-*Benzylbutanamide (3e)*: The alkylation of **3** with benzyl bromide (2.0 g, 12 mmol) similar to that with allyl bromide was performed using M-60-B. GLC showed that the selectivity was 97.1%. After the same treatment as **3d**, recrystallization from ether-hexane gave 1.4 g (79% yield) of **3e**, mp 49.5—50.5 °C; IR (KBr) 3290, 1630, 1550 cm^{-1}. Found: C, 74.34; H, 8.55; N, 7.90%. Calcd for $C_{11}H_{15}NO$: C, 74.58; H, 8.47; N, 7.91%.

N-*Allylbenzamide (1d)*: The alkylation of **1** using 85% KOH (3.3 g, 50 mmol)+M-60-B (10 g) with allyl bromide (1.45 g, 12 mmol) similat to that of **3** with allyl bromide was performed. The solid meterial was filtered off and washed with benzene (30 ml×2). After removal of the solvent, column chromatography (W-200-N, benzene and benzene-THF) gave 0.9 g (56% yield) of **1d** having bp 113—114 °C/0.2 mmHg (lit,[12] bp 173—174 °C/14 mmHg); IR (neat) 3300, 1640, 1535 cm^{-1}.

N-*Ethylacetamide (2a)*: Bp 69—70 °C/2 mmHg (lit,[13] bp 140—141 °C/91 mmHg); IR (neat) 3280, 1645, 1555 cm^{-1}.

N-*Butylacetamide (2c)*: Bp 89—90 °C/1.3 mmHg (lit,[13] bp 121—122 °C/13 mmHg); IR (neat) 3270, 1650, 1550 cm^{-1}.

N-*Ethylbutanamide (3a)*: Bp 80—81 °C/1.2 mmHg (lit,[14] bp 101—102 °C/7 mmHg); IR (neat) 3280, 1640, 1540 cm^{-1}.

N-*Butylbutanamide (3c)*: Bp 104—105 °C/1.2 mmHg (lit,[15] bp 138—140 °C/13 mmHg); IR (neat) 3280, 1640, 1545 cm^{-1}.

N-*Benzyl-2-phenylacetamide (4e)*: Mp 119—120 °C (lit,[10] mp 119 °C); IR (KBr), 3280, 1635, 1545 cm^{-1}.

N-*Benzylbenzamide (1e)*: Mp 105—106 °C (lit,[16] mp 106 °C); IR (KBr) 3280, 1640, 1550 cm^{-1}.

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