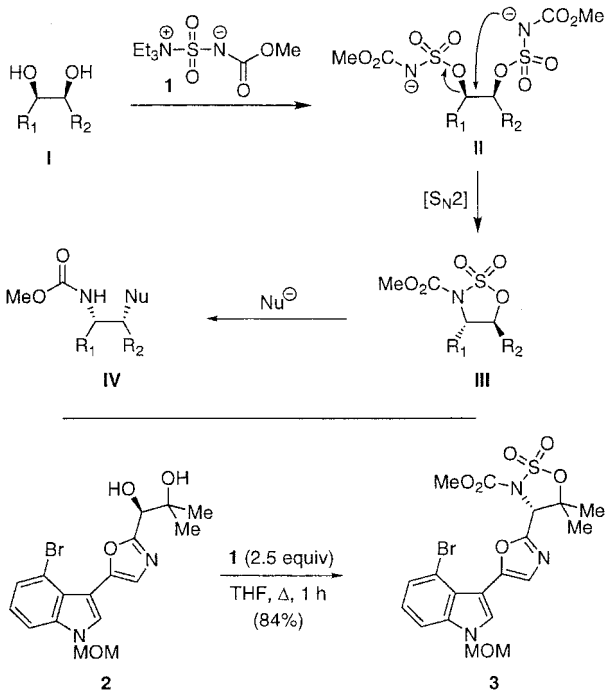
A Novel Regio- and Stereoselective Synthesis of Sulfamidates from 1,2-Diols Using Burgess and Related Reagents: A Facile Entry into β-Amino Alcohols**

K. C. Nicolaou,* Xianhai Huang, Scott A. Snyder, Paraselli Bheema Rao, Marco Bella, and Mali V. Reddy

Over the course of the past decade, chiral β-amino alcohols have become an increasingly targeted functional motif in organic synthesis owing to their ubiquity in biologically active compounds, as well as their value as ligands in asymmetric synthesis.[1, 2] Presently, several powerful methods exist to enantioselectively create such synthons, foremost of which is Sharpless' osmium-catalyzed asymmetric aminohydroxylation (AA).[3] Although the utility of this reaction is unquestionable, variable regio- and enantioselectivity is still observed in certain structural types, despite significant optimization of reaction conditions.[4, 5] Herein we provide an alternative two-step approach for the regio- and stereoselective synthesis of a wide variety of 1,2-amino alcohols centered on initial construction of chiral sulfamidates from enantiopure diols, orchestrated by Burgess reagent (**1**, Scheme 1), followed by mild treatment with aqueous acid. Furthermore, we disclose the development of several novel Burgess-type reagents which greatly extends the utility of this new protocol by enabling access to an orthogonal set of N-protected sulfamidates.

Based on insight garnered during our program directed towards the total synthesis of the marine-derived natural product diazonamide A,[6] we reasoned that it might be possible to generate a protected variant of a β-amino alcohol in the form of a cyclic sulfamidate (**III**) by exposing a diol (**I**) to excess Burgess reagent (**1**; Scheme 1).[7] Although this chemical is typically employed as a powerful dehydrating reagent (for example, effecting the formation of olefins from alcohols),[8] we envisioned that after the generation of an intermediate of type **II** from **I**, a unique and productive cyclization to sulfamidate **III** through the proposed S_N2 mechanism could potentially occur in preference to typical pathways that involve the loss of water. Assuming that this transformation proceeds with displacement of the more activated leaving group, then variation of the R^1 and R^2 substituents on enantiopure **I** would enable the stereo- and regioselective synthesis of diverse sulfamidates.



Scheme 1. Proposed conversion of diols **I** into cyclic sulfamidates **III** using Burgess reagent (**1**), and proof of principle (**2** → **3**). mom = methoxymethyl.

Typically, sulfamidates are prepared from chiral β-amino alcohol starting materials in several steps (based on the number of protecting-group manipulations required), and are then utilized to generate a diverse array of functionality based on the established ability of this synthon to undergo highly selective reactions with O-, S-, N-, C-, and F-based nucleophiles, to yield compounds of general structure **IV**.[9] As such, the proposed synthesis of **III** would not only represent a more efficient approach than is currently available, since the nitrogen atom is concomitantly protected, but more significantly because the technology does not rely on the use of β-amino alcohol starting materials, it would provide a unique way to prepare this important functional motif stereoselectively from **III** simply by using water as a nucleophile. To test this hypothesis, we heated a THF solution of diol **2** (synthesized from the precursor olefin by dihydroxylation under standard conditions) and 2.5 equivalents of Burgess reagent (**1**)[10] at reflux for 1 h and, most gratifyingly, observed the smooth formation of the desired sulfamidate **3** in 84 % yield as a single regioisomer (> 98:2) based on NMR spectroscopic analysis. Significantly, because attempted carbamate-based AA[11] of **2** led to the desired product in modest yield with little control of regioselectivity, while the Ritter reaction under acidic conditions[12] led solely to decomposition, the ease and selectivity of this particular Burgess-mediated transformation was suggestive of a potentially highly useful and applicable synthetic methodology.[13]

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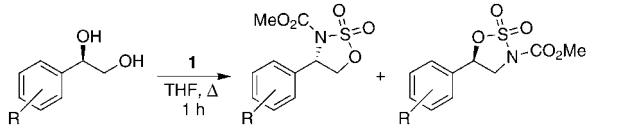
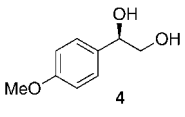
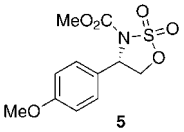
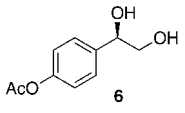
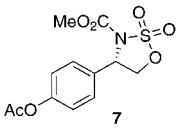
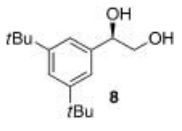
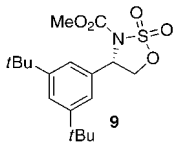
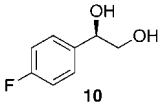
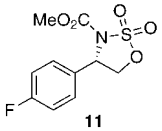
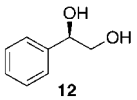
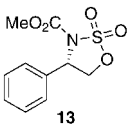
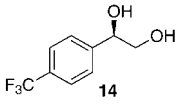
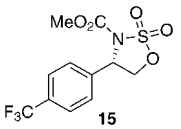
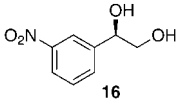
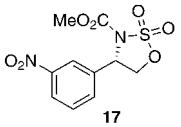
We then sought to test the generality of this reaction process on a selection of styrene-derived diols that possessed a broad range of aromatic substitution patterns in an effort to explore the anticipated role of inductive effects on the regioselectivity of the S_N2-based cyclization. We examined this particular class of compounds not only because it represents the best substrates for Sharpless asymmetric dihydroxylation (AD) in terms of both catalytic activity and enantioselectivity,[14] but also because styrene-type olefins display good but variable yields and regioselectivity in carbamate-based AA.[11] As shown in Table 1, Burgess-mediated sulfamidate synthesis followed the expected pattern for inductive influence in nucleophilic displacement at the benzylic position: electron-donating groups displayed excellent regioselectivity (Table 1, entries 1–4), whereas a lower selectivity was observed with electron-withdrawing substituents (Table 1, entries 6 and 7) relative to simple styrene (Table 1, entry 5). In all cases, the products were formed in high yield, and when two regioisomers were formed, the majority were separable by chromatography. Significantly, the poor regioselectivity observed in the conversion of **16** into **17** (Table 1, entry 7) was improved to 75:25 when the reaction was carried out at ambient temperature, albeit at the expense of yield (35%).

To explore the role of steric encumbrance on the reaction process, and to test the applicability of the procedure for other structural classes, we explored several additional substrates (Table 2). As expected, increasing steric bulk at the terminal position of the styrene core with a single methyl group (Table 2, entries 1 and 2) dramatically increased the regioselectivity of cyclic sulfamidate formation (cf. Table 1). Surprisingly, substituents adjacent to the reactive benzylic center on the aromatic ring did not affect either yield or selectivity

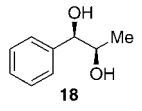
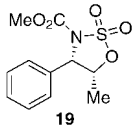
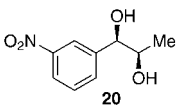
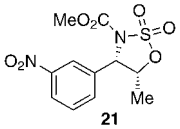
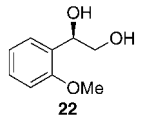
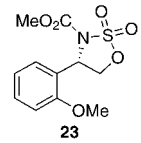
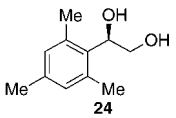
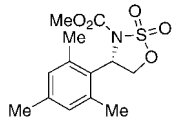
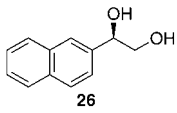
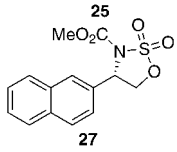
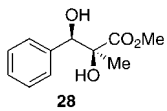
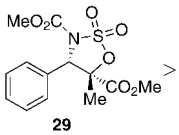
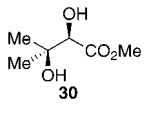
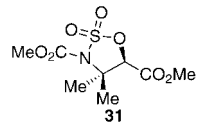
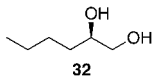
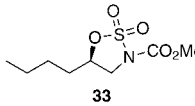
Tabelle 1. Regioselective synthesis of sulfamidates from diols by using Burgess reagent (**1**).



Entry	Starting material	Major product	Ratio of regioisomers[a]	Yield [%]
1	 **4**	 **5**	>98:2	91
2	 **6**	 **7**	95:5	88
3	 **8**	 **9**	95:5	87
4	 **10**	 **11**	95:5	79
5	 **12**	 **13**	93:7	92
6	 **14**	 **15**	85:15	83
7	 **16**	 **17**	55:45	86

[a] Determined by means of ^{1}H NMR spectroscopic analysis of the crude reaction products.

Tabelle 2. Further examples of the regioselective synthesis of sulfamidates from diols by using Burgess reagent (**1**).

Entry	Starting material	Major product	Ratio of regioisomers[a]	Yield [%]
1	 **18**	 **19**	>98:2	72
2	 **20**	 **21**	95:5	87
3	 **22**	 **23**	>98:2	92
4	 **24**	 **25**	>98:2	94
5	 **26**	 **27**	85:15	82
6	 **28**	 **29**	>98:2	81
7	 **30**	 **31**	71:29	41
8	 **32**	 **33**	>98:2	76

[a] Determined by means of ^{1}H NMR spectroscopic analysis of the crude reaction products.

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(Table 2, entries 3 and 4). Additionally, esters were well-tolerated in the reaction, with near complete regioselectivity observed for the formation of **29** from **28** (Table 2, entry 6), as a result of the mutually reinforcing effects of α-position deactivation by the ester moiety and the steric bulk imposed at that site by a methyl group. Competitive steric and electronic effects (Table 2, entry 7) led to retarded S_N2 displacement at the preferred terminal site, thereby reducing both regioselectivity and yield. Finally, reactions with simple aliphatic examples were highly regioselective, presumably because of the well-established preference for nucleophilic displacement of primary over secondary leaving groups. To verify the potential of this reaction for asymmetric synthesis, since all of the examples listed in Tables 1 and 2 were performed on racemic diol substrates, an X-ray crystal structure was obtained for sulfamidate **29** which confirmed that inversion of stereochemistry had occurred at the benzylic position relative to the racemic *cis*-diol starting material (Figure 1).[15] Additionally, both racemic and enantiopure **26** were synthesized,[16] and comparison of the chiral HPLC traces of the resultant products **27** indicated that preexisting stereochemical information was communicated in the reaction with complete fidelity.[17]

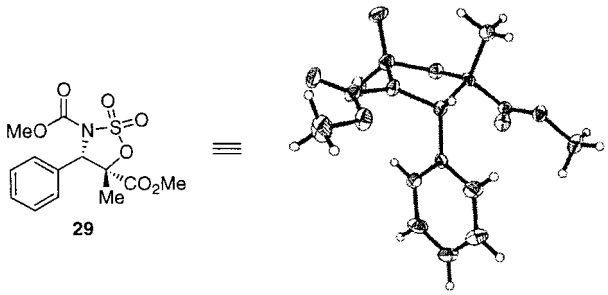
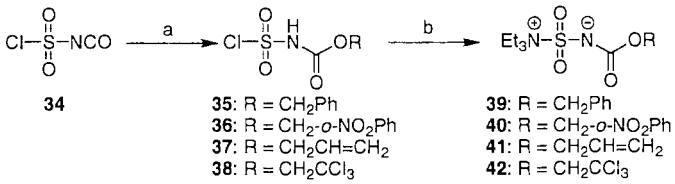


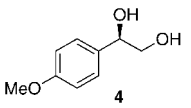
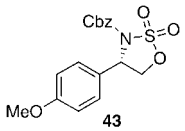
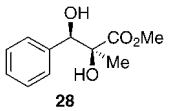
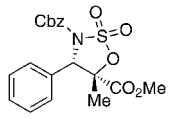
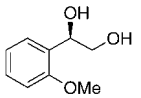
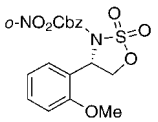
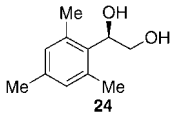
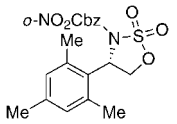
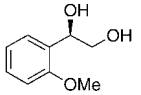
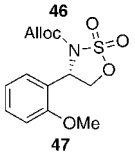
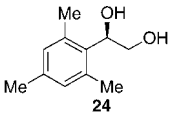
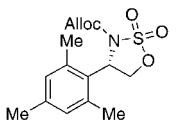
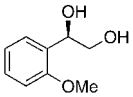
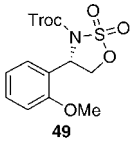
Figure 1. X-ray crystal structure of sulfamidate **29**.

To extend the overall utility of the present sulfamidate synthesis, we next sought to create compounds bearing N protection other than a methyl carbamate, a goal which could be achieved simply through modification of **1**. To our surprise, however, such reagents represented novel chemical entities, as an extensive search of the literature indicated that no efforts had been expended to create any Burgess-type salts other than those originally described almost thirty years ago. This result was unexpected, as **1** is known to passess both thermal and moisture sensitivity,[8a] features which might be modulated by differentiation of the carbamate portion. We readily prepared four different Burgess-type reagents (**39**–**42**), representing an orthogonal set of amine protecting groups (based on deprotection by hydrogenation, photolysis, exposure to palladium-based catalysts, or treatment with Zn, respectively) simply by treating chlorosulfonylisocyanate (**34**) with the alcohol of interest, followed by subsequent exposure to Et_3N (Scheme 2). The relative ease of these preparations implies that virtually any carbamate-based Burgess-type salt can be accessed by this approach.[18] Exposure of several diol substrates to **39**–**42** resulted in the facile formation of the desired sulfamidate products **43**–**49** (Table 3) in comparable efficiency and selectivity as was observed previously with **1**.



Scheme 2. Synthesis of the novel variants **39**–**42** of the original Burgess reagent: a) chlorosulfonyl isocyanate (**34**, 1.0 equiv), ROH (1.05 equiv), CH_2Cl_2, 0 °C, 30 min, 89–95 %; b) Et_3N (2.5 equiv), C_6H_6, 25 °C, 1 h, 81–87 %.

Tabelle 3. Use of the new Burgess-type reagents **39**–**42** to prepare orthogonally protected sulfamidates **43**–**49**.

Entry	Starting material	Major product	Ratio of regioisomers[a]	Yield [%]
1	 **4**	 **43**	> 98:2	90
2	 **28**	 **44**	95:5	81
3	 **22**	 **45**	> 98:2	87
4	 **24**	 **46**	> 98:2	82
5	 **22**	 **47**	> 98:2	89
6	 **24**	 **48**	> 98:2	87
7	 **22**	 **49**	> 98:2	78

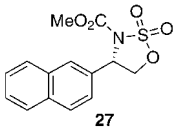
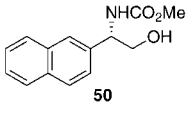
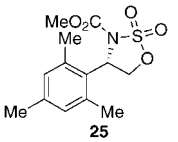
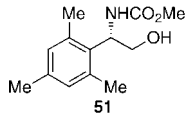
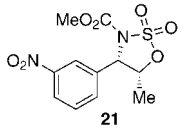
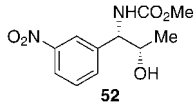
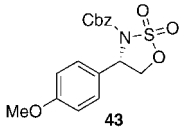
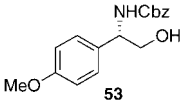
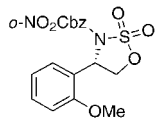
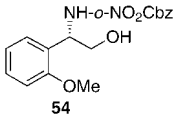
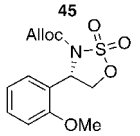
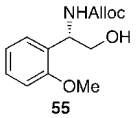
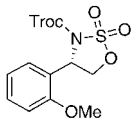
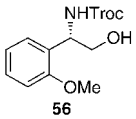
[a] Determined by means of ^{1}H NMR spectroscopic analysis of the crude reaction products. Cbz = CO_2CH_2Ph, Alloc = $CO_2CH_2CH{=}CH_2$, Troc = $CO_2CH_2CCl_3$.

Significantly, preliminary handling of **39**–**42** suggests that they possess unique thermal and moisture-sensitivity profiles relative to **1**, physical features which could prove significant in transformations that are typically effected by Burgess reagent on recalcitrant substrates. The ability of **39**–**42** to perform reactions already known with **1**, such as oxazole formation from precursor ketoamides,[19] is being explored.

  0044-8249/02/11405-0864 $ 17.50+.50/0

Finally, we sought to convert the sulfamidate products into β-amino alcohols. Although this conversion had been disclosed previously in the literature (1:1 mixture of HCl (aq.)/dioxane, ambient temperature), only one substrate was examined.[9k] To verify that this deprotection protocol had sufficient scope for general synthetic utility, several sulfamidates were readily deprotected under these conditions (Table 4). High yields were observed in all examples, despite relatively large variations in the reaction time necessary for complete conversion.[20]

Tabelle 4. Deprotection of cyclic sulfamidates using aqueous HCl in dioxane at ambient temperature to yield β-amino alcohols.

Entry	Starting Material	Product	t [h]	Yield [%]
1	 **27**	 **50**	10	94
2	 **25**	 **51**	30	95
3	 **21**	 **52**	12	92
4	 **43**	 **53**	2	92
5	 **45**	 **54**	26	95
6	 **47**	 **55**	24	93
7	 **49**	 **56**	16	90

To summarize, a novel regio- and stereoselective two-stage synthesis of β-amino alcohols has been achieved in which the key transformation is the creation of a cyclic sulfamidate from a precursor diol, mediated by Burgess-type reagents. The generality and scope of this approach is underscored by the considerable number and variety of substrates which display high levels of selectivity in the process. As such, this method provides facile access to compounds for use in a myriad of applications, whether as chiral ligands to perform asymmetric synthesis or as molecular probes to explore problems in chemical biology. Further extensions of the utility of the disclosed sulfamidate synthesis, as well as a full exploration into the physical properties and chemical reactivity of the newly disclosed Burgess-type reagents **39**–**42**, are the subject of present investigations.

Experimental Section

General procedure: the diol (0.5 mmol, 1.0 equiv) was dissolved in anhydrous THF (5 mL) and **1** (0.293 g, 1.25 mmol, 2.5 equiv) was added. The resultant solution was heated at reflux for 1 h, cooled to ambient temperature, concentrated, and then purified by chromatography on silica gel to afford the desired product in high purity.

Note: although analysis by thin-layer chromatography (TLC) indicates complete consumption of starting materials after a few minutes, uncyclized material **II** (Scheme 1) remains at the baseline, and further heating is required to effect complete conversion into **III**.

Deprotection of the sulfamidate group: the substrate was dissolved in a mixture of HCl (4 M, aq.)/dioxane (1:1) and the solution was stirred at ambient temperature until complete conversion was observed by TLC. The reaction mixture was then diluted with EtOAc, washed with aqueous $NaHCO_3$ (5%) and brine, dried over $MgSO_4$, and concentrated to afford spectroscopically pure **IV**.

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[1] For selected reviews on the synthesis and applications of 1,2-amino alcohols, see: a) T. Kunieda, T. Ishizuka in *Studies in Natural Products Chemistry*, *Vol. 12* (Ed.: Atta-ur-Rahman), Elsevier, New York, **1993**, p. 411; b) A. Golebiowski, J. Jurczak, *Synlett* **1993**, 241–245; c) Y. Ohfune, *Acc. Chem. Res.* **1992**, *25*, 360–366; d) T. Yokomatsu, Y. Yuasa, S. Shibuya, *Heterocycles* **1992**, *33*, 1051–1078; e) M. T. Reetz, *Angew. Chem*. **1991**, *103*, 1559–1573; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1531–1545.

[2] For additional reviews of this important area, see: a) E. J. Corey, C. J. Helal, *Angew. Chem*. **1998**, *110*, 2092–2118; *Angew. Chem. Int. Ed.* **1998**, *37*, 1986–2012; b) S. Wallbaum, J. Martens, *Tetrahedron: Asymmetry* **1992**, *3*, 1475–1504; c) R. Noyori, M. Kitamura, *Angew. Chem*. **1991**, *103*, 34–55; *Angew. Chem. Int. Ed. Engl*. **1991**, *30*, 49–69; d) V. K. Singh, *Synthesis* **1991**, 605–617; For some recent papers employing *cis*-1,2-amino alcohols, see: e) B. Di Simone, D. Savoia, E. Tagliavini, A. Umani-Ronchi, *Tetrahedron: Asymmetry* **1995**, *6*, 301–306; f) Y. Hong, Y. Gao, X. Nie, C. M. Zepp, *Tetrahedron Lett.* **1994**, *35*, 6631–6634.

[3] a) G. Li, H.-T. Chang, K. B. Sharpless, *Angew. Chem.* **1996**, *108*, 449–452; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 451–454; b) G. Li, K. B. Sharpless, *Acta Chem. Scand*. **1996**, *35*, 451–454.

[4] For selected examples of recent papers in the AA field, see: a) Z. P. Demko, M. Bartsch, K. B. Sharpless, *Org. Lett.* **2000**, *2*, 2221–2223; b) L. K. Goossen, H. Liu, K. R. Dress, K. B. Sharpless, *Angew. Chem.* **1999**, *111*, 1149–1152; *Angew. Chem. Int. Ed.* **1999**, *38*, 1080–1083; c) K. L. Reddy, K. R. Dress, K. B. Sharpless, *Tetrahedron Lett.* **1998**, *39*, 3667 - 3670; d) M. Bruncko, G. Schlingloff, K. B. Sharpless, *Angew. Chem.* **1997**, *109*, 1580–1583; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1483–1486.

[5] For an alternate and useful preparation of chiral 1,2-amino alcohols starting from substrates other than olefins, see: D. Ender, U. Reinhold, *Angew. Chem.* **1995**, *107*, 1332–1334; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1219–1222.

[6] For progress towards the total synthesis diazonamide A, see: a) K. C. Nicolaou, S. A. Snyder, K. B. Simonsen, A. E. Koumbis, *Angew. Chem.* **2000**, *112*, 3615–1620; *Angew. Chem. Int. Ed.* **2000**, *39*, 3473–3478; b) K. C. Nicolaou, X. Huang, N. Giuseppone, P. Bheema Rao, M. Bella, M. V. Reddy, S. A. Snyder, *Angew. Chem.* **2001**, *113*, 4841–4845; *Angew. Chem. Int. Ed.* **2001**, *40*, 4705–4709; for the development of other synthetic methodology as the result of this research program in total synthesis, see: c) K. C. Nicolaou, S. A. Snyder, A. Bigot, J. A. Pfefferkorn, *Angew. Chem.* **2000**, *112*, 1135–1138; *Angew. Chem. Int. Ed.* **2000**, *39*, 1093–1096; d) K. C. Nicolaou, A. E. Koumbis, S. A. Snyder, K. B. Simonsen, *Angew. Chem.* **2000**, *112*, 2629–2633; *Angew. Chem. Int. Ed.* **2000**, *39*, 2529–2533.

[7] a) G. M. Atkins, E. M. Burgess, *J. Am. Chem. Soc.* **1968**, *90*, 4744 – 4745; b) G. M. Atkins, E. M. Burgess, *J. Am. Chem. Soc.* **1972**, *94*, 6135 – 6141; c) E. M. Burgess, H. R. Penton, E. A. Taylor, *J. Org. Chem.* **1973**, *38*, 26 – 31.

[8] For reviews on the chemistry of **1**, see: a) P. Taibe, S. Mobashery in *Encyclopedia of Reagents for Organic Synthesis*, *Vol. 5* (Ed.: L. A. Paquette), Wiley, Chichester, **1995**, pp. 3345 – 3347; b) S. Burckhardt, *Synlett* **2000**, 559.

[9] a) L. Wei, W. D. Lubell, *Org. Lett.* **2000**, *2*, 2595 – 2598; b) L. T. Boulton, H. T. Stock, J. Raphy, D. C. Horwell, *J. Chem. Soc. Perkin Trans. 1* **1999**, 1421 – 1429; c) D. Ok, M. H. Fisher, M. J. Wyvratt, P. T. Meinke, *Tetrahedron Lett.* **1999**, *40*, 3831 – 3834; d) B. M. Kim, S. M. So, *Tetrahedron Lett.* **1998**, *39*, 5381 – 5384; e) B. Aguilera, A. Fernández-Mayorales, C. Jaramillo, *Tetrahedron* **1997**, *53*, 5863 – 5876; f) M. E. Van Dort, Y.-W. Jung, P. S. Sherman, M. R. Kilbourn, D. M. Wieland, *J. Med. Chem.* **1995**, *38*, 810 – 815; g) K. K. Andersen, M. G. Kociolek, *J. Org. Chem.* **1995**, *60*, 2003 – 2007; h) M. Okuda, K. Tomioka, *Tetrahedron Lett.* **1994**, *35*, 4585 – 4586; i) K. K. Andersen, D. D. Bray, S. Chumpradit, M. E. Clark, G. J. Habgood, C. D. Hubbard, K. M. Young, *J. Org. Chem.* **1991**, *56*, 6508 – 6516; j) G. J. White, M. E. Garst, *J. Org. Chem.* **1991**, *56*, 3177 – 3178; k) J. E. Baldwin, A. C. Spivey, C. J. Schofield, *Tetrahedron: Asymmetry* **1991**, *1*, 881 – 884; l) D. Alker, K. J. Doyle, L. M. Harwood, A. McGregor, *Tetrahedron: Asymmetry* **1991**, *1*, 877 – 880; m) T. A. Lyle, C. A. Magill, S. M. Pitzenberger, *J. Am. Chem. Soc.* **1987**, *109*, 7890 – 7891.

[10] Although **1** is available from several commercial sources at prices ranging from US$36 – 45 per gram, the material is easily synthesized during the course of an afternoon in multigram quantities at a price of less than US$1 per gram by following the procedure described in ref. [7c].

[11] a) K. L. Reddy, K. B. Sharpless, *J. Am. Chem. Soc.* **1998**, *120*, 1207 – 1217; b) G. Li, H. H. Angert, K. B. Sharpless, *Angew. Chem.* **1996**, *108*, 2995 – 2999; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2813 – 2817.

[12] a) C. M. Bellucci, A. Bergamini, P. G. Cozzi, A. Papa, E. Tagliavini, A. Umani-Ronchi, *Tetrahedron: Asymmetry* **1997**, *8*, 895 – 902; b) C. H. Senanayake, L. M. DiMichele, J. Liu, L. E. Fredenburgh, K. M. Ryan, F. E. Roberts, R. D. Larsen, T. R. Verhoeven, P. J. Reider, *Tetrahedron Lett.* **1995**, *36*, 7615 – 7618; c) C. H. Senanayake, F. E. Roberts, L. M. DiMichele, K. M. Ryan, J. Liu, L. E. Fredenburgh, B. S. Foster, A. W. Douglas, R. D. Larsen, T. R. Verhoeven, P. J. Reider, *Tetrahedron Lett*. **1995**, *36*, 3993 – 3996.

[13] For alternate, multistep approaches to *cis*-1,2-amino alcohols from diols, see: a) M. K. Lakshman, B. Zajc, *Tetrahedron Lett.* **1996**, *37*, 2529 – 2532; b) A. K. Ghosh, S. P. Mckee, W. M. Sanders, *Tetrahedron Lett.* **1991**, *32*, 711 – 714.

[14] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483 – 2547.

[15] This analysis does not exclude the possibility of inversion at the other center. However, this event is highly unlikely based on mechanistic details elucidated thus far. CCDC-174599 (**29**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit @ccdc.cam.ac.uk).

[16] Enantiopure (*R*)-**26** was prepared by using AD-mix-β: H. Becker, S. B. King, M. Taniguchi, K. P. M. Vanhessche, K. B. Sharpless, *J. Org. Chem.* **1995**, *60*, 3940 – 3941.

[17] Chiral HPLC analysis was performed by using a Diacel Chiralpack Column AD, hexane/2-propanol (85:15), 1.5 mL min^{-1}, 254 nm, 8.72 min ((*S*)-**27**), 12.2 min ((*R*)-**27**).

[18] Although carbamate-derived Burgess-type salts should be quite stable, the corresponding amide-based compounds are unlikely to be readily isolated; for efforts to use such reagents in synthesis, see: ref. [7c] and H. Vorbruggen, K. Krolikiewicz, *Tetrahedron* **1994**, *50*, 6549 – 6558.

[19] For representative examples, see: ref. [6b] and C. T. Brain, J. M. Paul, *Synlett* **1999**, 1642 – 1644.

[20] The chiral integrity of products that result from ring opening of the chiral sulfamidate by water under acidic conditions followed by neutralization with aqueous sodium bicarbonate has already been verified on a substrate far more prone to racemization (see: ref. [9k]).

A Supramolecular Array of Fullerenes by Quadruple Hydrogen Bonding**

Luis Sánchez, Minze T. Rispens, and Jan C. Hummelen*

Fullerenes have interesting properties that may be utilized in a variety of applications including organic photovoltaic (PV) devices.[1] Especially organic bulk-heterojunction PV cells consisting of a blend of a π-conjugated polymer and a fullerene derivative[2] have received much attention recently. A way to improve the efficiency of these so called "plastic" solar cells is the optimization of the morphology of the photoactive layer. A potential way to attain this goal is through supramolecular assembly of the constituents. Hydrogen bonding is particularly useful in the construction of supramolecular structures.[3] Relatively little work on C_{60}-based polymers[4] and supramolecular C_{60} derivatives has been performed.[5] So far, only dimeric compounds have been obtained by a supramolecular approach.[6] Monofunctionalized C_{60} derivatives bearing one or two hydrogen-bonding moieties on the substituent can serve as building blocks for the preparation of fullerene-containing dimers and arrays, by using the strength, directionality, and specificity, characteristic of hydrogen bonding.[3] Our group[7] and the group of Martín[8] have recently reported on the synthesis of supramolecular C_{60} dimers bearing Meijer's self-complementary 2-ureido-4-pyrimidinones which have a donor donor acceptor acceptor (DDAA) hydrogen bonding motif. This motif gives rise to a very high dimerization constant ($K_d \geq 6 \times 10^7\,\text{M}^{-1}$), as a result of attractive secondary interactions.[9] The presence of two ureidopyrimidinone groups in a molecule results in supramolecular polymers of exceptional properties.[10] After our first exercise on a fullerene with *one* coupling unit,[7] we now report the synthesis and spectroscopic characterization of the first hydrogen-bonded supramolecular array, formed by a (methano)fullerene with *two* coupling units.

The synthesis of target monomer **8** (Scheme 1) started with the conversion of diethyl-4-oxopimelate (**1**) into *para*-tosylhydrazone **2**. Heating the anion of **2** in the presence of C_{60} in 1,2-*ortho*-dichlorobenzene (ODCB) at 100 °C[11] gave fulleroid **3a**, together with methanofullerene **3b**, higher adducts, and C_{60}, through the intermediate diazo compound and diazoline adduct. The isomeric mixture **3a**/**3b** was isolated and photoisomerized quantitatively to the [6,6]-isomer **3b**. Hydrolysis of **3b** yielded acid **4**, which was fully characterized despite its insolubility in all common solvents. Target methanofullerene **8** was prepared using a one-pot procedure:

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