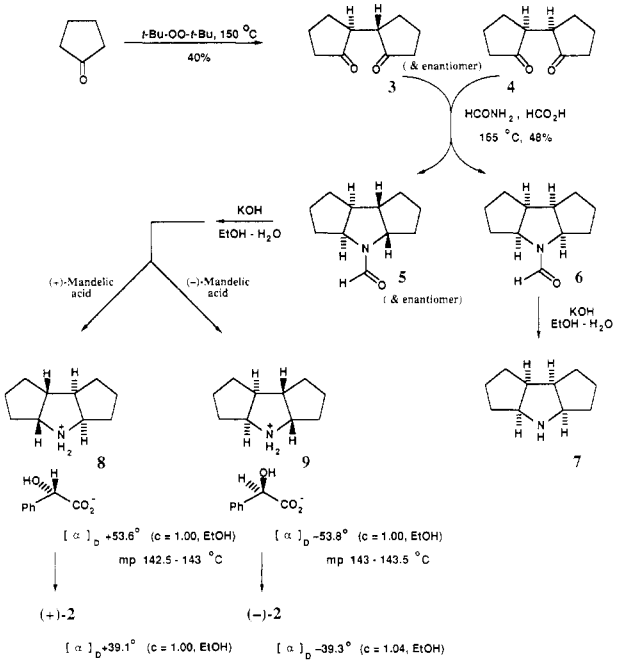

Figure 2.

oxidative dimerization[16] of cyclopentanone to a 1:1 mixture of *d,l* (**3**) and meso (**4**) diketones (Figure 2). Reductive amination of this mixture (or either separated diastereomer) with formamide (Leuckart reaction[17]) afforded a 2:1 mixture of formamides **5** and **6**. Removal of the undesired, "meso"[18] isomer was readily accomplished by selective hydrolysis with hydroxide in ethanol–water as the rate of conversion of formamide **6** to amine **7** is qualitatively 10 times faster than that for the analogous conversion of **5** to **2**. Subsequent hydrolysis of **5** after removal of **7** by simple aqueous acid extraction afforded racemic **2**. This amine was readily resolved as its mandelic acid salt, thereby providing ready and equal access to both enantiomers. Single-crystal X-ray analysis[19] of one of the diastereomeric salts[20] established the absolute configurations for (+)- and (-)-**2** to be as shown by internal reference to the mandelate residue. It is important to note that the synthesis of **2** involves no expensive reagents or solvents and that only simple distillation and aqueous–organic solvent partitioning are used for purifications.

Application of **2** to asymmetric induction is illustrated (Figure 3) by the formation of lactone **13**. The intermediate **12** was obtained with a diastereomeric excess of at least 95% (no evidence of a diastereomer by ^{13}C NMR spectroscopic analysis), and single-crystal X-ray analysis[19] established the absolute configurations of the two newly formed chiral centers (*) by internal reference to the amine subunit. Interestingly, it was found that 2 equiv of base

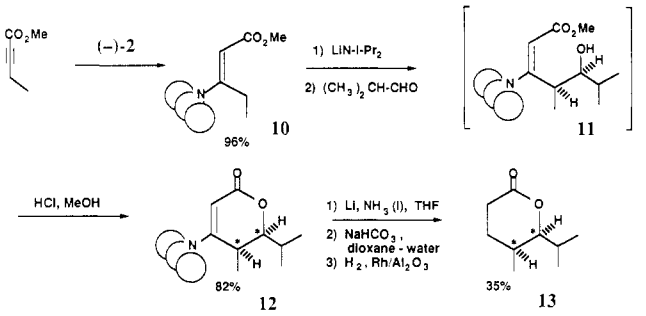

Figure 3.

was required for complete conversion in the alkylation step (**10** to **11**), but under these conditions, an 82% yield of recrystallized lactone **12** was obtained. Unlike the analogous sequence with dimethylpyrrolidine, the intermediate hydroxy ester **11** did not spontaneously lactonize. The final lactone (**13**) was obtained in optically pure form ($[\alpha]^{25}_D$ -96.5° (*c* = 1.5, $CHCl_3$), lit.[21] $[\alpha]^{25}_D$ +96° (*c* = 2.0, $CHCl_3$)) in 35% yield (unoptimized) from purified **12**.

There are numerous other potential applications of the amine **2** for asymmetric induction, including the use of the corresponding anion as a dialkylamide base as well as the incorporation of **2** into derived species such as bidentate ligands. We are vigorously pursuing these opportunities. In addition, we are building organic molecules from **2** for nonlinear optical applications where the chirality of the amine will enforce a noncentrosymmetric arrangement in the bulk materials.

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Supplementary Material Available: Full experimental details for the synthesis and resolution of the amine **2** (5 pages). Ordering information is given on any current masthead page.

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(18) Formamide **6** is in reality a mixture of enantiomers (interconverted by rotation about the amide linkage), the result of joining subunits of C_s symmetry with the mirror planes at right angles. Interestingly, the joining of subunits, one with C_2 and one with C_s mirror symmetry, to form formamides **5** does *not* provide for geometric stereoisomers.

(19) We are grateful to Dr. V. Lynch for these analyses, the details of which will be published elsewhere.

(20) The salt used, that derived from (-)-amine and (+)-mandelic acid, was one of the more soluble diastereomers ($[\alpha]_D$ +37.0° (*c* = 0.99, EtOH), mp 136–7 °C).

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James K. Whitesell,* Mark A. Minton
Kuo-Ming Chen
Department of Chemistry
The University of Texas at Austin
Austin, Texas 78712
Received July 6, 1988

Modification of Photochemical Reactivity by Zeolites: Selective Photorearrangement of α-Alkyldeoxybenzoins to *p*-Alkylbenzophenones in the Cavities of Faujasites†

Summary: Photolysis of α-alkyldeoxybenzoins included in Li–X and Li–Y zeolites gave the corresponding rearranged *p*-alkylbenzophenones in near quantitative yields via the Norrish type I α-cleavage process. Such a striking behavior contrasts their normal reactivity in solution.

Sir: The possibility that the internal cavities of zeolites can exert topological control on organic photochemical reactions has been recently established by Turro and others.[1] In this context, we have investigated the pho-

†Contribution No. 4697.

Scheme I

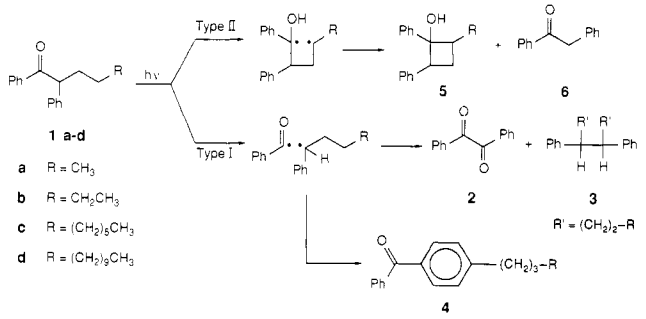


Table I. Product Distribution upon Irradiation of Alkyldeoxybenzoins in Zeolites

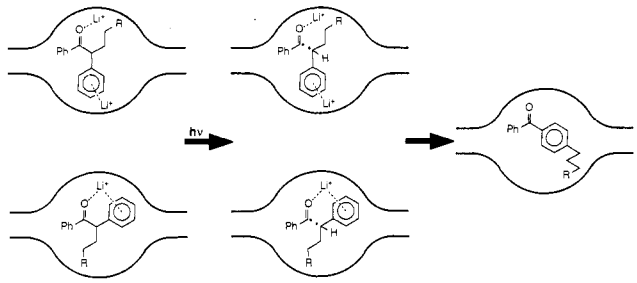
	percentage of products[a]				
medium	2	3	5	6	4
		Propyldeoxybenzoin			
benzene	5	24	54	17	
Li-X			4	1	95
Li-Y			15	10	75
		Butyldeoxybenzoin			
benzene	5	30	45	20	
Li-X			6	4	90
Li-Y			6	3	91
		Octyldeoxybenzoin			
benzene	6.1	44.6	20.6	23.8	4.6
Li-X				3.6	96.4
Li-Y				4	96
		Dodecyldeoxybenzoin			
benzene	4.3	21.5	33.3	36.9	3.7
Li-X				4.5	95.4
Li-Y				5.9	94.1

[a] Product yields were measured at ~15% conversion by gas chromatography; error limit ± 2%; all yields are relative and are an average of atleast four independent runs (variation between runs <5%). Reactions could easily be taken to near quantitative conversion with longer irradiation times (~6 h), and the product distribution did not change significantly under this condition.

tobehavior of α-alkyldeoxybenzoins included in the cavities of faujasites in the lithium exchanged form. Striking results presented below illustrate that modifications imposed by zeolites are not only of mechanistic but can also be of considerable synthetic importance.

Zeolites may be regarded as open structures of silica in which aluminum has been substituted in a fraction $[x/(x + y)]$ of the tetrahedral sites.[2] The framework thus obtained contains pores, channels, and cages. As the trivalent aluminum ions replace, to a given extent, tetravalent silicon ions at lattice positions, the network bears a net negative charge, which must be compensated by counter ions. The latter are mobile and may occupy various exchange sites depending on their radius, charge, and degree of hydration. They can be replaced, to varying degrees, by exchange with

Scheme II



other cations. If zeolitic water is removed, many other inorganic and organic molecular entities can be accommodated in the intracrystalline cavities. The zeolites and the guests that we have chosen for examination are Li-X and Li-Y[3] and α-alkyldeoxybenzoins, respectively.

α-Alkyldeoxybenzoins (**1a–d**) were chosen for investigation, and their primary photoprocesses and possible photoproducts are shown in Scheme I. Results of photolyses in benzene and Li-X and Li-Y zeolites are summarized in Table I. Although the results presented in the table correspond to ~15% conversion (2 h of irradiation), the product distribution remained the same even at higher conversion (>80%; 6 h). Remarkably different behavior is observed for all four ketones in zeolites with respect to that in benzene. While in benzene type II products dominate the product mixture, in zeolites the rearranged product, *p*-alkylbenzophenone **4**, derived in type I pathway, was obtained selectively (>90%). It is significant to note that the type I process is only minor and also that the rearrangement product is formed in negligible yields (<5%) in benzene. Such a dramatic medium-dependent product selectivity has not been obtained with **1** either in micelles or in cyclodextrin.[4]

Since the influence of zeolites on the reactivity of the included guests is very dependent on several factors[1,5] (e.g. method of preparation of the complex, percent loading, presence of water and other additives, procedure adopted to extract the products, etc.), the typical procedure we have employed is provided below. Dry zeolite[3] (100 mg) and the ketone (10 mg) were stirred in 2,2,4-trimethylpentane (10 mL) for about 10 h under dry nitrogen atmosphere. The complex was filtered, washed several times with absolute ether to remove any surface adsorbed material, degassed under reduced pressure (10^{-4} mm at 200 °C) for about 1 h, and irradiated with a 450-W medium-pressure mercury lamp. Following 2 h of irradiation, the products were extracted by stirring the complex with 20 mL of ether for about 10 h and analysed by GC (control experiments indicated that the products can not be extracted with hydrocarbon solvents efficiently). The loading as per carbon analysis, thermogravimetric analysis (TGA) and estimation of the extracted ketone was about 3%. Water content in all cases was about 2.5% according to TGA. Identical product ratios were obtained when the extraction procedure involved dissolution of the zeolite framework

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(3) Zeolite 13X (Na-X) and LZ-Y52 (Na-Y) were obtained from Linde. The powders were contacted with 10% $LiNO_3$ solution at 90 °C for 1 h. For each gram of zeolite, 10 mL of the nitrate solution were used. This was repeated three times. The samples were then thoroughly washed with water and dried. Chemical analysis showed exchange loadings of 46% and 34% for the X and Y zeolites, respectively. Prior to analysis the samples were heated in air 1 °C/min to 500 °C and held at 500 °C for 7 h. The samples were removed at 100 °C and stored under anhydrous conditions.

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with HCl. Mass balance in all cases was about 90%.

Li-X and Li-Y influence the reactivity of α-alkyldeoxybenzoins in two important ways. The normal type II reactivity is suppressed in favor of the type I process. Among the type I products the abnormal product **4** is selectively formed. The important role of cation in this selectivity is obvious as the extent of selectivity decreases with Na, K, Rb, and Cs as cations, in the same order.[6] The proposed reaction sequence upon excitation of **1** in the cavities of faujasites is illustrated in Scheme II. We believe that Li^+ holds the included ketone in a conformation that is not favorable for γ-hydrogen abstraction.[7] (It should be mentioned, however, that such an interaction may not completely arrest the rotational and translational motions of either the ketone or the intermediates derived from it.) Therefore, the normally favored type II process is inhibited inside the cavity facilitating the occurrence of the α-cleavage. Furthermore, once the α-cleavage occurs, the translational freedom of the fragments is reduced due to their coordination to the cation as shown in Scheme II. The caged fragments recombine either with or without rearrangement; the product resulting from the former pathway alone being different from the reactant.

Support for the interaction between the cation and the ketone derives from IR and laser Raman studies[8] and earlier literature observations on related systems. The carbonyl stretching band of **1a** is shifted (1665 cm^{-1}) in Li-X and Li-Y with respect to that as neat (1684 cm^{-1}) and in dealuminated zeolite (Si/Al = 500; 1680 cm^{-1}). The decreased specificity with other cations is also consistent with the decrease in energy of coordination along the series Li^+ to Cs^+.[9,10] Our above proposal is consistent with the reported examples of coordination of ketones[11] and aromatics[12] to the exchangeable cations in faujasites. Additional experiments are under way to understand the mechanism of the influence of zeolite framework on this and related photoprocesses.

Near quantitative formation of a new product upon photolysis of α-alkyldeoxybenzoins in the cavities of zeolite suggests that there exists a potential for utilization of molecular sieves to alter the inherent photobehavior of organic molecules.

Acknowledgment. We thank A. Pittman and J. McCartney for able technical assistance and Dr. B. Chase and N. D. Rapposelli for FT IR and laser Raman spectra.

Registry No. **1a**, 21383-02-8; **1b**, 2371-23-5; **1c**, 38821-25-9; **1d**, 110797-71-2; **2**, 134-81-6; **3a**, 42117-21-5; **3b**, 102555-75-9; **3c**, 115756-77-9; **3d**, 115756-76-8; **4a**, 55363-57-0; **4b**, 64357-40-0; **4c**, 64357-67-1; **4d**, 115732-32-6; **5a**, 110797-72-3; **5b**, 110797-73-4; **5c**, 115732-30-4; **5d**, 115732-31-5; **6**, 451-40-1; Li, 7439-93-2; Na, 7440-23-5; K, 7440-09-7; Rb, 7440-17-7; Cs, 7440-46-2.

(6) The relative yield of **4** decreased as the cation was varied from Li^+ to Cs^+ both in X and Y type zeolites for all four ketones. For example the yield of **4** from **1a** in M^+-X: Na-X, 88%, K-X, 48%; Rb-X, 32%; Cs-X, 21%. Details will be presented in the full paper.

(7) It is also likely that the interaction between the cation and the carbonyl chromophore results in the weakening of the α-CC bond. This would enhance the rate of α-cleavage with respect to γ-hydrogen abstraction.

(8) Diffuse reflectance IR spectra were recorded on Nicolet FT IR spectrometer (Model 7199). The samples were heated (200 °C) under vacuum (10^{-4} mm) for about 30 min prior to recording the spectrum.

(9) Preliminary TGA studies indicate that the temperature required to desorb **1a** from Li-Y, K-Y, and Cs-Y decreases in that order: Li-Y, 421 °C; K-Y, 396 °C; Cs-Y, 389 °C.

(10) It is known that the temperature required to desorb water from M^+-X decreases in the series Li, Na, K, Rb, and Cs as cations. Bertsch, L.; Habgood, H. W. *J. Phys. Chem.* **1963**, *67*, 1621.

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D. R. Corbin, D. F. Eaton, V. Ramamurthy*
Central Research and Development Department
E. I. du Pont de Nemours and Company
Experimental Station
Wilmington, Delaware 19898
Received March 22, 1988

Use of Polar Picolyl Protecting Groups in Peptide Synthesis

Summary: Protection of serine and threonine side chains with the 4-picolyl group and aspartic and glutamic acids with the 3-picolyl group is described. Picolyl-protected peptide segments are markedly more polar than benzyl-protected analogues, which can facilitate their purification.

Sir: Despite the continuous improvement in peptide synthesis methodology, no general strategy is yet available to permit a secure synthesis of large peptides or proteins. From a synthetic point of view, it seems advisable to base any attempt to develop such an strategy on a convergent approach. Current work of this laboratory deals with the test of several methodologies to design a convergent solid-phase approach to peptide synthesis.[1] A general problem in this strategy is the unpredictable, low solubility of protected peptide segments that causes difficulties in their purification as well as in the subsequent coupling steps. This problem is even more critical in solution synthesis where peptide segments must be soluble in the appropriate solvent at every stage.[2]

It seems likely that the poor solubility of protected peptide segments is due to the contrast between the polar nature of the peptide backbone and the hydrophobicity of some amino acid side chains (e.g. Phe, Leu, Ile, Val) and common protecting groups (e.g. benzyl, benzyloxycarbonyl, *tert*-butyl, *tert*-butyloxycarbonyl (Boc)) of trifunctional amino acids. At this point, one could expect that the use of polar protecting groups would help to circumvent the problem. To achieve such polarity, protecting groups must contain an additional function free from side reactions under the conditions of the peptide synthesis strategy designed. These orthogonality requirements are very stringent and must be accompanied by deprotection methods that are clean and essentially quantitative. Altogether this makes the development of polar protecting groups for the synthesis of large-size peptides a good challenge from the point of view of organic synthesis.

Little attention has been paid to the 4-picolyl group introduced by Young et al. in 1968[3] as a "handle" to protect the C-terminal amino acid and help in the purification steps of the growing peptide chain in solution peptide

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