HISTORICAL DROUGHT

Droughts and societal change: The environmental context for the emergence of Islam in late Antique Arabia

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In Arabia, the first half of the sixth century CE was marked by the demise of Himyar, the dominant power in Arabia until 525 CE. Important social and political changes followed, which promoted the disintegration of the major Arabian polities. Here, we present hydroclimate records from around Southern Arabia, including a new high-resolution stalagmite record from northern Oman. These records clearly indicate unprecedented droughts during the sixth century CE, with the most severe aridity persisting between ~500 and 530 CE. We suggest that such droughts undermined the resilience of Himyar and thereby contributed to the societal changes from which Islam emerged.

The Himyarite kingdom was the dominant power in Arabia from the late third to the early sixth century CE (Fig. 1A). Its dissolution over the course of the sixth century CE marked the end of a 1400-year-long pre-Islamic period of supratribal polities in Arabia (*1*–*6*), but the reasons for its demise remain debated. Himyar's decline was characterized by political disorder, socioeconomic change, shifting settlement patterns and demography (Fig. 1, B and C), and the decline of major irrigation systems (*2*, *4*, *5*, *7*, *8*). The annexation of Himyar by Aksum (today's Ethiopia) in 525 CE and frequent interventions from the Byzantine and Sasanian Empires were additional factors that contributed to profound social, economic, and political transformations during the sixth century CE in Arabia (*1*, *5*, *6*). Explanations for these changes focus on sociopolitical factors (*4*, *5*). The possibility that drought played a role has been largely ignored (*4*, *6*, *9*, *10*), despite the fact that Himyar and the southern Arabian region more widely were extremely vulnerable to droughts because their economy was based on rain-fed and irrigated agriculture (*5*, *6*, *9*).

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The lack of highly resolved and precisely dated palaeoclimate records from southern Arabia has prevented an assessment of whether droughts were a factor that contributed to Himyar's decline. Here, we combine hydrological, historical, and archaeological records from the Middle East and East Africa with a new stalagmite record of winter-spring precipitation and effective moisture (EM) in northern Oman to demonstrate that severe and persistent droughts may have been an important factor in the changes that took place in southern Arabia in the sixth century CE (*2*, *4*, *5*, *11*).

Stalagmite H12 from Hoti Cave in northern Oman (57°21′E, 23°05′N; 800 m above sea level) (Fig. 1A and figs. S1 and S2) provides a well-dated hydroclimatic record that spans this critical period of history. Rainfall in northern Oman and most of Arabia originates predominantly from Mediterranean frontal systems, whereas summer monsoon (SM) precipitation affects only the Yemeni highlands and southern Oman (*12*). Thunderstorms during summer and occasional cyclones are additional sources of rainfall. Regional precipitation varies between 50 and 255 mm year^{-1} (Al Hamra; 1978–1997) and occurs in winter and spring (~65% of annual rainfall) and summer (fig. S3). Importantly for this study, changes in rainfall (fig. S4) are consistent across southern Arabia, particularly for extreme droughts, which are often supraregional (*13*).

The chronology of H12 is based on 20 U-Th ages, with an average growth rate of ~0.23 mm year^{-1} over the past 2650 years (fig. S5 and tables S1 and S2). The oxygen ($\delta^{18}O$) and carbon ($\delta^{13}C$) isotope records have a ~2-year resolution and reflect fluctuations in rainfall amount and EM, respectively (*14*), as indicated by several observations. First, H12 $\delta^{18}O$ values correlate [correlation coefficient (r) = –0.69; $p \leq 0.001$] with mean annual rainfall in Oman and are consistent with rainfall anomalies for the entire Arabian Peninsula (*15*, *16*), with higher rainfall related to more negative $\delta^{18}O$ values (Fig. 2, A and B). Second, more positive H12 $\delta^{18}O$ values correspond to a reduced diameter of the stalagmite cap (Fig. 2C), indicative of lower drip rates and winter-spring precipitation, respectively (*17*). Third, the strong correlation between H12 $\delta^{18}O$ and $\delta^{13}C$ values (r^2 = 0.52) indicates that calcite did not precipitate in isotopic equilibrium with its parent drip water. Because $\delta^{13}C$ values are strongly governed by CO_2 degassing, more positive $\delta^{13}C$ values indicate lower drip rates and a lower partial pressure of CO_2 (P_{CO_2}) of cave air because of enhanced ventilation of Hoti Cave at times of lower precipitation and cave lake levels (fig. S1). Additionally, reduced vegetation density and soil microbial activity during drier

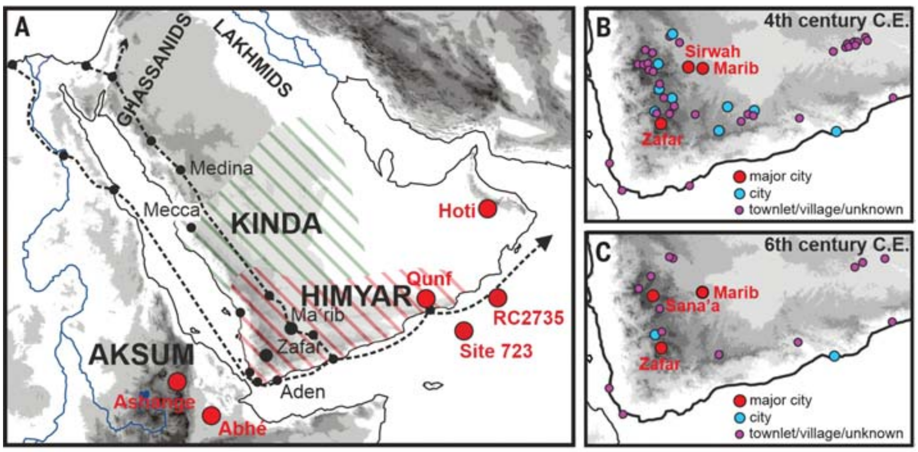

Fig. 1. Location and settlement maps. (**A**) Map showing the location of key proxy records and the suggested extent of Himyar (red line) and Kinda (green line) at the beginning of the sixth century CE (*6*). Black dashed lines denote the main trading routes (6). (**B** and **C**) Settlement patterns in Himyar in the (B) fourth and (C) sixth centuries CE (*8*).

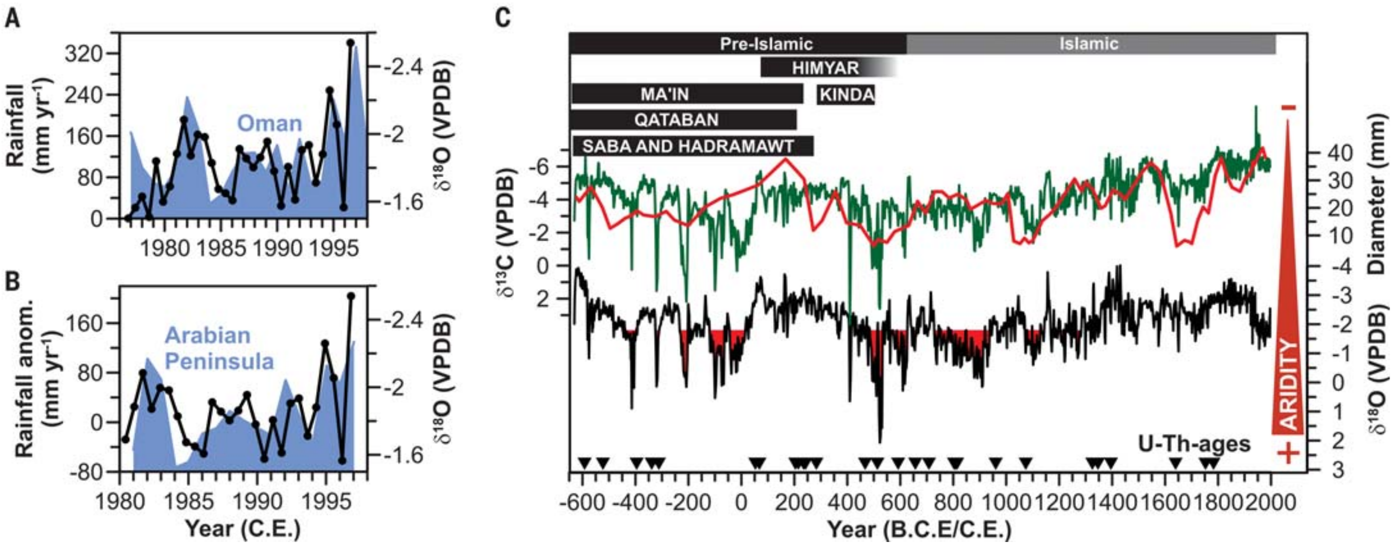

Fig. 2. Hoti Cave and meteorological records. (**A** and **B**) Comparison of H12 $\delta^{18}O$ values and (A) mean annual rainfall for Oman (*15*) and (B) precipitation anomalies [with respect to the 1978–1997 average of –1.8 per mil (‰)] averaged for the Arabian Peninsula (*16*). VPDB, Vienna Pee Dee Belemnite international standard. (**C**) H12 $\delta^{18}O$ (black), $\delta^{13}C$ (green), and stalagmite diameter (red line) records. The red-shaded area shows EM anomalies with respect to the 1978–1997 mean (–1.8‰). Black triangles denote ^{230}Th dates (tables S1 and S2). Black-shaded bars denote the estimated lifetime of kingdoms in southern and central Arabia (*11*).

years leads to lower biogenic soil P_{CO_2} and more positive calcite $\delta^{13}C$ values (*18*). Thus, H12 $\delta^{18}O$ and $\delta^{13}C$ values are primarily governed by precipitation and EM.

The H12 $\delta^{18}O$ profile displays high variability in EM over the past ~2600 years, with two periods of persistently lower EM from ~250 BCE to 25 CE and from ~480 to 1400 CE, on which distinct decadal to multidecadal fluctuations in $\delta^{18}O$ were superimposed (Fig. 2C). The most pronounced minimum in EM occurred from ~520 to 532 CE, with the most severe drought conditions of the entire H12 record centered at ~523 CE ± 30 years (Fig. 3B). This date is in excellent agreement with other independently dated winter-spring rainfall records from the Middle East (Fig. 3). In the Neor Lake record from northern Iran (*19*), a sharp rise in titanium (high dust flux) starts at the beginning of the sixth century CE. The lake level of the Dead Sea (*20*) declined from ~490 CE onward, and more positive $\delta^{13}C$ values (reduced EM) are observed in the Jeita Cave $\delta^{13}C$ record from Lebanon at ~510 CE (*21*). Likewise, the frequency of historical accounts of droughts in the Middle East peaks between 520 and 530 CE (Fig. 3F), with the spring of Siloam in Jerusalem reportedly drying up at ~520 CE (*22*, *23*). Overall, key hydrological records from the Middle East indicate drought conditions related to a decline in winter-spring precipitation and a substantial decrease in EM from ~480 CE onward. By contrast, the Nar Lake $\delta^{18}O$ record from Turkey (*24*) documents a substantial increase in precipitation, which is most likely related to a northward displacement of storm tracks in the eastern Mediterranean at the beginning of the sixth century CE, with fewer rain-bearing storms reaching the Fertile Crescent and Arabia.

Though winter-spring precipitation is the main source of annual rainfall throughout the Middle East, SM precipitation is an additional crucial source of rainfall in southern Arabia and Yemen (Himyar) in particular. SM records from southern Oman (Qunf Cave) (*12*, *14*), Ethiopia (Lake Ashange and Lake Abhé) (*25*, *26*), the Arabian Sea (sites RC2735 and 723) (*27*, *28*), India (Sahiya Cave) (*29*), and China (Dongge Cave) (*30*) indicate that SM wind strength and precipitation reached their absolute minimum during the sixth century CE as boreal summer insolation, a primary driver of monsoon intensity (*14*), reached its lowest Holocene values (Fig. 4). Furthermore, an abrupt decline in precipitation between 450 and 500 CE is evident in the SM records from Ethiopia (Lake Ashange) (*25*), the Arabian Sea (sites RC735 and 723) (*27*, *28*), and India (core 16A) (*31*), and, taking age uncertainties of the individual records into account, these are broadly concurrent with decreasing winter-spring precipitation in the H12 $\delta^{18}O$ and other hydroclimate records displayed in Fig. 4. In addition, the precisely dated Sahiya Cave (India) SM record (*29*) reveals a decrease in SM rainfall after ~490 CE (Fig. 3H). Taken together, mean annual precipitation in Arabia and northeastern Africa reached an absolute minimum at the beginning of the sixth century CE, with the most severe drought conditions persisting between ~500 and 530 CE (Fig. 4).

The synchronicity between peak aridity in southern Arabia and the sudden decline of Himyar points to a possible causal relationship between both. Himyar, with its centralized political system of kingship and subordinate chiefdoms, was the dominant power in southern and central Arabia (Fig. 1) (*2*, *6*). Though international trade in aromatics and metals had earlier also been a major source of revenue, agricultural production was fundamental to both central and regional economies (*5*, *7*, *32*). The importance of agriculture is evidenced by widespread terraced fields in the highlands, numerous irrigation systems along the desert margin, and a considerable expansion of hydraulic structures between the first and fourth centuries CE (*5*, *33*–*35*) (figs. S6 and S7). The dams, for instance, were a symbol and instrument through which Himyarite rulers exerted their authority, as indicated by inscriptions. Dams and terraced fields were designed to harvest rainfall and runoff ("runoff irrigation") because water was the most limited agricultural resource. The structural integrity of the terraced fields depended on the proper maintenance of the whole system of hillside terraces, and dams required constant repairs, which only a well-organized workforce and stable society could provide (*2*, *6*, *7*). Furthermore, a stable society and a functioning political entity were crucial to manage the proper allocation of water for the irrigated plots, particularly during drier years with more frequent water disputes (*36*). Himyar's agricultural productivity depended on a consistent rainfall cycle, with two rainy seasons in spring and summer (fig. S8). These factors combined made Himyar vulnerable to droughts, and low agricultural yields would have had a negative impact on Himyar's socioeconomic and political stability and thus the

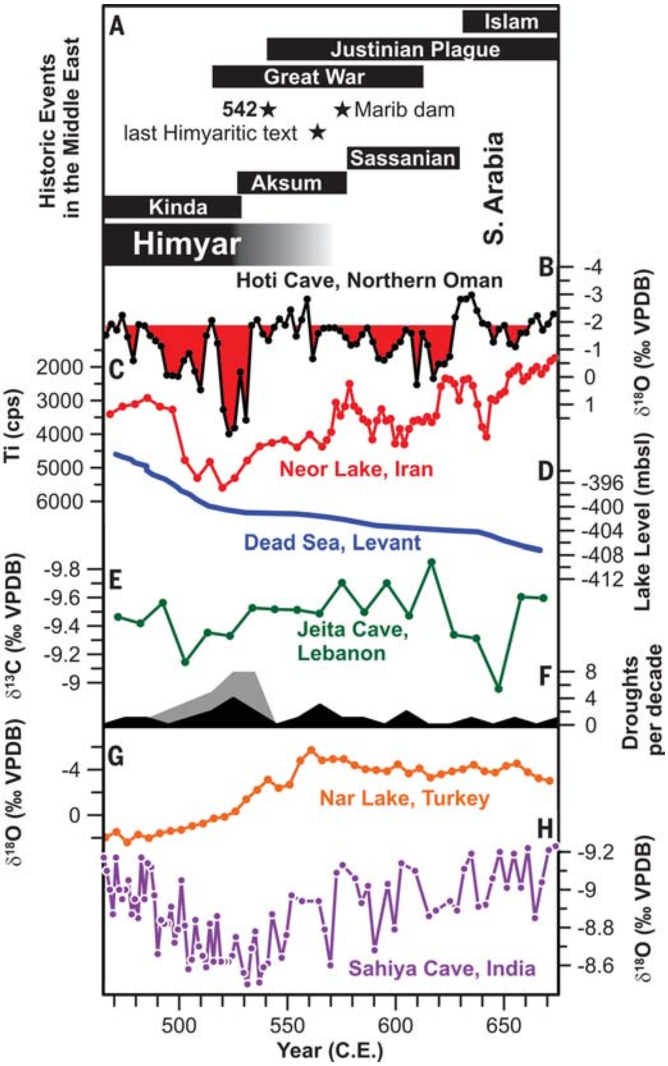

Fig. 3. Climate proxy records and historic events. (**A**) Key historic and cultural events in southern Arabia. Black bars denote ruling powers in southern Arabia, sociocultural events (star symbols) such as the disappearance of Himyarite inscriptions (*39*, *48*), and the destruction of the dam of Marib (*7*). (**B**) H12 $\delta^{18}O$ record from Hoti Cave. The red-shaded area marks periods of below-normal precipitation (with respect to the 1978–1997 average of –1.8‰). (**C**) Lake Neor titanium record from Iran (*19*). cps, counts per second. (**D**) Dead Sea level (*20*). mbsl, meters below sea level. (**E**) Jeita Cave $\delta^{13}C$ record (*21*). (**F**) Historic accounts (plotted as droughts per decade) derived from the Middle East after (*22*) (black-shaded curve) and (*23*) (gray-shaded curve). (**G**) Nar Lake $\delta^{18}O$ record from Turkey (*24*). (**H**) Sahiya Cave $\delta^{18}O$ record from India (*29*).

proper management of all water-harvesting structures. Thus, the abrupt and persistent decrease in rainfall and EM, respectively, throughout Arabia at the end of the fifth and beginning of the sixth century CE must have been a substantial stressor, undermining Himyar's resilience to both internal and external socioeconomic and geopolitical conflicts, particularly Christian Aksumite attempts to control the lucrative trading routes along the Red Sea and Arabian Sea coasts. Such stress may well have been further exacerbated by the possible effects of the global cooling that marked the beginning of the so-called Late Antique Little Ice Age that is visible in proxy data from the later 530s CE (*37*).

From the 480s CE, Himyar faced a number of problems. Internal conflict between rival elite lineages, partly informed by religious affiliations to either Judaism or Christianity, was exacerbated by Aksumite intervention between 518 and 530 CE that reduced Himyar to vassal status (*5*, *11*, *38*–*40*). This was followed by a brief revival of Himyarite power (but under an Aksumite general, Abreha) (*5*), to which a short-lived increase in winter-spring precipitation between 530 and 545 CE (Figs. 2 and 3) may perhaps have contributed. Yet it took this new regime at least four expeditions over more than 15 years to reestablish Himyarite political hegemony outside Yemen and Hadramaut, suggestive of both the weakening of its power and the extent of fragmentation of the traditional order in the region (*38*). Further indications of this include evidence for drought-induced migration across the region into Persian- and Byzantine-controlled Syria and Iraq, as well as southward into Yemen and Hadramaut, and the failure to maintain the dam of Marib, leading to a collapse of the system in ~580 CE and its final destruction in ~600 CE (an event important enough to find mention in the Koran 34:15–17) (*2*, *5*, *7*). The disappearance of Himyarite inscriptions after ~559 CE (*5*) may also indicate a breakdown of political authority and the established order. From about 570 CE, Himyar came under Persian domination and effectively ceased to exist as an independent polity (*1*–*3*, *5*, *6*, *40*).

The weakening of Himyar from the 480s CE onward, and its rapid conquest by Aksum in 525 CE, were thus directly coincident with both internal conflict as well as increasing aridity and declining agricultural yields that were due to a simultaneous reduction in winter-spring and SM precipitation, culminating in the most severe drought conditions of the entire Holocene in the early sixth century CE. Himyar's continued weakening through the middle decades of the sixth century CE, in spite of the temporary resurgence under Abreha, and its final dissolution in the 570s CE should thus be understood in the context of these conditions and the evidence for the persistence of drought conditions during the sixth century CE (Fig. 4). Aksum, however, was less affected by the drought because rainfall amounts were generally much higher (fig. S9) and a reduction in rainfall was therefore less detrimental to agricultural productivity. Although correlation is not necessarily causation, the singular magnitude and persistence of sixth-century drought, superimposed on a region that was highly dependent on rain-fed agriculture, is coincident with a clear turning point in Arabian history (*2*, *4*–*6*), when a cascade of regional political and socioreligious transformations occurred over the following decades.

Whether Himyar's decline as the dominant Arabian polity induced a sociopolitical vacuum remains unclear, although this is often assumed (*4*–*7*). But it has been plausibly argued that one result of the changed situation throughout Arabia during the sixth and early seventh centuries CE was a growth in the importance of pilgrimage and economic centers. Of these, Mecca (Muhammad's birthplace) gained considerable influence in central and southern Arabia in the first half of the sixth century CE (*41*). Furthermore, the reduction in the reach of Himyarite power drew the competing Byzantine and Sasanian empires into increasing and intensified competition for political and religious influence in the region as well as for economic resources, including precious metals (*42*, *43*). Such involvement was longstanding, and their influence was exercised both through their client kingdoms, the Ghassanid and Lakhmid confederacies (and their earlier equivalents) in northern Arabia, and through Aksum. Direct intervention was thus not new and had indeed occurred on several occasions from the third century on (*44*–*46*). But the crucial difference from the middle of the sixth century was precisely the absence of a stable Himyarite kingdom. Finally, external interventions stimulated a hostile

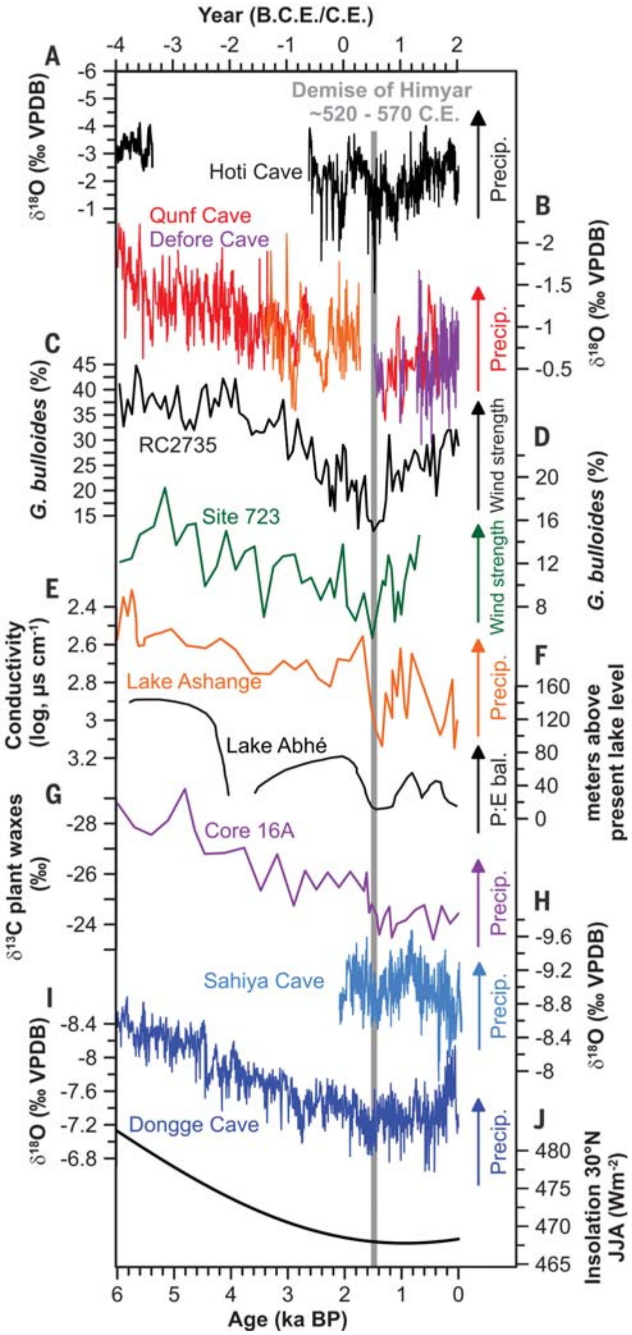

Fig. 4. Comparison of the H12 δ^{18}O record with SM records. (**A**) Hoti Cave δ^{18}O record. (**B**) Defore Cave (purple) and Qunf Cave (red and orange) δ^{18}O records from southern Oman (*12*). (**C** and **D**) *Globigerina bulloides*, a heterotrophic planktonic foraminifer, monsoon upwelling records from the Arabian Sea (*27*, *28*). (**E**) Lake Ashange conductivity record from Ethiopia (*25*). (**F**) Lake level record from Lake Abhé at the Etiopia-Djibouti border (*26*). P.E bal., precipitation minus evaporation balance. (**G**) δ^{13}C plant-wax record from core 16A offshore of India (*31*). (**H**) Sahiya Cave δ^{18}O record from India (*29*). (**I**) Dongge Cave δ^{18}O record from China (*30*). (**J**) Insolation curve at 30°N, averaged from June to August (*49*). All records reflect either SM wind strength or precipitation. The vertical gray bar marks the time interval between ~520 and 570 CE, which covers the period of Himyar's demise. ka BP, thousand years before present.

reaction, both to Christian Aksumite proselytizing and to the political maneuvering of the neighboring empires (*11*), although that this promoted a search for a new "Arab" identity remains questionable (*2*, *10*, *41*). Regardless, after 525 CE and the Aksumite invasion, both Arabian reactions and outside interventions occurred in a geopolitical context without an effective centralizing power. The decline and dissolution of Himyar was thus a critical element in the socioeconomic, political, and religious-cultural transformations in Arabia that ultimately framed the emergence of a range of new religious leaders or movements, many focused around monotheistic beliefs, including Islam. The challenges faced by the Islamic leadership in unifying the Arabian Peninsula in the 620s CE, in spite of substantial opposition from such competitors as well as from tribes that had converted to Judaism or were hostile to the Quraysh (Muhammad's tribe), reflected this situation (*2*–*4*, *6*, *47*). But by the late 620s CE, with Himyarite authority a distant memory and both Persia and Byzantium exhausted by their long war, the early Islamic leadership had the field to itself with respect to its ability to mount long-distance military expeditions.

We do not suggest that the extreme droughts of the late fifth to early seventh century CE in Arabia were the direct trigger for these fundamental changes (*43*), which were complex and, in several respects, of long duration. But we can now confirm from an entirely independent proxy that the Arabian Peninsula suffered from unusual and extreme aridity in the period between ~500 and 530 CE. This constituted an important, and hitherto largely neglected, factor that can only have undermined Himyarite resilience to both longer-term and more immediate internal and external stresses (*2*, *4*).

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SUPPLEMENTARY MATERIALS

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Materials and Methods
Figs. S1 to S10
Tables S1 to S3
References (*50*–*58*)

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BIOCONJUGATION

A chemoenzymatic strategy for site-selective functionalization of native peptides and proteins

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The emergence of new therapeutic modalities requires complementary tools for their efficient syntheses. Availability of methodologies for site-selective modification of biomolecules remains a long-standing challenge, given the inherent complexity and the presence of repeating residues that bear functional groups with similar reactivity profiles. We describe a bioconjugation strategy for modification of native peptides relying on high site selectivity conveyed by enzymes. We engineered penicillin G acylases to distinguish among free amino moieties of insulin (two at amino termini and an internal lysine) and manipulate cleavable phenylacetamide groups in a programmable manner to form protected insulin derivatives. This enables selective and specific chemical ligation to synthesize homogeneous bioconjugates, improving yield and purity compared to the existing methods, and generally opens avenues in the functionalization of native proteins to access biological probes or drugs.

With the increasing number of new modalities and biologics in pharmaceutical pipelines (*1*–*4*), the selective transformation of biomolecules, such as proteins and peptides, has emerged as an important challenge in organic synthesis. The need to maintain the complex tertiary structure of biological polymers, combined with the diversity and repetition of functional groups, demands both mild conditions and high chemoselectivity, each of which is difficult to achieve with existing methods (*5*–*7*). Current strategies to directly modify native proteins rely on the inherent reactivity of functional groups within the molecule, either by targeting modifications at the termini (*8*) or by exploiting subtle differences in the nucleophilicity, pK_a (*9*), or redox potential (*10*, *11*) of the repeating amino acid residues, which necessarily restricts the scope and selectivity of such methodologies (*5*–*7*) (Fig. 1A).

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Consequently, genetic modifications of the proteins where an (un)natural amino acid or recognition motif is inserted as a handle for site-selective functionalization have gained great interest (*5*–*7*). However, the introduction of recognition tags invariably alters the biomolecule, which may affect the very function that it performs as well as narrowing the scope of such approaches. These limitations have created a high demand for the invention of scalable strategies for site-selective bioconjugation of native proteins to accelerate the discovery and development of biological probes and therapeutics (*4*, *12*–*16*). Here we show that strategies based on enzyme catalysis can enable improved bioconjugation of native proteins such as insulin (**1**, Fig. 1, A and B).

Over the past several decades, the growing epidemic of diabetes mellitus has motivated many research laboratories to search for therapies that exhibit improved safety and pharmacology (*17*). The inherently low therapeutic index of insulin-based medicines, where overdosing can lead to hypoglycemia, remains a substantial medical risk and necessitates complex dosing regimens (*17*). Modified insulin molecules will advance understanding of how the insulin receptor is activated and the structure-activity relationships of its binders (*18*) and may ultimately lead to safer insulin-based medicines for glycemic controls (*17*). Our laboratories have been pursuing diverse human insulin bioconjugates with promising therapeutic potential and improved pharmacodynamic profiles, including insulin receptor partial agonists MK-1092 and MK-5160 (*19*) or glucose-responsive insulin MK-2640 (*20*) (Fig. 1C, **5a** to **5c**).