Sigma-Aldrich® Lab Materials & Supplies

# ISOTEC<sup>®</sup> Hyperpolarization MRI/MRS Products

Two polarization techniques, dynamic nuclear polarization (DNP) and parahydrogen-induced polarization (PHIP), have been used to produce magnetic resonance spectroscopic and imaging agents containing polarized <sup>13</sup>C and <sup>15</sup>N nuclei. While operating by different mechanisms of polarization, DNP and PHIP both have succeeded in producing substrates with high levels of signal enhancement.

### DNP

Hyperpolarization using dynamic nuclear polarization (DNP) has emerged as a versatile method to dramatically improve the MR signal of low-sensitivity nuclei. DNP facilitates the study of real-time metabolism in vivo using <sup>13</sup>C-enriched substrates and has been applied to numerous models of human disease. Within this field, pyruvic acid has been the most heavily and successfully studied substrate due to its long T<sub>1</sub>, ease of use and metabolic relevance. Research into the development of additional substrates has also shown the potential of other compounds.

Cat. No.	Product Description	Isotopic Purity
729655	Acetylene-13C <sub>2</sub> dicarboxylic acid	99 atom % <sup>13</sup> C
665223	Acetylene dicarboxylic acid-1-13C disodium salt	99 atom % <sup>13</sup> C
704164	N-Acetyl-∟-methionine-1- <sup>13</sup> C	99 atom % <sup>13</sup> C
489867	L-Alanine-1-13C	99 atom % <sup>13</sup> C
588741	4-Amino-TEMPO-piperidinyl-d <sub>17</sub>	98 atom % D
683604	3-Bromopyruvic acid-1-13C	99 atom % <sup>13</sup> C
722545	3-Bromopyruvic acid-3-13C	99 atom % <sup>13</sup> C
679860	tert-Butan-1 <sup>-13</sup> C, d <sub>9</sub> -ol	99 atom % <sup>13</sup> C, 98 atom % D
488372	Butyric acid-1-13C	99 atom % <sup>13</sup> C
609269	Choline chloride-15N	98 atom % <sup>15</sup> N
720593	Ethyl pyruvate-2-13C	99 atom % <sup>13</sup> C
676594	Ethyl pyruvate-3-13C	99 atom % <sup>13</sup> C
492140	D-Fructose-2-13C	99 atom % <sup>13</sup> C
749389	Fumaric acid-1,4-13C <sub>2</sub>	99 atom % <sup>13</sup> C
752576	Fumaric acid-1,4- $^{13}C_2$ , 2,3-d <sub>2</sub>	99 atom % <sup>13</sup> C, 98 atom % D
552151	D-Glucose- <sup>13</sup> C <sub>6</sub> -1,2,3,4,5,6,6-d <sub>7</sub>	99 atom % <sup>13</sup> C, 97 atom % D
604968	L-Glutamic acid-1-13C	99 atom % <sup>13</sup> C
605018	L-Glutamine-1-13C	99 atom % <sup>13</sup> C

The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.

Cat. No.	Product Description	Isotopic Purity
750506	L-Glutamine-4-13C	99 atom % <sup>13</sup> C
604690	L-Glutamine-5- <sup>13</sup> C	99 atom % <sup>13</sup> C
705748	4-Hydroxy-TEMPO- <sup>15</sup> N	98 atom % <sup>15</sup> N
487686	4-Hydroxy-TEMPO-d <sub>17</sub>	97 atom % D
704334	2-Ketoglutaric acid-1-13C	99 atom % <sup>13</sup> C
750832	2-Keto-4-methylpentanoic acid-1-13C	99 atom % <sup>13</sup> C
487716	2-Keto-4-methylpentanoic acid-1-13C sodium salt	99 atom % <sup>13</sup> C
738778	L-Lactic acid-1-13C	99 atom % <sup>13</sup> C
606057	L-Lactic acid-1- $^{13}$ C solution (85 % w/w in H <sub>2</sub> O)	99 atom % <sup>13</sup> C
703621	L-Malic acid-1-13C	99 atom % <sup>13</sup> C
696471	4-Oxo-TEMPO-1-15N	98 atom % <sup>15</sup> N
485268	4-Oxo-TEMPO-d <sub>16</sub>	97 atom % D
487740	4-Oxo-TEMPO-d <sub>16</sub> ,1- <sup>15</sup> N	98 atom % <sup>15</sup> N,
		98 atom % D
591173	4-Oxo-2,2,6,6-tetramethyl-	98 atom % <sup>15</sup> N,
	piperidine-d <sub>17</sub> ,1 <sup>-15</sup> N	97 atom % D
677175	Pyruvic acid-1- <sup>13</sup> C (free acid)	99 atom % <sup>13</sup> C
692670	Pyruvic acid-2- <sup>13</sup> C (free acid)	99 atom % <sup>13</sup> C
721298	Pyruvic acid-1,2 <sup><math>-13</math></sup> C <sub>2</sub> (free acid)	99 atom % <sup>13</sup> C
279293	Sodium acetate-1- <sup>13</sup> C	99 atom % <sup>13</sup> C
279315	Sodium acetate-2- <sup>13</sup> C	99 atom % <sup>13</sup> C
663859	Sodium acetate- <sup>13</sup> C <sub>2</sub> , S&P tested	99 atom % <sup>13</sup> C
372382	Sodium bicarbonate-13C	98 atom % <sup>13</sup> C
299359	Urea- <sup>13</sup> C	99 atom % <sup>13</sup> C
485349	Succinic acid-1,4-13C <sub>2</sub>	99 atom % <sup>13</sup> C
487813	Acetic anhydride-1,1'-13C <sub>2</sub>	99 atom % <sup>13</sup> C
717347	1,4-Bis[(phenyl-3-propanesulfonate) phosphine] butane disodium salt	NA
728918	N-Acetyl-1-13C-L-Cysteine-1-13C	99 atom % <sup>13</sup> C
720178	2,3-Butanedione-2,3-13C <sub>2</sub>	99 atom % <sup>13</sup> C
767891	1,3-Dihydroxyacetone-2-13C dimer	99 atom % <sup>13</sup> C
684279	2,2,3,3-Tetrafluoropropyl acrylate- $1^{-13}$ C,2,3,3-d <sub>3</sub>	98 atom % <sup>13</sup> C, 98 atom % D
793205	Pyruvic acid-3-13C	99 atom % <sup>13</sup> C
676071	Hydroxyethyl acrylate-1- <sup>13</sup> C, 2,3,3-d <sub>3</sub>	99 atom % <sup>13</sup> C, 98 atom % D
490954	Urea- ${}^{13}C, {}^{15}N_2$	99 atom % <sup>13</sup> C, 98 atom % <sup>15</sup> N



### **Custom Hyperpolarization Products**

#### **Parahydrogen-induced Polarization**

Parahydrogen-induced polarization (PHIP) is accomplished by performing a para- $H_2$  hydrogenation of an unsaturated substrate followed by polarization transfer to a <sup>13</sup>C label. PHIP is usually accomplished in a home-made polarizer at room temperature in a matter of seconds to minutes. Several substrates have been polarized using PHIP and have subsequently been used in MR experiments to study brain tumors and cellular glucose uptake.

#### References

- Koelsch BL1, Reed GD, Keshari KR, Chaumeil MM, Bok R, Ronen SM, Vigneron DB, Kurhanewicz J, Larson PE. Rapid in vivo apparent diffusion coefficient mapping of hyperpolarized <sup>13</sup>C metabolites. 25213126.
- Wilson DM1, Kurhanewicz J2. Hyperpolarized <sup>13</sup>C MR for molecular imaging of prostate cancer. 25168625.
- Keshari KR1, Sriram R, Koelsch BL, Van Criekinge M, Wilson DM, Kurhanewicz J, Wang ZJ. Hyperpolarized <sup>13</sup>C-pyruvate magnetic resonance reveals rapid lactate export in metastatic renal cell carcinomas. 23204238.
- Keshari KR1, Wilson DM. Chemistry and biochemistry of <sup>13</sup>C hyperpolarized magnetic resonance using dynamic nuclear polarization. 24363044.
- Ross BD1, Bhattacharya P, Wagner S, Tran T, Sailasuta N. Hyperpolarized MR imaging: neurologic applications of hyperpolarized metabolism. 19875468.
- Shchepin RV1, Coffey AM, Waddell KW, Chekmenev EY. PASADENA hyperpolarized <sup>13</sup>C phospholactate. 22352377.
- Bhattacharya P1, Chekmenev EY, Reynolds WF, Wagner S, Zacharias N, Chan HR, Bünger R, Ross BD. Parahydrogen-induced polarization (PHIP) hyperpolarized MR receptor imaging in vivo: a pilot study of <sup>13</sup>C imaging of atheroma in mice. 21538638.
- Keshari KR1, Sriram R, Van Criekinge M, Wilson DM, Wang ZJ, Vigneron DB, Peehl DM, Kurhanewicz J. Metabolic reprogramming and validation of hyperpolarized <sup>13</sup>C lactate as a prostate cancer biomarker using a human prostate tissue slice culture bioreactor. 23532911.
- Merritt ME1, Harrison C, Sherry AD, Malloy CR, Burgess SC. Flux through hepatic pyruvate carboxylase and phosphoenolpyruvate carboxykinase detected by hyperpolarized <sup>13</sup>C magnetic resonance. 22065779.
- Bhattacharya P1, Chekmenev EY, Perman WH, Harris KC, Lin AP, Norton VA, Tan CT, Ross BD, Weitekamp DP. Towards hyperpolarized <sup>13</sup>C-succinate imaging of brain cancer. 17303454.

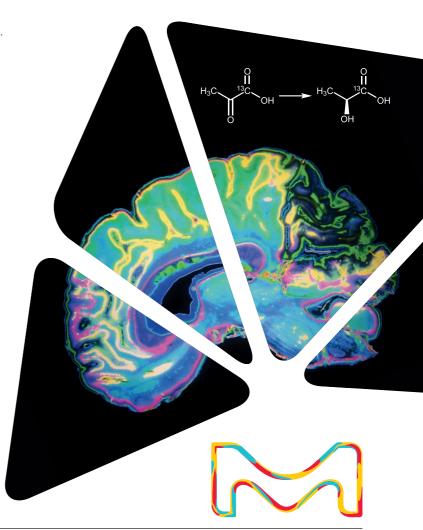
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#### **Custom Synthesized Substrates**

Due to the application specific nature of PHIP substrates, these products are usually made available through a custom request. This can often be the case for DNP substrates as well. As this field progresses, the identification of substrates that will produce sufficiently long  $T_1$  relaxation times while providing information about the metabolic cycle or disease being studied is important.

Isotec Stable Isotopes specializes in the custom synthesis of labeled compounds. Isotec employs a highly trained group of stable isotope scientists led by industry expert, Dr. C.T. Tan. This group is comprised of varied chemistry expertise, ensuring the synthesis of any compound. Our facilities give us the capability to perform syntheses ranging from milligram to kilogram quantities. In addition, we offer a variety of product grades including S&P tested to full GMP.



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NXI 83026 1015 02/2017