N-Alkylation of Pyrrole, Indole, and Several Other Nitrogen Heterocycles Using Potassium Hydroxide as a Base in the Presence of Polyethylene Glycols or Their Dialkyl Ethers

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The alkylation of pyrrole and indole in aqueous potassium hydroxide-organic two-phase systems in the presence of polyethylene glycols (PEG) or their dialkyl ethers (PEG-ether) as phase transfer catalysts (PTC) gave substantial quantities of the *C*-alkylated and *C,N*-polyalkylated products as well as the *N*-alkylated products. This fact is similar to that obtained in the presence of quaternary ammonium salts as PTC. In powdered potassium hydroxide-organic two-phase systems, the yields of the *N*-alkylated products were generally high. Especially, when PEG-ether were employed as solvents, the *N*-alkylated products were obtained in excellent yields under mild conditions. Imidazole, benzimidazole, carbazole, 2-methylindole, and benzotriazole were similarly *N*-alkylated in high yields by this method.

It has been reported that the *N*-alkylation of nitrogen heterocycles such as pyrrole and indole can be achieved by use of various bases such as potassium,[1] sodium amide,[2] sodium hydroxide in hexamethylphosphoric triamide,[3] potassium hydroxide in dimethyl sulfoxide,[4] and thallium(I) ethoxide.[5] Moreover, phase transfer procedures have been recently developed.[6] In many cases, concentrated aqueous sodium hydroxide was employed as a base in the presence of quaternary ammonium salts as phase transfer catalysts (PTC), and substantial quantities of the *C*-alkylated and *C,N*-polyalkylated (*C*- and *C,N*-alkylated) derivatives were obtained as by-products.

On the other hand, Santaniello *et al.*[7] have reported that *N*-alkylpyrrole and indole are obtained in good yields by use of potassium hydroxide as a base in the presence of crown ethers as PTC. Also Guida and Mathre[8] found that the *N*-alkylation of nitrogen heterocycles can be achieved in good yields by use of potassium *t*-butoxide as a base in the presence of crown ethers as PTC.

In this paper, the author reports the *N*-alkylation of nitrogen heterocycles using aqueous or powdered potassium hydroxide as a base in the presence of polyethylene glycols (PEG) or their dialkyl ethers (PEG-ether).

Results and Discussion

N-*Alkylation of Pyrrole and Indole in Aqueous Potassium Hydroxide-organic Two-phase Systems in the Presence of PEG or PEG-ether as PTC.* Table 1 shows that the results of *N*-alkylation of pyrrole and indole in aqueous potassium hydroxide-organic two-phase systems in the presence of PEG-1000, PEG-1000-diethyl ether (PEG-1000-Et_2) or PEG-600-dibutyl ether (PEG-600-Bu_2) as PTC. The yields of the *N*-alkylation were similar to those of the reported method[6] using quaternary ammonium salts as PTC.

It is well known[9] that the pyrrolyl and indolyl anion exhibit ambident behavior, and thus substantial quantities of the *C*- and *C,N*-alkylated products as well as the *N*-alkylated products are obtained. Under the present experimental conditions, the alkylation of pyrrole also gave many *C*- and *C,N*-alkylated products, which were detected by GLC. In the case of indole, GLC showed the presence of a few components except the *N*-alkylated products. In the cases of both pyrrole and indole, the alkylation with isopropyl bromide gave the *N*-alkylated products in extremely low yields because of the elimination of hydrogen bromide from isopropyl bromide, induced by the pyrrolyl or indolyl anion. This result contrasts with the result in which α-isopropylphenylacetonitrile is obtained in high yields under the same conditions,[10] indicating that the pyrrolyl and indolyl anions are much harder[11] than $PhC\bar{H}CN^{\ominus}$.

N-*Alkylation of Pyrrole and Indole in Powdered Potassium Hydroxide-organic Two-phase Systems in the Presence of PEG or PEG-ether as PTC.* Table 2 shows the results of the *N*-alkylation of pyrrole and indole using PEG-1000 or PEG-1000-Et_2. On the basis of the results reported by Santaniello *et al.*,[7] equimolar amounts of potassium hydroxide and pyrrole or indole (molar ratio: KOH/heterocycle=1/1) were used. However, the yields of the *N*-alkylation were lower than those reported by them.

Table 3 shows the effects of the relative amount of potassium hydroxide to pyrrole on the *N*-ethylation. For the molar ratio: KOH/pyrrole=1/1, an incomplete conversion of pyrrole to the product was observed. Furthermore, substantial quantities of the *C*- and *C,N*-ethylated products were obtained. For the molar ratio: KOH/pyrrole=2/1—3/1, the yields of the *N*-ethylation came to the constant value (88% by GLC).

On the basis of the data given in Table 3, the *N*-alkylations were carried out under the molar ratio: KOH/heterocycle=3/1, giving *N*-alkylated products in high yields (Table 2). These facts suggest that the water formed is absorbed by the excess potassium hydroxide and fixed in the solid phase, completing the conversion to the product.

N-*Alkylation of Pyrrole and Indole Using Powdered Potassium Hydroxide as a Base and PEG-ether as Solvents.* Table 4 shows the *N*-alkylation of pyrrole and indole using PEG-400-Et_2 as a solvent (molar ratio: PEG-400-Et_2/heterocycle=1/1 or 2/1). When the alkylating agents except isopropyl bromide and *t*-butyl bromide were employed, the *N*-alkylated products were obtained in extremely high yields. Moreover, the

Table 1. *N*-Alkylation of pyrrole and indole in aqueous-organic two-phase systems in the presence of PEG or PEG-ether as PTC[a]

	Alkyl halide		Catalyst[b] (mmol)	(Product) Yield[c]/% *N*-Alkylation	d)	Starting material
Pyrrole **1**	C_2H_5Br	**a**	A (2.5)	(**1a**) 84[e] (83)	(16)	(1)
	n-C_4H_9Br	**b**	A (2.5)	(**1b**) 65 (69)	(27)	(4)
			B (2.5)	(**1b**) 61[f] (65)	(32)	(3)
			C (2.5)	(**1b**) 66[f] (67)	(28)	(5)
	i-C_3H_7Br	**c**	A (5)	(**1c**) 46[g] (43)	(31)	(26)
	CH_2=$CHCH_2Br$	**e**	A (2.5)	(**1e**) (13)	(73)	(14)
	$PhCH_2Cl$	**f**	A (2.5)	(**1f**) 79 (85)	(10)	(5)
			B (2.5)	(**1f**) 78 (84)	(11)	(5)
			C (2.5)	(**1f**) 79 (84)	(10)	(6)
Indole **2**	C_2H_5Br	**a**	A (2.5)	(**2a**) 90 (94)	(6)	
			B (2.5)	(**2a**) 92 (94)	(6)	
	n-C_4H_9Br	**b**	A (2.5)	(**2b**) 86 (90)	(10)	
	i-C_3H_7Br	**c**	A (5)	(**2c**) (7)	(18)	(75)
	CH_2=$CHCH_2Br$	**e**	A (2.5)	(**2e**) 50 (56)	(44)	
	$PhCH_2Cl$	**f**	A (2.5)	(**2f**) 81 (86)	(14)	
			B (2.5)	(**2f**) 80 (86)	(14)	

a) All reactions were carried out with 0.1 mol of heterocycle, 0.15 mol of alkyl halide, 30 ml of benzene, and 0.5 mol of potassium hydroxide in 14 g of water at 45 °C for 2 h. b) A: PEG-1000-Et_2, B: PEG-1000, C: PEG-600-Bu_2. c) Isolated yields. Values in parentheses are the yields determined by GLC. Unless otherwise noted, the purities of *N*-alkylpyrrole and indole were 98 and 99% by GLC, respectively. d) Total yields of the C- and C, *N*-alkylated products, determined by GLC. However, all the products were not identified. e), f),g) Purities were 93, 97, and 78% by GLC, respectively.

Table 2. *N*-Alkylation of pyrrole and indole in solid-organic two-phase systems in the presence of PEG or PEG-ether as PTC[a]

	Alkyl halide		Catalyst[b] (mmol)	Temp °C	Time h	KOH (mol)	(Product) Yield[c]/% *N*-Alkylation	d)	Starting material
Pyrrole **1**	C_2H_5Br	**a**	A (2.5)	65	4	0.1	(**1a**) (67)	(13)	(20)
	n-C_4H_9Br	**b**	B (2.5)	70	4	0.1	(**1b**) 41[e] (55)	(25)	(21)
			A (2.5)	85	2	0.3	(**1b**) 74 (79)	(21)	
			B (10)	85	2	0.3	(**1b**) 80 (86)	(14)	
	CH_2=$CHCH_2Br$	**e**	A (2.5)	85	2	0.3	(**1e**) (24)	(64)	(12)
	$PhCH_2Cl$	**f**	A (2.5)	70	5	0.1	(**1f**) 65[f] (72)	(15)	(13)
			A (2.5)	85	2	0.3	(**1f**) 88 (90)	(10)	
			A (10)	85	2	0.3	(**1f**) 90 (98)	(2)	
Indole **2**	C_2H_5Br	**a**	A (2.5)	65	4	0.1	(**2a**) 78[g] (85)	(6)	(9)
	n-C_4H_9Br	**b**	B (2.5)	70	4	0.1	(**2b**) 68[h] (80)	(8)	(12)
			A (2.5)	85	2	0.3	(**2b**) 87 (95)	(5)	
			A (10)	85	2	0.3	(**2b**) 94 (98)	(2)	
	CH_2=$CHCH_2Br$	**e**	A (2.5)	85	2	0.3	(**2e**) 56[i] (67)	(33)	
	$PhCH_2Cl$	**f**	A (2.5)	65	3	0.1	(**2f**) 63[j] (68)	(15)	(17)
			A (2.5)	85	2	0.3	(**2f**) 83 (87)	(13)	
			A (10)	85	2	0.3	(**2f**) 88 (95)	(5)	

a) All reactions were carried out with 0.1 mol of heterocycle and 0.15 mol of alkyl halide in 30 ml of benzene. b) A: PEG-1000-Et_2, B: PEG-1000. c),d) see footnotes c), d) in Table 1, respectively. e),f),g),h),i),j) Purities were 92, 97, 92, 91, 97, and 98% by GLC, respectively.

yields of the *C*- and *C,N*-alkylated products were generally extremely low. The alkylation of indole with primary alkyl bromide or benzyl chloride gave *N*-alkylated products in almost quantitative yields. Even *N*-allylindole was obtained in 89—91% yields, which were comparable to that of the reported method using sodium hydride as a base in hexamethylphosphoric triamide.[3]

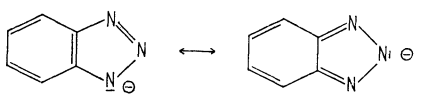
When isopropyl bromide was used as an alkylating agent, the considerable evolution of gas was observed during the reaction, and pyrrole or indole was recovered in 25-8 or 76—80%, respectively. As shown

in Table 1, the reaction of pyrrole or indole with isopropyl bromide using PEG or PEG-ether as PTC also gave pyrrole or indole in 26 or 75% yields, respectively. These facts indicate that the indolyl anion tends to induce the elimination reaction with isopropyl bromide in comparison with the pyrrolyl anion and is much harder[11] than the latter.

When PEG-400 was employed as a solvent in place of PEG-400-Et_2, the yields of *N*-alkylated products were extremely low because of the accompanied alkylation of PEG. For example, the alkylation of pyrrole with ethyl bromide gave pyrrole (49%), *N*-ethylpyrrole (43%), and *C*- and *C,N*-ethylated products (8% by GLC). The alkylation with *n*-butyl bromide gave pyrrole (39%), *N*-butylpyrrole (53%), and *C*- and *C,N*-butylated products (8% by GLC).

Since hydrogen bond is a hard-hard interaction,[11] under the condition containing large amount of water such as the aqueous-organic phase transfer system or in protic solvents such as PEG, water or PEG is capable of forming hydrogen bonding with the harder nitrogen atom of the heterocycle anion, suppressing the *N*-alkylation.[12] Therefore, the *C*-alkylation will increase. However, in PEG-ether, which is aprotic and would greatly increase the degree of dissociation[13] of the heterocycle anion, the exclusive *N*-alkylation could be achieved.

The method using potassium hydroxide as a base and PEG-ether as a solvent was applied to the alkylation of several nitrogen heterocycles. Table 5 shows the results. The alkylation of carbazole, imidazole, and benzimidazole gave 1-alkylated products in extremely high yields. However, in the case of benzotriazole, substantial quantities of 2-alkylbenzotriazole were obtained, in contrast to the alkylation of benzimidazole. This fact indicates that canonical structure of **13** would significantly contribute to the reactivity of the benzotriazolyl anion.



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In contrast to the alkylation of indole, the alkylation of 2-methylindole with ethyl bromide or benzyl chloride gave 1,3-dialkylated products as well as 1-alkylated products in 2 or 16% yields, respectively.

TABLE 3. INFLUENCE OF THE AMOUNTS OF POTASSIUM HYDROXIDE ON THE ETHYLATION OF PYRROLE[a]

KOH (mol)	Yield[b]/%		
	1a	c)	Starting material
0.1	67	13	20
0.15	78	14	8
0.2	86	13	1
0.3	88	12	—
0.4	88	12	—
0.5	89	11	—

a) All reactions were carried out with 0.1 mol of pyrrole, 0.15 mol of ethyl bromide, and 30 ml of benzene at 65 °C for 4 h in the presence of 2.5 mmol of PEG-1000-Et_2 as PTC. b) Determined by GLC. c) See footnote d) in Table 1.

TABLE 4. *N*-ALKYLATION OF PYRROLE AND INDOLE IN PEG-400-Et_2[a]

	Alkyl halide		PEG-400-Et_2 (mol)	Time / h	(Product) Yield[b]/%			
					N-Alkylation		c)	Starting material
Pyrrole **1**	C_2H_5Br	**a**	0.1	2	(**1a**) 88	(97)	(3)	
	n-C_4H_9Br	**b**	0.1	2	(**1b**) 91	(95)	(5)	
			0.2	2	(**1b**) 90	(95)	(5)	
	i-C_3H_7Br	**c**	0.1	3	(**1c**) 50[d]	(67)	(8)	(25)
			0.2	3	(**1c**) 53	(67)	(5)	(28)
	t-C_4H_9Br	**d**	0.1	3				(≈99)
	CH_2=$CHCH_2Br$	**e**	0.1	1	(**1e**) 43[e]	(40)	(53)	(7)
			0.2	1	(**1e**)	(42)	(47)	(11)
	$PhCH_2Cl$	**f**	0.1	2	(**1f**) 94	(99)	(1)	
	n-$C_8H_{17}Br$	**g**	0.1	2	(**1g**) 90	(96)	(4)	
Indole **2**	C_2H_5Br	**a**	0.1	2	(**2a**) 96 (≈100)			
	n-C_4H_9Br	**b**	0.1	2	(**2b**) 96 (≈100)			
	i-C_3H_7Br	**c**	0.1	3	(**2c**)	(21)	(3)	(76)
			0.2	3	(**2c**)	(18)	(2)	(80)
	t-C_4H_9Br	**d**	0.1	3				(≈99)
	CH_2=$CHCH_2Br$	**e**	0.1	1	(**2e**) 89	(92)	(8)	
			0.2	1	(**2e**) 91	(95)	(5)	
	$PhCH_2Cl$	**f**	0.1	2	(**2f**) 97 (≈100)			
	n-$C_8H_{17}Br$	**g**	0.1	2	(**2g**) 96 (≈100)			

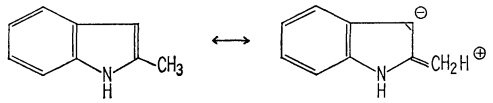
a) All reactions were carried out with 0.1 mol of heterocycle, 0.15 mol of alkyl halide, and 0.3 mol of potassium hydroxide in PEG-400-Et_2 at 30 °C. b), c) See footnotes c) and d) in Table 1, respectively. d),e) Purities were 80 and 84% by GLC, respectively.

Table 5. *N*-Alkylation of heterocycles in PEG-400-Et_2[a]

	Alkyl halide[b]		Reaction time/h	(Product) Yield[c]/% 1-Alkylated product		Other product		
2-Methylindole **3**	C_2H_5Br	**a**	2	(**3a**) 95	(98)	d)		(2)
	$PhCH_2Cl$	**f**	2	(**3f**) 80	(84)	1,3-Dibenzyl-2-methylindole (**8**)	14	(16)
Carbazole **4**	C_2H_5Br	**a**	2	(**4a**) 92				
	n-C_4H_9Br	**b**	3	(**4b**) 93				
	CH_2=$CHCH_2Br$	**e**	2	(**4e**) 90				
	$PhCH_2Cl$	**f**	3	(**4f**) 97				
Imidazole **5**	C_2H_5Br	**a**	3	(**5a**) 94	(≈97)			
	CH_2=$CHCH_2Br$	**e**	2	(**5e**) 93	(≈97)			
	$PhCH_2Cl$	**f**	3	(**5f**) 91	(≈97)			
Benzimidazole **6**	C_2H_5Br	**a**	3	(**6a**) 93	(≈100)			
	CH_2=$CHCH_2Br$	**e**	2	(**6e**) 90	(≈97)			
	$PhCH_2Cl$	**f**	3	(**6f**) 97	(≈100)			
Benzotriazole **7**	C_2H_5Br	**a**	3	(**7a**) 35[e]	(40)	2-Ethylbenzotriazole (**9**)	51[f]	(59)
	CH_2=$CHCH_2Br$	**e**	2	(**7e**) 66[g]	(69)	2-Allylbenzotriazole (**10**)	16[h]	(24)
	$PhCH_2Cl$	**f**	3	(**7f**) 70	(78)	2-Benzylbenzotriazole (**11**)		(19)

a) All reactions were carried out with 0.05 mol of heterocycle and 0.15 mol of potassium hydroxide in 0.05 mol of PEG-400-Et_2 at 30 °C. b) In the cases of **3** and **4**, 0.075 mol of alkyl halide was used. In the cases of **5**, **6**, and **7**, 0.0525 mol of alkyl halide was used. c) Isolated yields by distillation or recrystallization. *N*-Ethyl- and *N*-allylimidazole were directly distilled from the reaction mixture. The values in parentheses were the yields determined by GLC. Unless otherwise noted, the purities of the products were >99% by GLC. d) Probably 1,3-diethyl-2-methylindole. e), f), g), and h) Purities were 94, 95, 90, and 91% by GLC, respectively.

This fact suggests that canonical structure of **14** should not be ignored.



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Experimental

Materials. Pyrrole, indole, carbazole, benzimidazole, imidazole, 2-methylindole, benzotriazole, and alkyl halides (reagent grade, Tokyo Kasei Kogyo Co., Ltd.) were used without further purification. PEG, benzene, and 85% potassium hydroxide (reagent grade, Kishida Kagaku Co., Ltd.) were used also without further purification. PEG-ether were prepared by the method previously reported.[14]

The physical properties of **1a**,**b**,**f**,[7] **1c**,[15] **1e**,[16] **1g**,[17] **2a**, **b**,**f**,[7] **2e**,[3] **3a**,[7] **3f**,[18] **4a**,**b**,**e**,**f**,[19] **5a**,[20] **5e**,[21] **5f**,[22] **6a**,[23] **6e**,[24] **6f**,[25] **7a**,[26] **7e**,[27] **7f**,[21] **9**,[26] and **10**[27] were in good agreement with those reported in the literatures. *N*-Isopropylindole (**2c**)[12] and 2-benzylbenzotriazole (**11**)[28] were not isolated and were identified by comparing GLC retention times with those of authentic samples prepared by the literature procedures. *N*-Octylindole (**2g**) had bp 131—132 °C/0.3 mmHg (1 mmHg=133.322 Pa). Found: C, 83.60; H, 10.19; N, 6.00%. Calcd for $C_{16}H_{23}N$: C, 83.79; H, 10.11; N, 6.11%. 1,3-Dibenzyl-2-methylindole (**8**) had mp 95 °C (from ethanol). Found: C, 88.98; H, 6.94; N, 4.44%. Calcd for $C_{23}H_{21}N$: C, 88.70; H, 6.80; N, 4.50%.

General Procedure of N-*Alkylation in Aqueous Potassium Hydroxide-organic Two-phase Systems in the Presence of PEG or PEG-ether as PTC.* N-*Butylpyrrole (**1b**)*: *n*-Butyl bromide (20.6 g, 0.15 mol) was added dropwise over a period of 30 min at 45 °C with vigorous stirring to a mixture of 6.7 g (0.1 mol) of pyrrole, 2.7 g (2.5 mmol) of PEG-1000-Et_2, 33.0 g (0.5 mol) of 85% potassium hydroxide, 14 g of water, and 30 ml of benzene. After the mixture had been stirred at 45 °C for further 2 h, it was cooled to room temperature. To the mixture was added 50 ml of water and then the two layers were separated. The aqueous layer was extracted with 10 ml of benzene. The benzene layer was combined with the organic layer, extracted with 3.5% hydrochloric acid (50 ml×2), washed with water (50 ml×3), and then dried. After removal of the benzene, the residue was distilled under reduced pressure, giving *N*-butylpyrrole (**1b**), 8.0 g (65%), bp 75—77 °C/28 mmHg (lit,[7] 171 °C/760 mmHg). The hydrochloric acid extract was treated according to the method previously reported,[10] giving 2.6 g (98%) of PEG-1000-Et_2.

General Procedure of N-*Alkylation in Powdered Potassium Hydroxide-organic Two-phase Systems in the Presence of PEG or PEG-ether as PTC.* N-*Benzylindole (**2f**)*: A mixture of 11.7 g (0.1 mol) of indole, 2.7 g (2.5 mmol) of PEG-1000-Et_2, 19.8 g (0.3 mol) of powdered 85% potassium hydroxide, and 30 ml of benzene was heated under reflux with vigorous stirring for 1 h. Benzyl bromide (19.0 g, 0.15 mol) was added dropwise to the mixture over a period of 30 min at 80—85 °C with vigorous stirring. After the mixture had been heated at 85 °C with vigorous stirring for 2 h, it was cooled to room temperature. To the mixture was added 50 ml of water. The mixture was worked up as described above, giving 17.2 g (83%) of *N*-benzylindole (**2f**), bp 142—144 °C/0.5 mmHg, mp 43 °C (lit,[4] 133—138 °C/0.3 mmHg, mp 42—43 °C).

General Procedure of N-*Alkylation Using Powdered Potassium Hydroxide as a Base and PEG-ether as Solvents.* N-*Allylindole (**2e**)*: A mixture of 11.7 g (0.1 mol) of indole, 46 g (0.1

mol) of PEG-400-Et_2, and 19.8 g (0.3 mol) of powdered 85% potassium hydroxide was vigorously stirred at room temperature for 30 min. Allyl bromide (18.2 g, 0.15 mol) was added dropwise over a period of 30 min at 30 °C with vigorous stirring to the mixture. After the mixture had been vigorously stirred for further 1 h, 50 ml of water was added. The two layers were separated. To the organic layer was added 100 ml of 3.5% hydrochloric acid and extracted with benzene (30 ml × 3). The benzene extract was extracted with 3.5% hydrochloric acid (50 ml × 2), washed with water and then dried. After removal of the benzene, the residue was distilled under reduced pressure, giving 14.0 g (89%) of *N*-allylindole (**2e**), bp 96—98 °C/2 mmHg (lit,[3] bp 114—116 °C/6 mmHg, 72—73 °C/0.12 mmHg). The hydrochloric acid solutions were combined, washed with 10 ml of benzene, added 40 g of sodium hydroxide, and then extracted with benzene (50 ml × 2). The benzene extract was dried and the benzene was removed to recover 45.5 g (99%) of PEG-400-Et_2.

*1-Benzylbenzimidazole (**6f**)*: A mixture of 5.9 g (0.05 mol) of benzimidazole, 23 g (0.05 mol) of PEG-400-Et_2 and 9.9 g (0.15 mol) of powdered 85% potassium hydroxide was vigorously stirred at room temperature for 30 min. Benzyl chloride (6.6 g, 0.0525 mol) was added dropwise over a period of 30 min at 30 °C with vigorous stirring to the mixture. The mixture was vigorously stirred for further 3 h at 30 °C. The reaction mixture was poured into 200 ml of 1.9% hydrochloric acid (0.104 mol). The precipitated solid was collected, washed with water, dried, and recrystallized from ethanol, giving 10.1 g (97%) of 1-benzylbenzimidazole (**6f**), mp 116—117 °C (lit,[25] mp 116—117 °C). The filtrate was washed with 10 ml of benzene and treated according to the manner used for *N*-allylindole (**2e**) to recover 22 g (96%) of PEG-400-Et_2.

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References

1) C. F. Hobbs, E. P. Papadopoulos, and C. A. Vanderwerf, *J. Am. Chem. Soc.*, **84**, 43 (1962); E. P. Papadopoulos and K. I. Y. Tabello, *J. Org. Chem.*, **33**, 1299 (1968).
2) K. T. Potts and J. E. Saxton, *Org. Synth.*, **40**, 68 (1960).
3) G. M. Rubotton and J. C. Chabala, *Org. Synth.*, **54**, 60 (1974).
4) H. Heanery and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 499; *Org. Synth.*, **54**, 58 (1974).
5) C. F. Candy and R. A. Jones, *J. Org. Chem.*, **36**, 3993 (1971).
6) A. Jonczyle and M. Makosza, *Rocz. Chem.*, **49**, 1203 (1975); *Chem. Abstr.*, **84**, 30793 (1976); A. Barco, S. Benetti, G. P. Pollini, and P. G. Baraldi, *Synthesis*, **1976**, 124; V. Bocchi, G. Casnati, A. Dossena, and F. Villani, *ibid.*, **1976**, 414.
7) E. Santaniello, C. Farachi, and F. Ponti, *Synthesis*, **1979**, 617.
8) W. C. Guida and D. J. Mathre, *J. Org. Chem.*, **45**, 3172 (1980).
9) Ref. 8 and references cited therein.
10) K. Sukata, *Yuki Gosei Kagaku Kyokai Shi*, **39**, 1132 (1981).
11) R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.*, **89**, 1827 (1967); *J. Org. Chem.*, **32**, 2899 (1967); T.-L. Ho, *Chem. Rev.*, **75**, 1 (1975).
12) B. Cardillo, G. Casnati, A. Pochini, and A. Rica, *Tetrahedron*, **23**, 3771 (1967).
13) L. L. Chan, K. H. Wong, and J. Smid, *J. Am. Chem. Soc.*, **92**, 1955 (1970).
14) K. Sukata, *Yuki Gosei Kagaku Kyokai Shi*, **39**, 86 (1981).
15) C. F. Candy, R. A. Jones, and P. H. Wright, *J. Chem. Soc., C*, **1970**, 2563.
16) P. A. Cantor and C. A. Vanderwerf, *J. Am. Chem. Soc.*, **80**, 970 (1958).
17) A. O. Pittet, J. V. Pascale, and D. E. Hruza, U. S. Patent 3980089 (1976).
18) Beil. 20 I, 126.
19) H. Nishi, H. Kohno, and T. Kano, *Bull. Chem. Soc. Jpn.*, **54**, 1897 (1981).
20) H. J. J. Loozen, J. J. M. Drouen, and O. Piepers, *J. Org. Chem.*, **40**, 3279 (1975).
21) R. Gassend, J. C. Maire, and J-C. Pommier, *J. Organomet. Chem.*, **133**, 169 (1977).
22) H. A. Staab and A. Mannschrock, *Chem. Ber.*, **95**, 1284 (1962); *Chem. Abstr.*, **57**, 5848 (1962).
23) Beil. 23 II, 152.
24) E. L. Ringwald and A. B. Craig, U. S. Patent 2623879 (1952); *Chem. Abstr.*, **47**, 9367 (1953).
25) A. M. Simonov, N. O. Vitkevich, and B. K. Martsokha, *Zh. Obshch. Khim.*, **30**, 3062 (1960); *Chem. Abstr.*, **55**, 16520 (1961).
26) F. Krollpfeiffer, A. Rosenberg, and C. Mühlhausen, *Justus Liebigs Ann. Chem.*, **515**, 113 (1935); *Chem. Abstr.*, **29**, 2166[1] (1935).
27) F. Krollpfeiffer, A. Rosenberg, and H. Pötz, *Ber.*, **71B**, 596 (1938); *Chem. Abstr.*, **32**, 4162[1] (1938).
28) R. Beahm, *Pharmazie*, **33**, 83 (1978).