tions. The final organic products of these multicomponent reactions have molecular weights of 432 (**14**) and 472 (**16**), yet the fluorous-labeled precursors of these products were successfully extracted into the fluorous phase for purification. These and related fluorous-labeled products have molecular weights in the range of 2000, of which roughly three-fifths is fluorine, one-fifth is other atoms in the label (C, H, Si), and one-fifth is the labeled substrate itself. In these examples, the fluorous label has a role roughly analogous to that of the "traceless linkers" recently introduced in solid-phase synthesis (*3*).

In light of the increased demand for combinatorial and parallel synthesis of libraries of small organic molecules, the issue of purification is no longer a technical concern but needs to be addressed at the strategy level in synthetic planning. Reactions should be designed such that the desired product has a different phase from all of the other components of the final reaction mixture. The fluorous synthesis techniques outlined here introduce new strategic options to meet this goal.

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Recharge in Volcanic Systems: Evidence from Isotope Profiles of Phenocrysts

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Strontium isotope ratios measured from core to rim across plagioclase feldspar crystals can be used to monitor changes in the isotope composition of the magma from which they grew. In samples from three magma systems from convergent margin volcanoes, sudden changes in major element composition, petrographic features, and strontium isotope composition were found to correspond to discrete magmatic events, most likely repeated recharge of more mafic magma with lower ratios of strontium-87 to strontium-86 into a crustally contaminated magma.

Mineral assemblages and individual crystal phases from magmatic suites record differentiation processes in magmatic systems. Compositional zoning, textural discontinuities, inclusion zones, and reaction rims in crystals all reflect changes in magmatic conditions. Compositional changes may be produced either by changes in intrinsic variables (such as changes in water content, temperature, or pressure, reflecting eruptive or convective cycles from a magma chamber) or by open system processes such as recharge (the introduction of a fresh batch of generally hotter and less evolved magma into the chamber) and contamination (the assimilation of country rock and its incorporation into the magma).

Plagioclase feldspar can serve as a recorder of differentiation processes in many volcanic rocks (*1*). In mafic to intermediate volcanic rocks of subduction-related suites, it typically occurs as large (2 to 20 mm) phenocrysts. Growth zones within plagioclase crystals form an effective stratigraphy reflecting changes through time in the magma from which it grows. Dissolution surfaces preserved in the crystals, and revealed by petrographic and Nomarski interferometry analysis (*2*), reveal rapid changes in the magmatic environment. We show that Sr isotope profiling of plagioclase phenocrysts is a potentially powerful tool in elucidating differentiation processes and discuss three examples that underscore the importance of repeated mafic recharge in subduction-related volcanic systems. We studied plagioclase from Chaos Crags in California, Purico-Chascon in Chile, and El Chichón in Mexico. In the first two systems, the presence of mafic magmatic inclusions provides direct evidence that recharge occurred, whereas at El Chichón, the phenocrysts themselves provide the most compelling evidence for recharge by a mafic magma.

We obtained the crystal isotope stratigraphy by mechanically drilling polished, thick sections. Drill sites were planned to sample discrete zones within the crystal, which may be bounded by dissolution surfaces. This objective was rarely achieved, however, because the width of distinct zones is typically similar to, or less than, the drill diameter. Furthermore, adjacent zones may also be penetrated in the vertical dimension. Thus, individual drill sites commonly include mixtures of two or more adjacent growth zones, but careful overlap-

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ping of drill holes made possible reasonably comprehensive characterization of $^{87}Sr/^{86}Sr$ variations from core to rim.

Chaos Crags comprises a group of six discrete dacite domes sequentially emplaced between 1000 to 1200 years ago (*3*) as part of the Lassen Volcanic Center, the southernmost extension of current subduction-related magmatic activity of the Cascade range of North America. The domes contain a suite of mafic (basaltic andesite) magmatic inclusions, which increase in volumetric abundance with time throughout the emplacement sequence. The inclusion magmas and host dacites have incompletely hybridized but have mingled to the extent that crystal populations have been exchanged and show various degrees of disequilibrium. A model in which two magmas intermingled (*4*) appears to explain chemical and petrographic characteristics of the Chaos Crags system.

Plagioclase crystals in the mafic inclusions are typically large and compositionally similar [in terms of anorthite (An) content, about An_{40} (*5*)] to those in the host dacite. Many crystals have a spongy-textured overgrowth (Fig. 1A), which apparently indicates immersion of plagioclase crystals from the host dacite into the mafic magma. The marked increase in An content near the rim is consistent with this interpretation.

The $^{87}Sr/^{86}Sr$ ratios from the cores of the crystals in the inclusions are similar to those of the bulk host dacite (~0.7040 to 0.7041), whereas the $^{87}Sr/^{86}Sr$ ratios of the rims are close to those of the basaltic andesite inclusions (~0.7037 to 0.7038) in which the crystal now resides (Fig. 1). A simple interpretation consistent with petrographic observations is that the plagioclases grew in a dacite magma system that was injected by a basaltic andesite with a lower $^{87}Sr/^{86}Sr$ ratio and that the low $^{87}Sr/^{86}Sr$ ratios of the rims reflect overgrowth after immersion in the inclusions. The presence of dissolution surfaces in the crystals and the occurrence of mafic clots dispersed throughout the dacite hosts, which may represent the remnants of earlier inclusion suites (*6*), suggest that mafic recharges occurred also during earlier phases of crystal growth. Detailed profiling confirms that the $^{87}Sr/^{86}Sr$ ratio is variable in the interiors of some crystals.

Purico-Chascon is a Quaternary lava dome complex in the Altiplano region of northern Chile, similar in many respects to Chaos Crags. The dacites that form the domes contain a suite of mafic inclusions, which have interacted and variably hybridized with the host dacites. The dacite domes represent a suite of rocks formed from crustal melting of the local ignimbrite basement ($^{87}Sr/^{86}Sr$ ratio of ~0.709), whereas the basaltic andesites (lower $^{87}Sr/^{86}Sr$ ratio of ~0.7062), which form the mafic inclusions, are melts from a deeper source (*7*, *8*).

The $^{87}Sr/^{86}Sr$ ratios of plagioclase crystals from Purico-Chascon mafic inclusions, also decrease overall from core to rim. The most complete profile, however, shows an oscillation (Fig. 2, A and B). The detailed petrography (*8*) suggests that crystal populations have been exchanged, possibly multiply recycled, between mafic and silicic magmas; a balance between recurring mafic recharge and crustal assimilation is implicated. The overall crystal isotope stratigraphy reflects progressive addition of mafic magma to a silicic end member. The intraprofile reversal in this trend at 1.5 to 1.0 mm from the rim in Fig. 2B then reflects a period of growth in which assimilation was dominant over recharge.

The silicic melt that formed the domes is isotopically similar to the Purico ignimbrite (1.3 × 10^6 years old) that underlies the dome complex (*9*). It may be magma residual from the ignimbrite eruption, implying the existence of a long-lived magma chamber (*10*). If so, then the cores of the plagioclase crystals may be much older than the isotopically variable rims and may be derived from the Purico ignimbrite. Alternatively, the silicic end member could be remelted ignimbrite at shallow depth or a melt of the same source as the ignimbrite at depth, and the plagioclase crystals record nearly continuous growth from that melt. Plagioclase crystals sampled from the Purico ignimbrite have cores with high $^{87}Sr/^{86}Sr$ ratios and rims with only slightly lower $^{87}Sr/^{86}Sr$ ratios, far less variation than recorded in plagioclase crystals from the inclusions (Fig. 2B). These data suggest that, rather than representing xenocrysts, the crystals from the inclusions grew more or less continuously during the evolution of the Purico-Chascon magma system. Plagioclase crystals from the dacite hosts reveal comparable core-to-rim variations, suggesting that they experienced similar differentiation histories and that their current environment (host versus inclusion) was the result of a comparatively recent inclusion-forming event. Thus, the crystal isotope stratigraphy of the Purico-Chascon plagioclase crystals records a protracted differentiation history revealing far more detail than bulk rock chemistries alone.

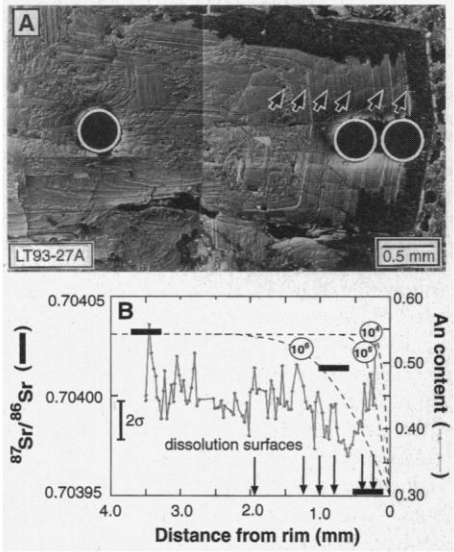

Fig. 1. Example of drilling results for a plagioclase phenocryst in a mafic magmatic inclusion from Chaos Crags, Lassen National Park, California (*20*). (**A**) Drill hole locations on a Nomarski image of the crystal; dissolution surfaces are marked by arrows. (**B**) The $^{87}Sr/^{86}Sr$ results are shown relative to the An contents and to the locations of obvious dissolution surfaces. The small-scale variations in An content probably reflect perturbations in local conditions (*21*), whereas the sudden jumps in An content, which occur near dissolution surfaces, are thought to reflect a major change in growth conditions (*22*), such as a change in temperature, composition, and water content that would accompany the introduction of basalt magma into the chamber. The length of the bars corresponds to the width of the drill hole. Dashed curves are simple diffusion profiles (labeled for time in years) appropriate for temperatures of about 950°C, demonstrating the unrealistically long time scales required for diffusion to affect Sr isotope compositions within the crystal (*11*). Core-to-rim decreases in $^{87}Sr/^{86}Sr$ ratios have been recorded in seven other plagioclase crystals.

For both Chaos Crags and Purico-Chascon, systematic core-to-rim decreases in

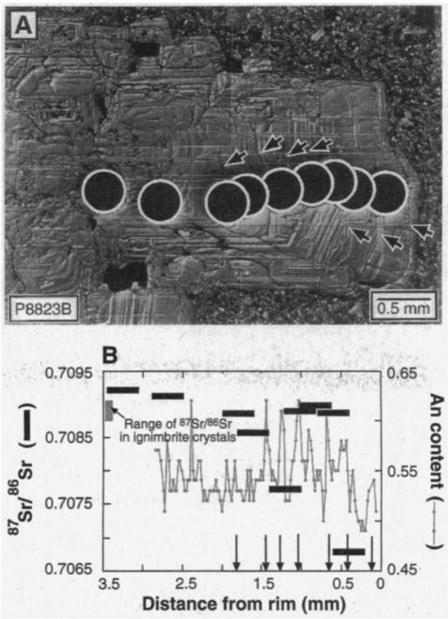

Fig. 2. (**A**) Results for a plagioclase crystal from a mafic inclusion, the Purico-Chascon dome complex, northern Chile. (**B**) The $^{87}Sr/^{86}Sr$ profile is plotted together with the electron microprobe traverse. Locations of major dissolution surfaces are shown by arrows. The precision of the $^{87}Sr/^{86}Sr$ ratios lies within the thickness of the bar. Large core-to-rim decreases have been observed in six other plagioclase phenocrysts from Purico-Chascon.

^{87}Sr/^{86}Sr ratios might be argued as reflecting partial equilibration through self-diffusion of an initially homogeneous plagioclase immersed in a hot, mafic magma with a lower ^{87}Sr/^{86}Sr ratio. However, several lines of evidence argue against this interpretation. First, if the ^{87}Sr/^{86}Sr profiles are interpreted as due simply to diffusion (*11*), then the implied time scales would be excessively long (Fig. 1). Second, the rates of diffusion are typically orders of magnitude slower than those of crystal growth. Only at negligible degrees of undercooling can diffusion in the crystal keep pace with crystal growth (*12*). Heating, such as may attend immersion in the mafic inclusions, would initially inhibit crystal growth but would also lead to dissolution of the crystal margins, again at rates far greater than diffusion of Sr can affect the crystal interior. Finally, incompatible element concentrations determined by secondary ion mass spectrometry do not show simple systematic diffusion profiles in response to a core-to-rim concentration gradient but rather vary irregularly, most likely in response to changes in the incompatible element concentration of the evolving magma and to changes in the effective distribution coefficient with pressure, temperature, composition, and kinetic factors controlling crystal growth.

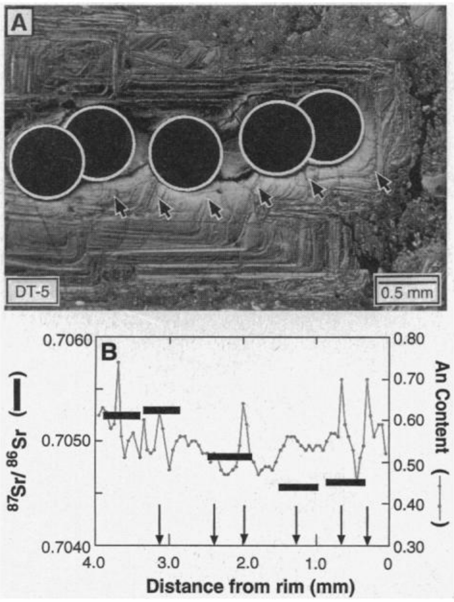

Fig. 3. (**A**) Results for a plagioclase phenocryst from the 1982 El Chichón eruption, Mexico. (**B**) The ^{87}Sr/^{86}Sr profile is plotted together with the electron microprobe traverse. Locations of major dissolution surfaces are shown by arrows. For this sample, the compositional profile (An content) was not measured along the line of the microdrill traverse and has been mapped onto the Sr data by correlation of stratigraphic growth features. The precision of the ^{87}Sr/^{86}Sr ratios lies within the thickness of the bar. Large core-to-rim decreases have been observed in four other plagioclase phenocrysts from the 1982 lava.

El Chichón is a subduction-related volcanic edifice of Quaternary age forming part of the Mexican Volcanic Belt. The recent eruption (March through April 1982) was part of a recurring cycle of eruptive activity, taking place at intervals of ~600 (±200) years (*13*). The erupted products of 1982 and previous events are basaltic andesite to andesite, plagioclase-porphyritic lavas, and pyroclastic rocks, with subsidiary amphibole, clinopyroxene, and apatite. Mafic magmatic inclusions have not been observed. Anhydrite was observed in fresh blocks collected from the 1982 eruption (*14*). Seven whole rock samples from this eruption are isotopically relatively homogeneous and have lower ^{87}Sr/^{86}Sr ratios than do the older lavas. However, Tilling and Arth (*15*) showed that ^{87}Sr/^{86}Sr ratios increased in the order from groundmass to clinopyroxene, apatite, anhydrite, bulk rock, and plagioclase, thus challenging the assumption that the constituent components of magmas—groundmass or glass and the minerals crystallized therefrom—are isotopically homogeneous.

Plagioclase crystals from the 1982 lava show particularly well-developed growth zones punctuated by zones of melt inclusions that correspond to "spikes" in An content (Fig. 3B). It has been suggested that these growth zones are a response to variations in volatile pressure accompanying cycles of pressure buildup and eruption (*16*). Isotope stratigraphy of the crystals enables us to test this contention because variations only in pressure or temperature should not affect isotope ratios. The ^{87}Sr/^{86}Sr ratios of the crystals consistently decrease from core to rim (Fig. 3, A and B), indicating that the growth zones reflect open system processing rather than simply changes in intrinsic variables (pressure and water content). The Sr isotope ratios change across the crystal. Although our technique does not permit unequivocal sampling of individual growth zones, it does appear that changes in isotope ratio are correlated with magmatic events indicated by the intracrystal unconformities (Fig. 3).

The Sr isotope variations across the phenocrysts most likely record growth in a magma system, to which a magma with a lower ^{87}Sr/^{86}Sr ratio was periodically added, possibly resulting in eruption. The recharge events are recorded in the plagioclase dissolution surfaces, and perhaps in the lower ^{87}Sr/^{86}Sr ratios of more mafic phenocryst phases such as clinopyroxene (*15*). If the periodicity of eruptions (~600 years) reflects the minimum frequency of recharge events, which in turn are marked by dissolution surfaces in the plagioclase crystals, then we can calculate maximum crystal growth rates. If 0.5 to 1.0 mm is the typical distance between dissolution surfaces (Fig. 3), the growth rate is of the order 10^{-12} cm/s. This is far slower than minimum growth rates determined experimentally (10^{-6} to 10^{-8} cm/s) but is similar to growth rates estimated for natural systems (*17*). Recharge events, however, do not necessarily always lead to eruption, so it is possible that some of the dissolution surfaces correspond to events occurring more frequently than actual eruptions (that is, the time period represented by the distance between discontinuities in the phenocrysts is considerably less than 600 years). Furthermore, a finite volume of the crystal must have been dissolved during recharge in order to produce the observed crystallographic unconformities. Both of these considerations may increase our estimated growth rate by a factor of up to 10.

The high ^{87}Sr/^{86}Sr ratios of plagioclase cores are consistent with higher ratios in the older (~2000 years) bulk rocks. Plagioclase crystals may have started to grow in magmas such as these early erupted products. Similarly, ^{87}Sr/^{86}Sr ratios have been observed to decrease in bulk lavas over the past 2000 years. Thus, the plagioclase phenocrysts may preserve the differentiation history over that order of time.

The isotopic difference between the differentiated magma and the recharge magma was likely a result of crustal assimilation. The systematic decrease in ^{87}Sr/

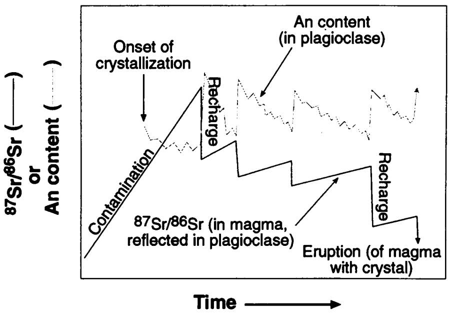

Fig. 4. Schematic illustration of the possible evolution of convergent margin magma systems as interpreted from the isotope stratigraphy of plagioclase crystals. Mafic recharge occurs periodically and causes growth discontinuities in the plagioclase crystals. Contamination by the assimilation of crustal rocks with higher ^{87}Sr/^{86}Sr ratios remains an important process, provided heat is supplied by the recharge magma and provided the wall rock does not become severely depleted by partial melting of a fusible fraction or thickly armored by sidewall cumulates. Although the recharge magma is assumed to have lower ^{87}Sr/^{86}Sr ratios than the contaminated magma in the chamber, its ^{87}Sr/^{86}Sr ratio is not necessarily constant. Alternative scenarios involving more complex magma chamber dynamics might be equally plausible but all require open system differentiation during plagioclase growth.

^{86}Sr ratios in the phenocrysts therefore requires that assimilation occurred at an early stage of magmatic evolution. Each subsequent recharge event added Sr with a lower ^{87}Sr/^{86}Sr ratio (Fig. 4). Although assimilation between recharge events may gradually increase the ^{87}Sr/^{86}Sr ratio of the magma (as may be illustrated by the Purico-Chascon example in Fig. 2), this question typically cannot be resolved at the scale of microdrilling. A progressive decrease in the ^{87}Sr/^{86}Sr ratio must reflect the frequency and relative amount of mafic recharge compared with assimilation. This effect may well be accentuated by the contribution of Sr from dissolving of plagioclase rims attendant with each injection of mafic magma (*18*). Recharge of the magma system must maintain a rather steady-state magma chamber (*19*), as the small variations in An content across dissolution surfaces and lack of unidirectional overall zoning preclude growth from magmas that vary greatly in composition. In the case of El Chichón, the uniformity of erupted products over 300,000 years of total activity (*16*) seems to support the operation of a steady-state magma system.

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Selective Use of TBP and TFIIB Revealed by a TATA-TBP-TFIIB Array with Altered Specificity

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Interaction between the TATA box–binding protein TBP and TFIIB is critical for transcription in vitro. An altered-specificity TBP-TFIIB interaction was rationally designed and linked in sequence to an altered-specificity TATA box–TBP interaction to study how TBP and TFIIB function together to support transcription in human cells. The activity of this altered-specificity TATA-TBP-TFIIB array demonstrated that many activators use the known TBP-TFIIB interaction to stimulate transcription. One activator, however, derived from a glutamine-rich activation domain of Sp1, activated transcription independently of this interaction. These results reveal that selectivity in activator function in vivo can be achieved through differential use of TBP and TFIIB.

In vivo analysis of the basal transcriptional machinery is difficult because the basal factors are highly conserved, ubiquitously expressed, and probably essential proteins. One way to circumvent these limitations is to exploit mutations that alter the specificity of interaction between two factors, allowing their activities to be measured in vivo in the presence of their wild-type counterparts. We have previously used a form of TBP with an altered TATA box–binding specificity (TGTA) (*1*) to probe the role of TBP in activated transcription in human cells (*2*). We found that TBP activity in vivo is sensitive to certain combinations of clustered point mutations across the surface of the molecule, and that in vivo activity correlates closely with the ability to associate in vitro with the largest TBP-associated factor, hTAF$_{\mathrm{II}}$250 (*3*), suggesting that the TBP-associated factors (TAFs) are important for activated transcription in vivo, as they are in vitro (*4*).

Biochemical studies indicate that the interaction of TBP with TFIIB is also critical for activated transcription in vitro (*5*), but none of our original TBP mutations targeted residues involved in interaction with TFIIB (*2*, *6*, *7*). To probe the importance of the TBP-TFIIB interaction for transcription in vivo, we examined the effects of single or double amino acid substitutions (*8*) at three TBP residues critical for interaction with TFIIB in vitro (*7*) (Fig. 1A), measuring the response to two GAL4-fusion activators carrying either the

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